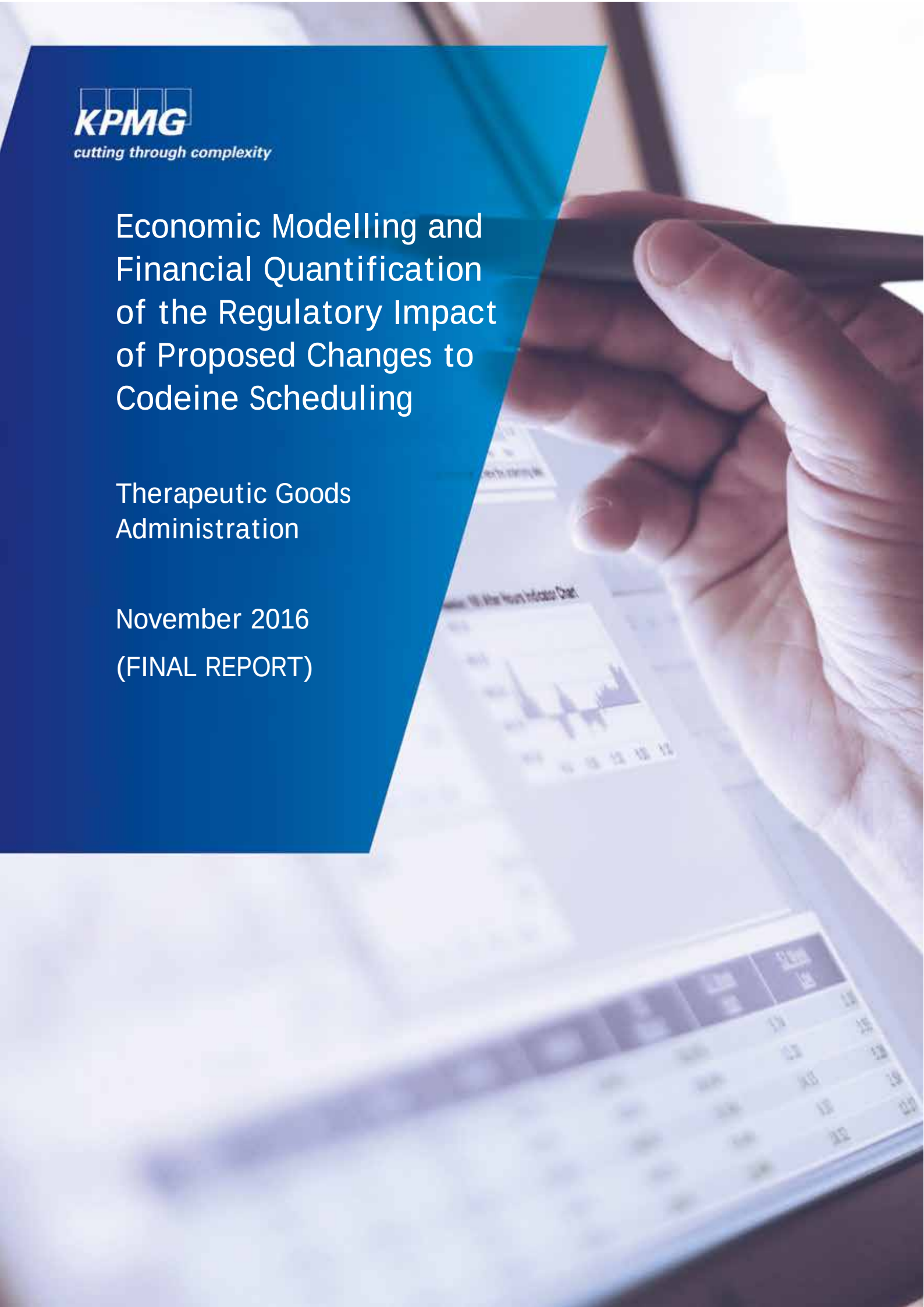

KPMG
cutting through complexity

Economic Modelling and Financial Quantification of the Regulatory Impact of Proposed Changes to Codeine Scheduling

Therapeutic Goods Administration

November 2016

(FINAL REPORT)

Inherent Limitations

This report has been prepared as outlined in the Background section. The services provided in connection with this engagement comprise an advisory engagement, which is not subject to assurance or other standards issued by the Australian Auditing and Assurance Standards Board and, consequently no opinions or conclusions intended to convey assurance have been expressed.

No warranty of completeness, accuracy or reliability is given in relation to the statements and representations made by, and the information and documentation provided by the Therapeutic Goods Administration management and personnel consulted as part of the process.

KPMG have indicated within this report the sources of the information provided. We have not sought to independently verify those sources unless otherwise noted within the report.

KPMG is under no obligation in any circumstance to update this report, in either oral or written form, for events occurring after the report has been issued in final form.

The findings in this report have been formed on the above basis.

Third Party Reliance

This report is solely for the purpose set out in the Background section and for the Therapeutic Goods Administration, and is not to be used for any other purpose or distributed to any other party (with the exception of providing the report for review by the Office of Best Practice Regulation in the Department of the Prime Minister and Cabinet) without KPMG's prior written consent.

This report has been prepared at the request of the Therapeutic Goods Administration in accordance with their Official Order for 'The provision of economic modelling and financial quantification of the regulatory, social and economic impacts of the proposed regulatory options for the rescheduling of codeine as outlined in the Department of Health request for quote and statement of requirements and with the response provided by KPMG' dated 02 August 2016. Other than our responsibility to the Therapeutic Goods Administration, neither KPMG nor any member or employee of KPMG undertakes responsibility arising in any way from reliance placed by a third party on this report. Any reliance placed is that party's sole responsibility.

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Executive Summary

Background

There is growing concern amongst some key stakeholders over the ready availability of codeine-containing medicines in over-the-counter (OTC) formulations and whether this may be contributing to a reported increase in codeine abuse and, consequently, negative health impacts and public health costs. A number of submissions to this effect were made to the July 2015 meeting of the Advisory Committee on Medicines Scheduling and, on 1 October 2015, the Delegate made an Interim Decision to restrict the availability of codeine-containing products to prescription only level. The Interim Decision was widely contested, resulting in deferral of the final decision to allow for thorough consideration of stakeholder input and a range of regulatory options.

KPMG was engaged by the Therapeutic Goods Administration (TGA) on 2 August 2016 to assist in the preparation of a Regulation Impact Statement (RIS) assessing the regulatory options (as identified by the TGA) through the provision of economic modelling and financial quantification services; specifically, the provision of input for the Impact Analysis and Regulatory Costing of the RIS. In the following four weeks, KPMG identified and documented potential regulatory, economic and social consequences of each of the codeine scheduling options.

At the request of the TGA, KPMG was asked to consolidate the results of its regulatory and economic modelling into a standalone report suitable for public release.

Purpose of this document

This document sets out KPMG's approach to undertaking both the regulatory and economic modelling, including summaries of consultation activities and explanations of the workings of the two models. Both an Impact Analysis and the Regulatory Costing, for inclusion in the RIS, are provided with this document (annexes C and D respectively). Annex E provides additional detail on the economic model to supplement that provided in the main body of the report.

Noting that this report may be read separately to the RIS produced by the TGA, some additional commentary is provided in the Executive Summary to provide more detailed explanations of the process undertaken, including its limitations. This additional commentary also provides some additional context for the inputs and outputs to the models that are likely to be of greatest interest to external stakeholders.

Overall context for this document

The modelling detailed in this report was conducted in accordance with the guidance provided by the Office of Best Practice Regulation (OBPR) for undertaking a cost-benefits analysis. It is worth noting that the policy driver for this study was not to reduce the regulatory burden on business but rather to achieve a public health outcome. As such, an understanding of the evidence base for the proposed rescheduling of codeine, as detailed in the TGA RIS, provides essential context for viewing the results of the regulatory and economic modelling. This report will not comment on the merits of this policy driver.

Throughout the report, reference is made to the base year of the report being 2017. Readers should not infer that this necessarily means that the proposed regulatory change will be in effect from 1 January 2017 or even 1 July 2017. Rather, 2017 was selected as the base year purely for the purposes of the regulatory and economic modelling.

Data limitations

The models, in particular the economic model, were developed in a 'data-poor' environment over an initial four-week period. Validated data was limited to essentially historical IMS[1] for the FY 12/13, which was extrapolated forward to provide the base year volume data. A key Input factor was provided by the Department of Human Services in relation to the public cost of additional GP and specialist pain consultations. Other inputs, such as the discount rate and the default wage rate were sourced from OBPR guidance. A limited review of the relevant academic literature was undertaken to inform the development of the economic model. The theoretical construct for this approach was that if conservative inputs for projected benefits were used, and the model still returned a net economic benefit across a range of sensitivity analysis for a particular scenario, then that scenario, of the scenarios examined, would provide the greatest overall benefit.

In addition to quantitative data sources, as detailed above, KPMG also sought inputs from a range of qualitative sources. In addition to desktop reviews of submissions made to the TGA with respect to this matter, KPMG conducted consultation activities within the four-week timeframe, engaging with representatives from:

- TGA;
- broader Department of Health;
- Office of Best Practice Regulation (OBPR);
- five pharmaceutical companies involved in the production and sale of low dose codeine medicines; and
- three peak bodies.

The models

For this project KPMG developed a regulatory costing model and an economic and social impacts model (health economic model), each informed by a range of sources, including the aforementioned industry and peak body consultations, as well as guidance from the TGA and the OBPR.

KPMG has sought to be as transparent as possible in relation to the assumptions made, and the inputs and outputs from the regulatory and economic models. Given its relative simplicity, a high level of transparency has been achieved for the regulatory model. However, the economic model is more complex; the population is segmented into five groups based on codeine usage characteristics and assumptions do not operate collectively across all groups but rather in combination, depending on the pathway of each group through the modelled time period (ten years). Hence transparency is achieved by detailing the model design and structure and comparing it against alternative potential structures (see Annex E).

Key findings

In consultation with TGA, KPMG and the TGA determined that Options 1- 6 (see Table ES1) (pertaining to distinct regulatory options), while separated in the modelling for the purposes of clarity, would, in practice, result in the following scenarios (logical grouping of regulatory options) due to the natural alignment and dependency of certain options.

[1] Wholesale pharmaceutical data (IMS) is collated by a commercial organisation (QuintilesIMS) and was provided to KPMG by the Department of Health. See <https://www.imshealth.com/en/about-us/news/top-line-market-data>.

Table ES1. Regulatory options for the rescheduling of codeine (based on TGA guidance)

Scenario 1: (Option 1)	No change to the status quo.
Scenario 2: (Options 2 and 5)	Schedule 2 and Schedule 3 entries for codeine (including, but not limited to, cough and cold medicine preparations and codeine containing analgesics) be amended to reduce the pack size to not more than 3 days' supply and include a label warning that codeine can cause addition. *Summary* · Reduce pack size and include warning label for S2 and S3
Scenario 3: (Options 3 and 5)	The current Schedule 2 entries for codeine in cough and cold medicine preparations be up-scheduled to Schedule 3, and then all Schedule 3 entries (i.e. those currently Schedule 3 and those previously Schedule 2) for codeine (including, but not limited to, cough and cold medicine preparations and codeine containing analgesics), be amended to reduce the pack size to not more than 3 days' supply, and include a label warning that codeine can cause addiction. *Summary* · S2 up-scheduled to S3 · Reduce pack size and include warning label for S3
Scenario 4: (Options 4 and 6)	Schedule 2 and Schedule 3 entries for codeine (including, but not limited to, cough and cold medicine preparations and codeine containing analgesics) be up-scheduled to Schedule 4. *Summary* · S2 and S3 up-scheduled to S4

Source: TGA and KPMG workshop 4 August 2016

As discussed in further detail throughout the report, only the implementation of Scenario 4 (Options 4 and 6) results in a net benefit to society (as detailed in Table ES2). OBPR specifies different methods for summarising ten years of projected regulatory and economic costs. Regulatory costs projected over ten years are summed (without discounting) and then summarised and reported as an average annual impact (total divided by ten). In contrast, economic costs for a cost-benefit analysis have their impact over the life of the proposed regulation (set at 10 years in this case) monetised and discounted at 7% per annum to obtain present value of the ten years of costs. Noting these differences in calculation methods, Tables ES2 sums the results of the regulatory costs (the undiscounted ten years summed) and economic modelling (ten years discounted to obtain a predicted net benefit). Subsequent tables in the Executive Summary provide additional detail on each of the component costs and benefits.

Option 5 has an increase in economic costs; the reduction in pack size means that consumers who are currently using packs of more than 3 days' supply (38% of packs sold in the 12 months to September 2013) will purchase more packs to maintain their use of the medicines, and smaller packs are at a higher cost per tablet. The economic benefits are driven by gains in quality of life, deaths prevented and also net financial savings to consumers, for example those who substitute OTC codeine with paracetamol and/or ibuprofen, post regulatory change. These benefits are only realised for Options 4 and 6, hence the absence of an economic benefit estimate for Options 2, 3 and 5 (Scenarios 2 and 3).

The health economic model sought to project the changes to a range of costs to the Commonwealth and individual consumers, deaths prevented and changes in quality of life as a consequence of the specified scenarios. There were a number of key assumptions regarding both baseline parameters (e.g. the proportion of consumers who are dependent on low dose codeine medicines) and projection parameters (the proportion of dependent users whose health outcomes will improve)) that have limited supporting evidence. By using the

most appropriate model structure, conservative assumptions and sensitivity analysis, the following key results were demonstrated:

- only Scenario 4 will result in an expected net benefit;
- the drivers of the net benefit are improved quality of life following better treatment pathways, deaths prevented, and net financial savings to consumers; and
- even under sensitivity analyses that materially reduce benefits and increase costs, a positive net benefit, albeit small, remains the projected result of Scenario 4.

Table ES2. Summary costs and benefits for regulatory scenarios over the period 2017-26 ($ million)

Element	Scenario 2		Scenario 3		Scenario 4	
	Option 2	*Option 5*	*Option 3*	*Option 5*	*Option 4*	*Option 6*
Regulatory costs (total over ten years (2017-26) not discounted)	*($0.50)*	*($1.30)*	*($101.40)*	*($1.30)*	*($102.40)*	*($22.10)*
Economic costs (PV 2017-26 at 7% discount $M)	*($20.70)*	*($409.87)*	*($14.49)*	*($409.87)*	*($56.03)*	*($209.87)*
Economic benefits (PV 2017-26 at 7% discount $M)	*0*	*0*	*0*	*0*	*$243.95*	*$5,353.17*
Net benefit (option basis) ($M)	*($21.20)*	*($411.17)*	*($115.89)*	*($411.17)*	*$85.52*	*$5,121.20*
Net benefit (scenario basis) ($M)	*($432.37)*		*($527.06)*		*$5,206.72*	

Note: the regulatory costs are undiscounted and the economic costs discounted, as is consistent with OBPR guidelines.
Source: KPMG

An extensive sensitivity analysis was undertaken to provide the necessary degree of confidence in the robustness of the model's key result: that the net benefit of Scenario 4 is positive whereas scenarios 2 and 3 are negative. The summary contains a discussion of the drivers and key inputs for each broad outcome; specifically (1) health gains and death prevented; (2) the net savings and costs to consumers; (3) additional MBS activity and costs; and (4) additional PBS scripts and their cost to PBS. This summary also includes a comparison of the outputs and results of the economic model with some relevant indicators of context: (1) additional MBS expenditure from Scenario 4 as a proportion of total national MBS expenditure; (2) the results of separate public domain analyses that investigated additional MBS cost and the share of all consumers who would continue to use low dose codeine if they required a prescription; and (3) the cost effectiveness of pharmaceuticals newly approved for listing on the PBS using a cost per Quality of life year (QALY) metric.

Additional commentary on key aspects of the findings

Regulatory compliance costs to pharmaceutical industry

In accordance with OBPR guidance, regulatory costings were annualised over 10 years. However, projected regulatory costs will likely be fully realised over the assumed implementation period (12 – 24 months) for a decision by the delegate that impacts on the labelling, pack-size or up-scheduling of low-dose codeine medicines. Regulatory costings were informed by insights provided by the industry consultations and assumed that any of the proposed options would result in some product portfolio rationalisation by current sponsors of codeine phosphate products listed on the Australian Register of Therapeutic Goods (ARTG). Annex D provides the detailed assumptions and inputs used to undertake the regulatory costing. Tables ES3 shows the projected industry compliance costs (excluding impacts on consumers, pharmacists and doctors). Scenario 4 will produce the least projected increase in compliance costs for industry (less than 20% of the figure for the other scenarios), primarily resulting from the projected significant rationalisation of product portfolios if OTC codeine based medicines were up-scheduled to S4.

Table ES3: Projected increase in industry compliance cost ($ million)

Element	Scenario 2		Scenario 3		Scenario 4	
	Option 2	*Option 5*	*Option 3*	*Option 5*	*Option 4*	*Option 6*
Regulatory compliance costs (industry)	($0.49)	($1.27)	($0.4)	($1.27)	($0.09)	($0.2)
Net cost (scenario basis)	($1.76)		($1.67)		($0.29)	

Additional costs to doctors and pharmacists (regulatory model)

Data was not available on the current capacity of GPs to take on additional consultations or for specialist pain clinics (which is assumed to pose a greater limitation given anecdotal evidence of current wait times for appointments at such clinics). Some key clinical stakeholders noted that the initial increase in the number of people who are additionally treated and experience a health benefit is likely to decline in a few years until the system recalibrates. That is, patients who are currently using low dose codeine medicines and who, following up-scheduling will pursue therapeutic pathways that improve health outcomes, are part of a cohort. They will receive additional treatment and care for the following year, but this additional treatment, compared to what they would otherwise have received, will reduce each year. Stakeholders who raised this issue indicated that this additional activity would start to reduce after one to two years and maybe be absorbed into standard care after three or four years. Hence, the economic model captures this factor by assuming, in the base case, a 30% annual reduction on previous year's treatment and health gains. This factor was incorporated into the model by using an average (over ten years) number of additional GP appointments (200,000 additional appointments per year for Option 4 and 51,000 additional appointments per year for Option 6). Unlike the regulatory compliance costs for sponsors, detailed above, the additional regulatory compliance costs for doctors and pharmacists are likely to occur over the entire ten-year period used for the regulatory modelling. These costs are detailed in Tables ES4.

Table ES4: Projected average increase in cost (time) for health professionals per year (2017-26) ($ million)

Element	Scenario 2		Scenario 3		Scenario 4	
	Option 2	*Option 5*	*Option 3*	*Option 5*	*Option 4*	*Option 6*
Regulatory compliance costs (doctors and pharmacists)	($0)	($0)	($6.91)	($0)	($2.52)	($0.22)
Average net cost (scenario basis) per year for the period 2017-26	($0)		($6.91)		($2.74)	

Additional costs to consumers (regulatory model)

As noted above the cohort of consumers changing their behaviour from the status quo is likely to reduce over time. Tables ES5 details the projected costs to consumers (in relation to increased time spent), as per OBPR guidance. Scenario 4 will results in a significantly greater time impost (almost 450% greater than Scenario 3) on consumers. However, this results should not be considered in isolation but rather in conjunction with the costs and benefits as determined by the economic model.

Table ES5: Projected average increase in cost (time) for consumers per year (2017-26) ($ million)

Element	Scenario 2		Scenario 3		Scenario 4	
	Option 2	*Option 5*	*Option 3*	*Option 5*	*Option 4*	*Option 6*
Regulatory compliance costs (doctors and pharmacists)	($0)	($0)	($3.2)	($0)	($7.71)	($1.97)
Average net cost (scenario basis) per year for the period 2017-26	($0)		($3.2)		($9.68)	

Additional deaths prevented and health gains (economic model)

A total of five (2017) and 50 (2017-26) prevented deaths are projected by the economic model. The number of deaths prevented per year was assumed to be five; equivalent to 0.445 deaths prevented per 100,000 current customers. This is a conservative assumption. An Australian study[2] found that over 2000-2013 (14 years) 1,437 deaths (accidental and intentional) were assessed by the authors as having 'codeine toxicity' as a 'contributory cause of death'. Of these codeine related deaths, 83.7% were 'attributed to multiple drug toxicity'. In 572 (41.1%) of these cases, the study's authors found that 'information about whether the codeine consumed before death was prescribed or obtained over the counter' had been recorded. Of these cases, in 229 'OTC codeine products were recorded'. In the remaining 343 cases, prescribed codeine products were recorded, most commonly Panadeine Forte. Hence, on average 16 (229/14) codeine related deaths per year had OTC codeine products recorded, and possibly up to 20 to take into account the deaths for which this information was missing (conservatively assuming that 10% of all the unidentified sources were OTC codeine) . The authors found that the rate of codeine related deaths had increased between 2000 and 2009, from 3.5 to 8.7 deaths per million population. They also noted that a potential driver of this increase 'may have been the introduction in Australia of OTC products containing larger amounts of codeine, including codeine combined with ibuprofen'. Given the underreporting of type of codeine product and the ongoing increase in codeine related deaths, then, for the purpose of this model, it was assumed that up to 30 codeine deaths in 2017 could occur and also have had OTC codeine as the codeine product. The critical assumption is however the number of deaths that could be prevented if OTC low dose codeine were rescheduled to S4. A conservative assumption, 5 rather than 16 or 30 deaths prevented was used to reflect the additional information also reported in the study: (1) 83.7% of all of the codeine related deaths were attributed to multiple drug toxicity; (2) the combination of mental health and chronic pain issues were found in 25.7% of cases; (3) 53.6% of cases had a history of mental health issues; and (4) 36.1% had a history of substance use problems. Hence, it is reasonable to assume that up scheduling from S3 to S4 could prevent some of these death and that 5 deaths (which represents between 15% and 30% of these deaths) is a conservative assumption.

In the economic model each prevented death is valued at $4.2 million, to ensure consistency with OBPR guidelines.[3]

A gain in quality of life years (QALY) of 9,208 in 2017 is the result of patients receiving treatment they would otherwise not have accessed that leads to more effective therapy compared to low dose codeine combination medicines. This gain is offset by the loss experienced by a small proportion of clients for whom low dose codeine combination medicines are the most effective option available to them and who do not attend a GP to obtain a prescription under Scenario 4. This loss is projected to be 134 QALYs, based on the assumptions about the rate at which this situation occurs (assumed to be small) and the annual QALY loss per person. This situation was identified by some stakeholders. Systematic reviews indicate[4] that, on average, current acute users and chronic users of low dose codeine combination medicines who change to OTC only paracetamol

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[2] See <https://www.mja.com.au/journal/2015/203/7/trends-and-characteristics-accidental-and-intentional-codeine-overdose-deaths>.
[3] Office of Best Practice Regulation, 'Best Practice Regulation Guidance Note: Value of statistical life', dated December 2014.
[4] Cochrane reviews are systematic reviews of primary research in human health care and health policy, and are internationally recognised as the highest standard in evidence-based health care resources. See <www.cochrane.org/whjat-is-cochrane-evidence>. Relevant reviews are: Derry S, Moore RA, McQuay HJ. Single dose oral codeine, as a single agent, for acute postoperative pain in adults. Cochrane Database of Systematic Reviews 2010, Issue 4. Art. No.: CD008099. DOI: 10.1002/14651858.CD008099.pub2. Toms L, McQuay HJ, Derry S, Moore RA. Single dose oral paracetamol (acetaminophen) for postoperative pain in adults. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD004602. DOI: 10.1002/14651858.CD004602.pub2. Derry CJ, Derry S, Moore RA, McQuay HJ. Single dose oral ibuprofen for acute postoperative pain in adults. Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD001548. DOI: 10.1002/14651858.CD001548.pub2. Toms L, Derry S, Moore RA, McQuay HJ. Single dose oral paracetamol (acetaminophen) with codeine for postoperative pain in adults. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD001547. DOI: 10.1002/14651858.CD001547.pub2. Derry S, Karlin SM, Moore RA. Single dose oral ibuprofen plus codeine for acute postoperative pain in adults. Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD010107. DOI: 10.1002/14651858.CD010107.pub3. Derry CJ, Derry S, Moore RA. Single dose oral ibuprofen plus paracetamol (acetaminophen) for acute postoperative pain. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD010210. DOI: 10.1002/14651858.CD010210.pub2.

and/or ibuprofen will experience no change in pain relief and hence do not experience a QALY loss. This assumption was used in the economic model to ensure consistency with the clinical evidence. (See Table ES15 for details of the number of patients who participate in additional therapy and the average gains.)

The monetary valuation of a QALY ($182,000) was used to ensure consistency with OBPR guidelines.[5] This resulted in a gain of $1,651.5 million (in 2017) and a gain (present value) of $4,399.5 million over 2017-26. The ten year result is not simply ten times the first year result, for two reasons. First, the majority of the QALY gains occur in the first two years as customers pursue different options as a consequence of attending a GP consultation. Stakeholders stated that this initial activity would reduce over time. The model assumes the reduction in the number of patients participating in additional therapy occurs at a rate of 30% per year. (The QALY gained is assumed conservatively to occur only in the year that treatment occurs). Secondly, the QALY gained were discounted using a rate of 7% to ensure consistency with OBPR guidelines.

There are other potential sources of QALY gains and losses that are noted in the literature and by stakeholders but which were not quantified as part of the economic model. The reasoning for this is that the data on both the added gains and losses is limited but this might not impact the net QALY gain because it is plausible that these aims and losses will net each other out. To illustrate further, the sources of QALY gain relate to the reduction in risk of dependence and the reduction in risk of adverse events relating to overdose or long-term use of codeine, paracetamol and/or ibuprofen. Moreover, some stakeholders also identified that some patients might have an increased risk of adverse events as a result of changes to higher dose prescription codeine, for example. However, neither of these effects were quantified, and to the extent that the former outweighs the latter this results in an underestimate of the net QALYs gains under Scenario 4.

It was assumed that Scenario 4 would not result in an improvement in the quality of life for current customers whose use of codeine medicines is non-therapeutic.

Table ES6 presents the deaths prevented and QALYs gained in the first year, and Table ES7 the present value of these outcomes over 2017-26.

Table ES6: Additional deaths prevented and health gains, Economic Model, 2017 ($ million)

Health outcomes 2017 ($M)	Scenario 2		Scenario 3		Scenario 4	
	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6
Deaths prevented						
Estimated deaths prevented (number)	0	0	0	0	0	5
Monetised deaths prevented (using OBPR valuation of $4,200,000) ($M)	*0*	*0*	*0*	*0*	*0*	*$21.0*
Improved quality of life (ex. Deaths prevented)						
Patients with QALY benefits (number)	0	0	0	0	0	221,034
Above as % of all current customers	0	0	0	0	0	19%
QALY gains from improved treatment (number)	0	0	0	0	0	9,208
QALY loss for some consumers no longer using Low dose codeine medicines (number)	0	0	0	0	0	*(134)*
Monetised QALY gain (using OBPR valuation of $182,000) ($M)	*0*	*0*	*0*	*0*	*0*	*$1,651.5*
Monetised value of health gains and deaths prevented						
Total monetised value of health gains and deaths prevented ($M)	*0*	*0*	*0*	*0*	*0*	*$1,672.5*

[5] Office of Best Practice Regulation, 'Best Practice Regulation Guidance Note: Value of statistical life', dated December 2014.

Table ES7: Monetised present value additional deaths prevented and health gains, Economic Model, 2017-26 ($ million)

Monetised health outcomes and deaths 2017-26 Present value (7% as per OBPR guidelines) *(all dollar amounts are in italics)*	Scenario 2		Scenario 3		Scenario 4	
	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6
Monetised present value of Deaths prevented	*0*	*0*	*0*	*0*	*0*	*$147.5*
Monetised present value of net QALYs gained	*0*	*0*	*0*	*0*	*0*	*$4,399.5*
Total monetised present value						*$4,547.0*

Projected additional MBS consultations and costs (economic model)

The projected additional MBS consultations in 2017 arise for one of two reasons:

- First, under Option 6 some patients are expected to attend consultations to gain the benefits of alternative treatment options, including pain clinic consultations with specialists and pain management at general practices provided by GPs. The potential for some current customers to attend a medical practitioner to improve their current therapy was identified by all stakeholders and this increase in consultations for treatment purposes is consistent with best practice. The number of consultations for treatment for a given patient will depend upon whether they participate in more or less intensive pain management; current chronic dependent users were assumed to be the most likely to participate in more intensive pain management, including the care provided by pain clinics.
- The second reason is that some customers will attend GPs to obtain prescriptions for their ongoing use of low dose codeine medicines under Scenario 4. For both treatment and prescription only consultations, some will be accommodated in consultations that would otherwise have occurred. In the case of treatment consultations, the share that would otherwise have occurred depends on whether the patient requires a more or less intensive clinical pathway, with consultations related to less intensive pathways (primarily changed pharmacotherapy) morel likely to occur as part of consultations that would otherwise have occurred. For low dose codeine prescription consultations, 25% of consultations were assumed to be additional for both S2 (Option 4) and S3 (Option 6).

The additional low dose codeine prescription GP consultations under Option 6 (46,979) are substantially less than under Option 4 (185,184) (See table ES8), despite the estimated packs sold for current S2 products currently (3.7 million) being substantially lower than for S3 (20.8 million packs)[6]. The reason is the difference in the number of packs per year that are expected to be purchased under Scenario 4. First, the economic model assumes that up to five repeat prescriptions will be available as is currently the case for prescription codeine products on private prescription.[7] This allows for up to 6 scripts per visit to a GP. Hence, current acute users of S3 medicines, who are assumed to purchase five (20 tablet) packs a year currently (see Table ES14 for the basis of this assumption) will only require one consultation a year, and in 25% of cases are assumed to be additional consultations. In contrast, current S2 users who continue to use the product are assumed in Scenario 4 to require only one pack a year and hence one consultation is required per person per year, 25% of which are assumed to be additional.

[6] This estimates are derived from IMS data for sales for the 12 months to September 2013, projected to 2017 using an assumed reduction in sales for both of 10% over this period, based on stakeholder advice.
[7] Private prescriptions have been used as the comparator as these products are under the PBS co-pay threshold

The additional GP consultations were translated to an additional cost to the MBS using an average cost to MBS per consultation calculated from data provided by the Department of Human Services. This data provided the total cost to MBS for a given volume of consultations, each year for the next five years starting in 2017. The average cost per consultation was derived from this data for each year. This average cost was applied to the number of consultations projected by the model to determine the cost to the MBS in the base case and all of its sensitive analyses. This average cost increased each year. On advice from the data custodians, the values for the final year were kept constant and continued for each year up to 10 years. This average cost was calculated using assumptions made by the data custodians including: the mix of consultations; safety net effects and bulkbilling rates. This rate was $40.43 per average consultation in 2018 for example. An analogous method was used to derive the average cost per specialist consultation (pain clinic related costs), for example $89.89 in 2018.

Table ES8 details the additional MBS consultations and costs in the first year (2017), and Table ES9 the present value of these costs over 2017-26. The additional MBS costs in 2017 are estimated at $59.4 million, of which 83% relate to the costs of improved treatment for pain relief that would otherwise not have occurred. The remainder ($5.6 million) relate to the costs of additional consultations to obtain prescriptions for low dose codeine medications. The present value of additional costs to the MBS over the ten-year period 2017-26 are $185.2 million, of which 61% relate to treatment costs. This difference in the proportion that relate to treatment costs over the ten-year period is the result of the need for treatment for patients with chronic therapeutic use (dependent and non-dependent) decreasing as the use of low dose codeine medications reduces due to the requirement for patients to obtain a prescription from a GP.

Table ES8: Projected additional MBS consultations and costs, Economic Model, 2017

MBS Consultations and Costs 2017 *(all dollar amounts are in italics)*	Scenario 2		Scenario 3		Scenario 4		
	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6	Scenario 4 total
General Practice Consultations							
Treatment related							
Consultations (number)	0	0	0	0	0	1,062,891	1,062,891
Cost to MBS of additional consultations ($M)	*0*	*0*	*0*	*0*	*0*	*($42.9)*	*($42.9)*
LDC prescription related							
Number of consultations	0	0	0	0	185,184	46,979	232,162
Cost to MBS of additional consultations ($M)	*0*	*0*	*0*	*0*	*($7.5)*	*($1.9)*	*($5.6)*
Specialist consultations (All treatment related)							
Number of consultations	0	0	0	0	0	80,333	80,333
Cost to MBS of additional consultations ($M)	*0*	*0*	*0*	*0*	0	*($7.2)*	*($7.2)*
Total additional MBS							
Number of consultations	0	0	0	0	185,184	1,190,203	1,375,387
% that are treatment related consultations	0	0	0	0	0%	96%	**83%**
Cost to MBS of additional consultations ($M)	*0*	*0*	*0*	*0*	*($7.5)*	*($52.0)*	*($59.4)*
% that are cost of treatment related consultation	0	0	0	0	0%	96%	84%

Table ES9: Present value of projected additional MBS consultations costs, Economic Model, 2017-26

MBS Costs 2017-26 Present value (7% as per OBPR guidelines) *(all dollar amounts are in italics)*	Scenario 2		Scenario 3		Scenario 4		
	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6	Scenario 4 total
GP consultation costs	*0*	*0*	*0*	*0*	*($56.03)*	*($129.16)*	*($185.19)*
Comprising:							
treatment related	*0*	*0*	*0*	*0*	*0*	*($16.56)*	*($16.56)*
Low dose codeine scripts related	*0*	*0*	*0*	*0*	*($56.03)*	*($112.59)*	*($168.63)*
Specialist consultation costs	*0*	*0*	*0*	*0*	*0*	*($19.27)*	*($19.27)*
Total Additional MBS costs	*0*	*0*	*0*	*0*	*($56.03)*	*($148.43)*	*($204.46)*

Additional prescription medicines and additional costs to PBS (economic model)

The additional prescription medicines dispensed are primarily the result of patients who have chronic conditions and current chronic use of low dose codeine medicines and, under GP or specialist pain management, are prescribed pharmacotherapy with less risk of adverse events/and or improved pain management outcomes compared to low dose codeine combination medicines and OTC options. Stakeholders provided examples of these medications; the appropriateness of the regimen (medicine(s), dose, frequency number of repeats, pack size and duration of therapy) depending on the situation for the individual patient as assessed by the GP or specialist: tramadol, high dose codeine,[8] pregabalin, and gabapentin.

The model assumes that 223,149 (20%) of all current consumers are 'chronic users' (see tables E13 and E14 below) and that 174,056 (78%) of these users will have some kind of additional pharmacotherapy in Scenario 4. Also, some patients with acute conditions, such as migraines, are expected to be prescribed alternative analgesics such as anti-migraine preparations where they are more effective compared to low dose codeine medicines and/or have less side effects. The model assumed that 46,979 (5% of acute consumers) would participate in pain management that would lead to additional health benefits compared to low dose codeine and that pharmacotherapy would be one part of this management.

A share of these medicines would attract a PBS subsidy, however, there was little data available to inform an estimate of either the share of these scripts that would attract a subsidy, or the size of that subsidy if it occurred. Some of these alternative analgesic medicines will be below the general concessional co-payment ($38.30 at July 2016) and around $10 above the concessional co-payment ($6.20 at July 2016), for example, tramadol and high dose codeine combination medicines. Others will be above the general co-payment, for example, pregabalin. PBS will only incur a cost if the medicine is above the threshold for the relevant patient group (concessional or general beneficiary). In the absence of data and evidence of the likely uptake of these medicines the following simplifying assumption was made: 50% of all prescription medicines would attract a PBS subsidy and the average subsidy would be $10.

Clinical stakeholders indicated that these additional scripts would reduce over time as chronic pain for this group became more appropriately managed and new cases that would otherwise have used low dose codeine went directly to their GP and received the appropriate pharmacotherapy. The model accommodated this advice.

[8] Panadeine Forte, for example, has the following active ingredients Paracetamol 500 mg; Codeine phosphate hemihydrate 30 mg

Additional costs to PBS for these additional medications that are expected to improve pain relief and or reduce the risk of side effects relative to low dose codeine medications is analogous to a new drug with additional effect and additional cost compared to usual care approved through the PBAC process because it is cost effective. Hence, given these medications are already approved for PBS listing it is reasonable to assume that this additional cost represents a cost effective increase in PBS expenditure. The issue of assessment of cost effectiveness is discussed in more detail in the section 'Results in Context' at the end of this Executive Summary.

Low dose combination medicines are assumed not to be listed on the PBS under options 4 and 6. This assumption is consistent with stakeholder perspectives. Hence patients prescribed and dispensed this medicine will not attract a PBS subsidy.

Table ES10 presents the additional prescription medicines dispensed (4.6 million) and costs to the PBS ($23.1 million) in the first year (2017), and Table ES11 the present value of the additional costs to the PBS ($61.4 million discounted at 7%) over 2017-26. Only some of the 4.6 million additional prescriptions in 2017 that are expected to occur under Scenario 4 will incur cost to the PBS.

Table ES10: Additional prescription medicines and additional costs to PBS, Economic Model, 2017

Prescription medicines and PBS Costs 2017 *(all dollar amounts are in italics)*	Scenario 2		Scenario 3		Scenario 4	
	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6
Total additional prescription medicines (Inc. under and over co-payment PBS scripts and private scripts)	0	0	0	0	0	4,612,359
Additional Cost to PBS (this estimate excludes under co-payment and private scripts)	*0*	*0*	*0*	*0*	*0*	*($23.1)*

Table ES11: Present value of additional costs to PBS, Economic Model, 2017-26

PBS Costs 2017-26 Present value (7% as per OBPR guidelines) *(all dollar amounts are in italics)*	Scenario 2		Scenario 3		Scenario 4	
	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6
PBS costs	*0*	*0*	*0*	*0*	*0*	*($61.4)*

Additional costs and benefits to consumers (economic model)

The calculations of additional cost to consumers due to changes in pack size for low dose codeine (S2 and S3, all scenarios) were calculated by starting with the IMS wholesale data provided by the Department of Health describing current volume, its distribution across pack size, and the total wholesale expenditure by pack size. The cost per tablet was calculated and then the total number of smaller packs that represent an equivalent total tablet volume to the total tablets with current pack sizes was estimated. Smaller pack sizes have a higher cost per tablet, hence the wholesale cost are expected to be higher under all scenarios for the same volume. The cost to consumers was calculated by assuming a 44% mark-up on wholesale price, based on a review of the published priced compared to the prices by pack size derived from IMS data. For S3 medicines, this change in pack size would result in an increase of 23% in the number of packs sold in a year to maintain volume of tablets (from 20,844,727 to 25,750,705) and a 33% increase in the average expenditure per year per consumer from $138 to $185. The smaller sales of S2 items (an estimated 3.7 million packs in 2016) results in a smaller increase in out-of-pocket costs due to the change in pack size.

Another source of additional cost to consumers are the co-payments for additional GPs and specialists consultations, which were assumed to be at an average of $10 and $75 respectively; these are weighted average co-payments and take into account that some of these consultations will be bulkbilled. The weighted value of $10 corresponds to 20% of consultations requiring a co-payment at $50 per consultation and the

remaining requiring no co-payment ($50 x 20% =$10). The cost per prescribed medicine was assumed to be $15 and takes into account the factors discussed in the PBS section, above. Additional OTC medications (paracetamol and/or ibuprofen) were assumed to be purchased at an average cost per pack of $3.[9]

The additional financial savings due to reduced use of low dose combination medicines are the source of financial savings to consumers in Scenario 4. In a conventional regulatory situation, an additional cost impost on an item that leads to a reduction in its use and the replacement with a lower cost substitute would indicate a reduction in consumer surplus. In the case of a health economic model, where the loss of interest is health (QALYs), and the lower cost alternative is demonstrated to be no more effective and no greater risk of adverse events compared to the higher cost alternative, there is no loss in health, only a reduction in expenditure. Hence, the reduction in out-of-pocket-cost to consumers who have substituted lower cost OTCs that are equally effective and/or with less side effects comes, on average, without a loss to the consumer. From table E13 it can be seen that chronic users could be spending between $600 and $700 on low dose codeine combination medications currently per year. The additional savings are calculated relative to Scenario 1, with no change in pack size.

Table ES12 presents the additional benefits (deaths prevented, QALYs gained and net financial savings) and costs (net out of pocket costs) in the first year (2017), and Table ES13 the present value of these outcomes over 2017-26. This table is presented to provide the overall perspective of the gain and loss to consumers. The basis of the estimates of deaths prevented and net QALYs gained are presented in a previous section. These two tables also include the net financial costs (in Scenarios 2 and 3) and net financial savings to consumers under Scenario 4.

[9] This price is based on the following results of a Choice survey in July 2015. 'Supermarket generic paracetamol was a lot cheaper than Panadol, costing from 65c (Aldi) to 70c (Coles and Woolworths) for a pack of 20. In pharmacies, however, a pack of 100 Panamax can be had for less than $2, making this one of the cheapest painkillers you can buy. Nurofen (ibuprofen) was generally cheaper in pharmacies than supermarkets, with the bigger packs making it even more so. However, supermarkets were the cheapest source of generic ibuprofen, at $1.65 (Aldi) to $1.80 (Coles) per pack of 24. In Chemist Warehouse we found 50 Rafen tablets for $2.39, but in other pharmacies, house brands such as Amcal and Chemists Own were more expensive than supermarket generics.' <https://www.choice.com.au/health-and-body/medicines-and-supplements/prescription-medicines/articles/supermarkets-vs-pharmacies-for-otc-medicine>.

Table ES12: Additional benefits and costs to consumers, Economic Model, 2017

Consumer costs and benefits 2017	Scenario 2		Scenario 3		Scenario 4		
	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6	Scenario 4 total
Deaths prevented and QALYs gained							
Deaths prevented (number)	0	0	0	0	0	5	5
net QALYs gained (number)	0	0	0	0	0	9,074	9,074
Financial savings to consumers							
Additional cost of co-payments for MBS and PBS, OTC medications less the savings from less purchases of low dose codeine ($M)	*0*	*0*	*0*	*0*	*$32.5*	*$40.2*	$72.73
Comprising:							
Savings from reduction in Low dose Codeine ($M)	*0*	*0*	*0*	*0*	*$34.4*	*$132.8*	$167.19
Additional costs of medicines (OTC and prescription) and co-payment ($M)	*0*	*0*	*0*	*0*	*($1.9)*	*($92.6)*	($94.47)
Net additional out of pocket costs to consumers							
Additional cost due to change in pack size less savings due to less purchases of low dose codeine in options 2 and 3 ($M)	*($2.8)*	*($54.6)*	*($1.9)*	*($54.6)*	*0*	*0*	$0.00

Table ES13: Present value of additional benefits and costs to consumers, Economic Model, 2017-26

Consumer costs and benefits 2017-26 Present value of QALYs gained, and financial costs or savings (7%)	Scenario 2		Scenario 3		Scenario 4	
	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6
Deaths prevented and QALYs gained						
Deaths prevented (number)	0	0	0	0	0	50
net QALYs gained (number)	0	0	0	0	0	24,173
Net financial savings or cost						
Net financial savings or costs ($M)	*($20.7)*	*($409.9)*	*($14.5)*	*($409.9)*	*$244.0*	*$806.2*

Other key model assumptions (Economic model)

The first important element of the model design for Option 6 was that it used five different patient groups, rather than an average patient, to determine: (1) current use; (2) response by consumers under Option 6; (3) the resource use for consumers; and (4) the health impact. All stakeholders identified that there were distinct groups amongst current users: (1) therapeutic and non-therapeutic users; (2) chronic and acute users: and (3) dependent and non-dependent chronic therapeutic users. Stakeholders also identified that these consumers would respond differently, and, importantly for the net benefit calculations, only a small minority of acute users would have a health gain from important treatment options whereas chronic users, would potentially benefit from improved treatment options (less adverse events and/or more health effects). Critically for the economic modelling, there was little data available to distribute consumers across these types, nor was there data on the total number of consumers.

There was data on the total volume of sales for the 12 months to September 2013, by pack size, and this was assumed to have reduced by 10% to approximate 2017 use, based on advice from stakeholders that the

market had reduced since that time. This represented a total of 20.8 million packs, as presented in table ES14 as the total of the row labelled 'number of packs'.

Some stakeholders provided possible daily and annual use patterns for these types of consumers; there was no single agreed figure and the assumptions presented in Table ES14 for daily use, and days per year of use are broadly consistent with these expert opinions, but do not reflect any single opinion. An important consideration is that both duration of use and daily use were indicated as drivers of potential adverse events. Chronic dependent users were assumed to exceed the maximum recommended daily dose, whereas chronic non-dependent were assumed to not exceed the dose but to have a duration of use that was beyond the recommended use and increased the risk of dependency.

To obtain the result of packs per year and pack size for each group, it was assumed that acute users purchase smaller packs than chronic users. The actual distribution of pack size in the IMS was maintained in the model and the packs reported in the IMS data were essentially allocated from smallest (first) to largest (last) across acute therapeutic users and last, dependent non therapeutic users. This approach resulted in the estimates of packs per person and average pack size presented in Table ES14, with acute user packs smaller than those for chronic users.

The number of people in each group was estimated by 'back solving' given the modelled input 'constraints' of daily and annual individual use, proportion in each group, and overall volume. Hence the number of people in each group in table ES14 below is the only possible 'solution', that is consistent with inputs regarding total volume, use profile and proportion in each group. Solution is referring to both: (1) total number of customers in a year; and (2) distribution of customer numbers across customer groups. This approach ensured that for the sensitivity analysis, if any of the inputs of user profile or share in each group changed, then the total volume of sales (a fixed and relatively certain input) was maintained, and the 'slack' was taken up by changing the number of customers in total and/or their distribution across groups.

Table ES14: Baseline activity: number and type of current consumers and their pattern of use (Economic Model)

S3 use only	Therapeutic use			Non therapeutic use		
	Acute	Chronic dependent	Chronic not dependent	Chronic	Acute	Total
Annual use of individual consumers						
Tablets per day when taken (8 is max)	8	12	8	20	6	
Days per year taken	12	250	250	365	20	
Average tablets per pack	20	40	28	40	20	28
Average packs per year	5	75	71	183	6	18
Expenditure per year per person	*$25*	*$701*	*$591*	*$1,706*	*$30*	*$129*
Total baseline use by type of consumer						
Number of consumers						
Number of consumers in each group	939,572	44,630	178,519	1,174	10,570	1,174,465
As % of all users	80.0%	3.8%	15.2%	0.1%	0.9%	100%
As % of Australian population over 12	4.73%	0.22%	0.90%	0.01%	0.05%	5.91%
Packs						
Number of packs	4,624,637	3,347,226	12,595,103	214,340	63,421	20,844,727
As % of all packs sold	22.2%	16.1%	60.4%	1.0%	0.3%	100%
Total baseline expenditure						
Total expenditure ($M)	*$23.1*	*$31.3*	*$105.5*	*$2.0*	*$0.3*	*$151.7*

A number of important characteristics of the current profile are suggested by the results presented in ES14

- Around 6% of the Australian population over the age of 12 (19,874,413 at June 2015) purchase at least one pack of low dose codeine per year. Given that there will be an estimated 20.8 million packs sold in 2017 and that many consumers purchase more than one pack, this result of 6 per cent of the population purchasing at least one pack has face validity.
- 80 per cent of all consumers are 'acute', however, as a group they purchase 22.2% of all packs.
- 19% of all consumers are chronic therapeutic users and they purchase 76.5% of all packs sold.

A second key element of the model structure was that the use of resources (consultations and medicines) and the health benefits (QALY gains) would vary across consumers, and that chronic consumers were more likely to participate in therapeutic options that would require medical consultations and prescription medicines. In summary, six potential pathways were identified, and were defined by increasing use of pharmacotherapy and GP and specialist consultations and increasing average health benefits. The first two pathways, use of OTC only and ongoing use of low dose codeine prescriptions, had no health effect. The remaining four had an average health effect for patients. The participation in increasingly intensive treatment pathways is higher for chronic therapeutic users compared to acute therapeutic users, and then higher for dependent compared to non-dependent therapeutic users.

Table ES15 presents the components that constitute the estimated QALY gains and reflects the allocation of the population across treatment pathways (as described above). Only 5% of acute users were assumed to participate in improved therapy that leads to QALY gains, but they represent 21% of all participants in such treatment. An example of acute users in this group is people with migraines. (Migraines were an acute condition treated with low dose codeine combination products and potentially more effectively treated with prescription medicines that was most frequently cited by stakeholders.) In contrast, 90% of dependent and 75% of non-dependent therapeutic users are projected to participate in improved therapy with an average QALY gain per year therapy of 0.05 and 0.045 respectively. These higher gains per person come at additional cost to the MBS, PBS and the consumer, as discussed. However, from Table E15 it can be seen that chronic users could currently be spending between $600 and $700 on low dose codeine combination medications. Hence these costs of alternative treatments will be offset by the reduced expenditure on low dose codeine medicines.

Table ES15: Treatment participation and effectiveness (Economic Model)

Participation in treatment that could potentially lead to a gain in QALYs Only gains in first year are presented - proportion participating in treatment is reduced by 30% a year each year	Therapeutic use			Non therapeutic use		Total
	Acute	Chronic dependent	Chronic not dependent	Chronic	Acute	
% in group or participate	5%	90%	75%	0%	0%	
Number who participate	46,979	40,167	133,889	0	0	221,034
% of all participants who are in group	21%	18%	61%	0%	0%	100%
Number who attend pain clinics	0	4,463	8,926	0	0	13,389
Average QALY gain from therapy per participant	0.025	0.05	0.045	0	0	
Total QALY gain from improved therapy	1,174	2,008	6,025	0	0	9,208
% of all QALY gains from improved therapy	13%	22%	65%	0%	0%	100%

Sensitivity analysis (economic model)

The result of a positive net benefit for Scenario 4 (see table ES2) is robust to a wide range of sensitivity analyses, including the following set of cost maximising and benefit minimising assumptions:

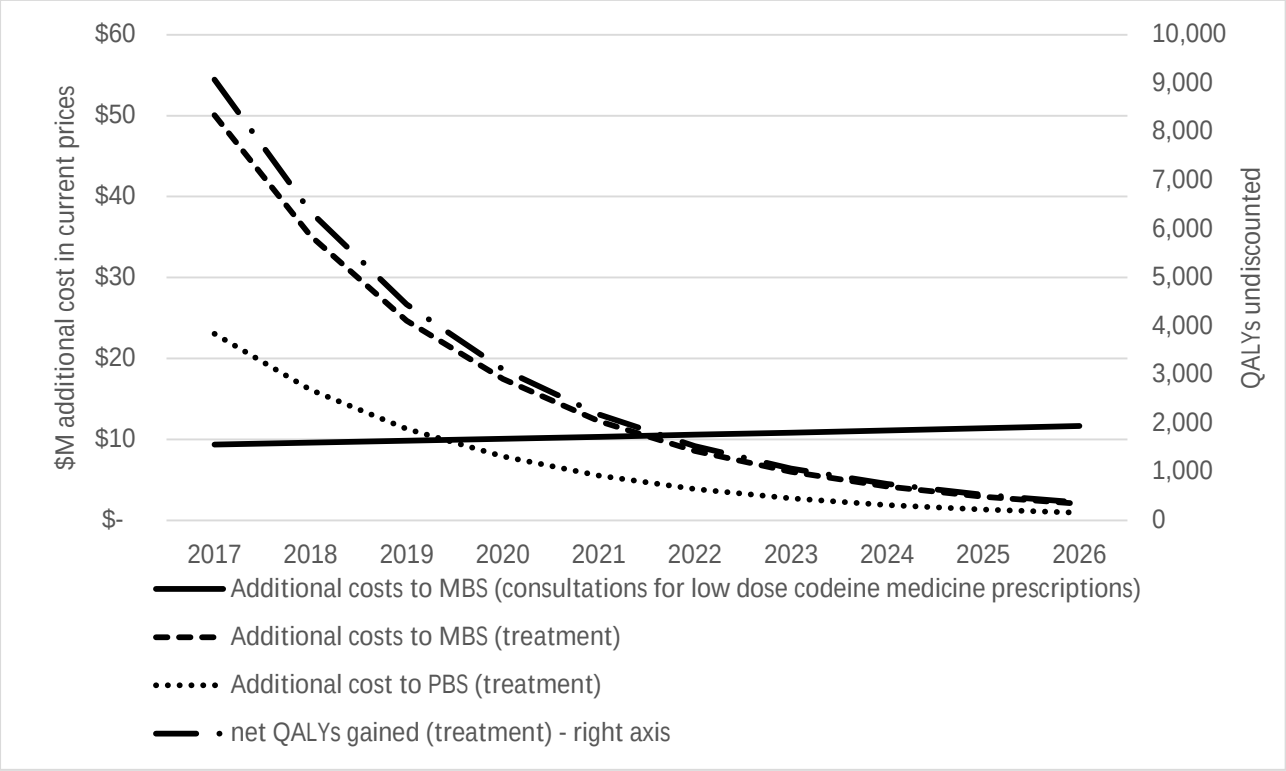
- no deaths prevented;
- the costs of gaining any quality of life improvements through improved treatment for chronic pain, for example, are increased by 80%; and
- the quality of life gain from treatment is reduced by 80%.

The variables that this result of a positive net benefit were most sensitive to were the average QALY gain resulting from additional treatment received, and the number of repeat scripts. The result was only moderately sensitive to the discount rate, number of deaths prevented, and the co-payment for GP and specialist consultations. The net benefit for Scenario 4, however, remained positive across all sensitivity analysis conducted.

Results in context

The tables above report results either for 2017, or for the present value over the period 2017-26, at a discount rate of 7%, to ensure consistency with OBPR guidelines. The following graphic presents the results on an undiscounted basis for each year over this period. It demonstrates that the rate of reduction in treatment related costs and also in the benefits of treatment (QALYs) decline over time, as indicated by stakeholders. It also demonstrates the ongoing use of low dose codeine by some consumers.

Figure ES1: Annual additional MBS treatment consultation costs, MBS low dose codeine medicine prescription consultation costs PBS costs and QALYs - Scenario 4



The additional costs to MBS for Scenario 4, in the first year, represent 0.5% (for treatment related) and 0.1% (for low dose codeine prescription related) of total MBS expenditure ($9.8 billion) in the professional attendances group in 2015-16.[10] The difference in treatment related consultations and low dose codeine prescription related consultations are discussion in more detail in the section above (Projected additional MBS consultations and costs (economic model)). In summary, the former relate to improved treatment and management of pain which occurs as a consequence of change in patient behaviour, triggered by Scenario 4. The latter relate to the additional costs to the MBS of patients continuing to use low dose codeine medicines without any other changes in therapy, care or health related outcomes.

One way of summarising and assessing the health and financial consequences of Scenario 4 is as a net benefit, where the QALYs and deaths are summarised as monetised values and compared to the costs. This approach is consistent with OPBR guidelines and presented in this report. Another approach, which is used by the Pharmaceutical Benefits Advisory Committee (PBAC) and the Medical Services Advisory Committee (MSAC), is cost effectiveness analysis: a comparison of the additional costs with the additional effects (QALYs) expressed as an incremental cost effectiveness ratio (ICER). A formal cost effectiveness analysis was outside the scope of this project. It is possible to use the results generated by the economic model to make a broad estimate of the ICER of Scenario 4 compared to Scenario 1 (current practice). Using the results report in previous tables, the additional costs to MBS and PBS from Scenario 4 relative to current practice were compared to the additional QALYs, for both the first year and the present value over ten years and estimates $9,092 per QALY and $11,097 per QALY respectively are reported. (See Table ES16). Although the decision threshold for PBAC is not publicly reported, it is reasonable to conclude that at around $10,000 per QALY that these preliminary results indicate that Scenario 4 is projected to achieve additional QALYs at a cost per QALY that would be considered to be 'cost effective'.

Table ES16: A preliminary estimate of the likely cost effectiveness of Scenario 4 relative to current (Scenario 1)

Cost and effect (QALYs) - all sourced form previous tables	2017	PV of 2017-26
Additional MBS low dose codeine prescription consultation costs ($M)	$9.36	$72.60
Additional MBS treatment consultation costs ($M)	$50.08	$134.22
Additional PBS costs ($M)	$23.06	$61.43
Total MBS and PBS costs ($M)	$82.50	$268.25
Additional QALYs (ex. Deaths) (QALYs)	9,074	24,173
ICER = additional cost/additional QALYS ($)	$9,092	$11,097

The Macquarie University Centre for the Health Economy (MUCHE) reported the results of a study on the value of OTC medicines, the gain in value should some medicines be rescheduled from S4 to S3, and the loss in value should some of them not be available OTC.[11] The report stated that their survey found that, in the case of analgesics/pain relievers, when asked what they would do if the medication for their condition became unavailable over the counter: 63% of respondents said they would see their doctor, 24% said they would do nothing, 15% said they would use a home remedy and 7% said they would 'supplement'.

More options were explored in the model presented in this report. The 48% of all current users who do not go to their doctor to obtain the now prescription only product, could instead use OTC paracetamol and/or ibuprofen medicines. Another 12% were assumed to visit their GP who would advise them to use OTC analgesics and/or non-pharmaceutical pain management options. It was not possible to determine from the

[10] 2015-16 expenditure by MBS group was sourced from Medicare Statistics online : http://medicarestatistics.humanservices.gov.au/statistics/mbs_group.jsp

[11] The Macquarie Centre for the Health Economy, Macquarie University, 'The value of OTC medicines in Australia: March 2014', < http://www.asmi.com.au/media/14036/final_web_copy_asmi_valuestudy_a4.pdf>. The report notes that 'it was funded by the Australian Self Medication Industry and a Macquarie University research grant'.

MUCHE report whether these patients would go to their doctor only for low dose codeine medicines or whether they would undertake alternative therapeutic options that could have less risks or are more effective. Of those who do go to their doctor, some will continue to use low dose codeine medications and others will use different pharmacotherapy options as part of a pain management strategy.

It was not possible to verify the sample frame used in the study to determine the representativeness of the sample with respect to the current Australian consumers. For example, it was not possible to determine whether the sample frame was pharmacy customers. Selection bias (and reduced representativeness) would occur in this case because customers who are more frequent purchasers would attend the pharmacy more often and hence more likely to be invited to participate in such as study. Hence frequent purchasers of OTC products would be over represented in this study and while 63% of such customers might go to their doctor, it is possible that only 20% of non-frequent purchasers would go to the doctor. Hence the result of the survey is not representative of current consumers. In addition to not being able to verify the sample frame to assess selection bias, it was also not possible to verify exactly what questions had been asked of these respondents and whether this study referred specifically to S3 products or OTC medicines that are also available at a supermarket.

A report prepared for the Pharmacy Guild by Cadence[12] projected that there would be an additional 8.7 million GP visits as a consequence of up-scheduling low dose codeine combination medicines at a cost of $316.44 million as a result of patients attending a doctor for these scripts. The Cadence model assumes that 53% of all current use will continue if low dose codeine medicines if they were up-scheduled and the additional GP costs correspond to one consultation per prescription. The main reason for the difference in the Cadence results and the results presented for this analysis is that the Cadence model assumes that there will be one visit for every script whereas the model presented in this report uses the assumption, provided by the TGA and clinical stakeholders, that that patients can have up to five repeat scripts (as is currently the case for prescription codeine products on private prescription), that is, a ratio of up to six scripts per GP visit, reducing the figure of $316.44 million to as low as $52 million. Further, the Cadence model assumes that patients will either continue to use low dose codeine or presumably use other OTC medicines. The model presented in this report provides other options for patients. Furthermore, this Cadence report uses the results of the MUCHE study (discussed above) to inform their estimate of 53% of usage continuing. The limitations of the representativeness of the MUCHE study are discussed in the previous paragraph. The modelling presented in this report moves away from the average consumer approach in order to accommodate the variations reported by all stakeholders across patients and their potential responses and resource implications, and the variation in opportunities for improvements in QALYs.

The public domain reports on the MedsASSIST initiative were reviewed, and the most recent public data that was found was from an August 16th publication.[13] Referencing the IMS data, the two million transactions recorded in MedsASSIST from March to July 2016 represent around 10% of the total sales in 2015. This lower than expected coverage could be a consequence of the 65% coverage of pharmacies generally, the rate of uptake over these five months or it could be the result of patients selecting to go to pharmacies that did not use MedsASSIST; it is not possible to determine these drivers this from available data. It is also not possible to determine from this public data whether the 43,000 instances of non-supply over this period were for 1,000, 20,000 or 40,000 people, nor how many individual customers had purchased these items. Therefore, this data was not used to inform the inputs in this model.

[12] Cadence Economics Pty Ltd, 'Fiscal Impact of Codeine Changes: Report for the Pharmacy Guild of Australia', dated 6 November 2015, viewed 24 August 2016, <http://www.auspharmacist.net.au/images/cad.pdf>.

[13] http://issues.pharmacydaily.com.au/2016/Aug16/pd110816.pdf

Conclusion

Only the implementation of Scenario 4 (Options 4 and 6 – up-scheduling S2 and S3 codeine-containing medicines to S4) results in a net benefit to society. The drivers of the net benefit are improved quality of life following better treatment pathways (as patients pursue different options as a consequence of attending a GP consultation), deaths prevented, and net financial savings to consumers. The result of a positive net benefit for Scenario 4 is robust to a wide range of sensitivity analyses.

1 Background

1.1 Codeine scheduling

In Australia, medicines and poisons are classified according to the level of regulatory control over the availability of the substance to the public. The greater the control, the higher the schedule number and the greater the risk to public health and safety. The Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP), known as the Poisons Standard, publishes the scheduling of medicines and poisons, which can in turn be given legal effect in state and territory legislation.

Codeine is understood to have analgesic and/or antitussive properties, and is present in many medicines classified under four schedules in the SUSMP, as detailed below.

- Schedule 2: Pharmacy medicine – These medicines are generally only available for purchase from pharmacies. They are referred to as over-the-counter (OTC) medicines, but professional pharmacist advice is *not* required for purchase of Schedule 2 medicines.
- Schedule 3: Pharmacist only medicine – These medicines are only available for purchase from pharmacies. They are also referred to as OTC medicines, and professional pharmacist advice *is* required for purchase of Schedule 3 medicines.
- Schedule 4: Prescription only medicine – These medicines are only available for purchase from pharmacies with presentation of a valid prescription (i.e. from a medical or dental practitioner).
- Schedule 8: Controlled drug – These substances should be available for use but require restriction of manufacture, supply, distribution, possession and use to reduce abuse, misuse and psychological dependence.[14]

Over the past decade, the Advisory Committee on Medicines Scheduling (ACMS) and its predecessor committee, the National Drugs and Poison's Committee (NDPSC), have given consideration to the scheduling of codeine and its availability as an OTC medicine, as well as codeine labelling and dosage controls.[15]

Concerns have been raised by some key stakeholders about the potential for the abuse of codeine made possible through its ready accessibility in OTC medicines, and the associated risks, including morbidity, toxicity and dependence, and related public health costs.

For these reasons, amongst others, proposals to up-schedule codeine-containing medicines to Schedule 4 were referred to the July 2015 meeting of the ACMS. Pre-meeting comments were invited from the public, and 60 submissions were received. On 1 October 2015, the Delegate made an Interim Decision to delete the current Schedule 2 and 3 entries for codeine and amend the current Schedule 4 and 8 entries to reflect these changes, effectively making codeine only available by prescription. The public was invited to provide further comments in response to the Interim Decision and 127 submissions were received. Subsequently, on 18 November 2015, the Delegate deferred a final decision on codeine scheduling to thoroughly consider the large number of submissions and to seek additional advice from the ACMS.[16] An additional public consultation in December 2015 resulted in a further 49 submissions.

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[14] It should be noted that, in the SUSMP, references to the concentration, strength or quantity of codeine are calculated for anhydrous codeine (molecular weight: 299.36). However, codeine is commonly present in products as codeine phosphate (molecular weight: 397.4). Weights of codeine referred to in the SUSMP are multiplied by 1.33 to obtain the weight of codeine in codeine phosphate formulations. Codeine weights in this document refer to its presence in codeine phosphate formulations.

[15] See Therapeutic Goods Administration website for more detail: https://www.tga.gov.au/book-page/interim-decisions-matters-referred-expert-advisory-committee-11.

[16] See Therapeutic Goods Administration website for more detail: https://www.tga.gov.au/book-page/part-final-decisions-matters-referred-expert-advisory-committee-11-14.

1.2 Objective

The objective of this report and the project that informed its development was to provide economic modelling and financial quantification of the regulatory, social and economic impacts of the proposed options for the rescheduling of codeine being considered by the ACMS. More specifically, KPMG's role was limited to providing the TGA with input for Impact Analysis (cost-benefit) and Regulatory Costing in order to satisfy the requirements of a Regulation Impact Statement (RIS). KPMG was not required to undertake an exhaustive review of the evidence/medical literature for or against the up-scheduling of codeine, as this is a policy consideration and is addressed in the RIS proper.

1.3 Approach

KPMG's approach to this task comprised two parallel but overlapping work streams: regulatory modelling, and economic modelling. As proposed by KPMG and agreed with the TGA, the approach consisted of the following activities:

Background research

- Desktop review of the Australian and International peer reviewed and other literature, publications and data sources to support development of the economic and social impact modelling in relation to the model's input variables including the following:
  - the rates of deaths and morbidity associated with low dose codeine combination medicines;
  - the comparative effectiveness in pain relief for low dose codeine combination medicines compared to paracetamol and/or ibuprofen without low dose codeine;
  - the number of people who purchase low dose codeine combination medicines: the proportion who use it chronically, and if used chronically, the proportion who are dependent;
  - the number of packs purchased; and
  - the Quality of Life Year (QALY) gains associated with improved treatment of chronic pain.

Generalisability of overseas results to the Australian setting regarding the prevalence of dependent users was limited due to difference in the regulatory and clinical contexts.

Engagement with relevant government agencies

- Engagement with the Regulatory Engagement & Planning Branch, Health Products Regulation Group, Department of Health (DoH), so as to confirm scope; discuss and obtain feedback on progress; seek advice or direction regarding assumptions, qualifications and inputs; and communicate challenges. This included a workshop wherein regulatory touch points for the 5 regulatory options (noting that Option 1 entailed no change) were discussed and confirmed, and where it was agreed that there were four logical groupings of the six options, resulting in four potential scenarios (see Section 2.1).
- Engagement with relevant business units in DoH to discuss potential impacts and modelling of proposed options as follows:
  - *Pharmaceutical Benefits Scheme (PBS).* Potential increased costs due to additional prescription of PBS listed medicines in the case of up-scheduling to Schedule 4.
  - *Medicare Benefits Schedule (MBS*). Increased costs due to additional medical practitioner visits to obtain prescriptions in the case of up-scheduling to Schedule 4.
- Engagement with subject matter experts within the TGA to understand potential regulatory impacts and modelling of proposed options for OTC and prescription medicines.
- Two meetings with the OBPR to confirm proposed approach and seek advice or direction regarding assumptions, qualifications and inputs.

Interviews with industry

- KPMG initially conducted interviews with current sponsors of products on the Australian Register of Therapeutic Goods (ARTG) that had codeine as an active ingredient. The following pharmaceutical companies, which provided a cross-section of current sponsors of S2 and S3 medicines containing codeine on the ARTG, were interviewed:
  - Sandoz Pty Ltd - as a major provider of Schedule 2 and Schedule 3 (OTC) medicines containing codeine to the Australian market.
  - Sanofi-Aventis Australia Pty Ltd - as a major provider of Schedule 3 (OTC) and Schedule 4 (prescription only) medicines containing codeine to the Australian market.
  - GlaxoSmithKline Consumer Healthcare Pty Ltd - as a major provider of Schedule 2 and Schedule 3 medicines containing codeine to the Australian market.
  - Soul Pattinson Manufacturing Pty Ltd - as a major provider of Schedule 2 and Schedule 3 medicines containing codeine to the Australian market.
  - Johnson & Johnson Pacific - as a major provider of Schedule 2 and Schedule 3 medicines containing codeine to the Australian market.
- In preparation for these interviews, KPMG provided sponsors with background material and a list of questions for discussion (Annex F). Industry input contributed to the development of the regulatory costing model, allowed for the testing of baseline assumptions and gave some insight into anticipated supply and demand behaviour of market participants in response to the rescheduling options.

Interviews with peak bodies

- KPMG also participated in interviews with peak bodies in order to inform the development of the economic and social model. These interviews were with representatives from the:
  - Australian Medical Association (AMA) - as the peak body representing registered medical practitioners and medical students of Australia.
  - Pharmaceutical Society of Australia (PSA) - as the peak body representing pharmacists in Australia.
  - Australian Self Medication Industry (ASMI) - as the peak body representing companies involved in the manufacture and distribution of consumer healthcare products in Australia.

Development of regulatory and economic models

- The regulatory and economic models were developed in consultation with the OBPR, and were informed and guided by the background research, consultation with relevant government agencies and interviews mentioned above, as well as a range of primary data sources (discussed in greater depth in Section 1.4.).

1.4 Sources and manipulation of data

To inform the regulatory and economic modelling, data was sought from authoritative sources where possible, and was used to inform the logic of the regulatory and economic models, as well as the data inputs and assumptions for these models. Primary data sources are referenced throughout the report, and include:

- Australian Register of Therapeutic Goods (ARTG, August 2016): product name, formulation, sponsor (company) and manufacturer details of all therapeutic goods lawfully supplied in Australia.
- IMS Health (June 2013, supplied by TGA): product sales data.
- Pharmaceutical Benefits Scheme (PBS, August 2016, supplied by TGA): details of the medicines subsidised by the Australian Government.
- Medicare Benefits Schedule (MBS, August 2016, supplied by TGA): details of the Medicare services subsidised by the Australian Government.

- Public submissions to the TGA (May 2015 – January 2016): from interested members of the public, individual specialists (i.e. pharmacists and medical practitioners), pharmaceutical companies, representative / peak bodies, and other agencies.[17]
- Confidential submissions to the TGA (May 2015 – January 2016, supplied by TGA): submissions as above, but not permitted for public release.
- Interviews (August 2016): see Section 1.3 for more detail.
- MedsASSIST (PGA, September 2016): the real-time recording and monitoring program established by the Pharmacy Guild of Australia to support patient safety and improve the clinical outcomes for medicines containing codeine.
- Academic literature concerning health effects of long-term codeine use.

[17] See Therapeutic Goods Administration website for all publicly available submissions: https://www.tga.gov.au/scheduling-submission/public-submissions-scheduling-matters-referred-acms-15-august-2015.

2 Approach

2.1 The options being considered by the Medicines Scheduling Delegate

Table 1 details the regulatory options (or combinations of regulatory options) being considered by the Medicines Scheduling Delegate.

Table 1. Regulatory options for the rescheduling of codeine

Option 1	No change - the current scheduling of codeine remains appropriate.
Option 2	The current Schedule 2 entry for codeine in cough and cold medicine preparations be amended to reduce the pack size to not more than 3 days' supply and include a label warning that codeine can cause addition.
Option 3	The current Schedule 2 entries for codeine in cough and cold medicine preparations be up-scheduled to Schedule 3, and that the pack size be reduced to not more than 3 days' supply, and include a label warning that codeine can cause addiction.
Option 4	Up-schedule the current Schedule 2 entries for codeine to Schedule 4 and amend the current Schedule 4 and 8 entries.
Option 5	The current Schedule 3 entries for codeine (including, but not limited to codeine containing analgesics) be amended to reduce the pack size to not more than 3 days' supply and include a label warning that codeine can cause addiction.
Option 6	Up-schedule the current Schedule 3 entries for codeine to Schedule 4 and amend the current Schedule 4 and 8 entries.

Source: TGA RFI documentation (TGA2016-325)

As discussed above, it was confirmed at the planning workshop between KPMG and relevant TGA internal stakeholders that, while these implementation options are separated out into individual scheduling changes for clarity, in practice, they are necessarily grouped. For example, both Options 4 and 6 reflect the Interim Decision. The following scenarios were agreed in the workshop to reflect the most likely practical groupings and were used to inform subsequent analysis.

Table 2. Grouping of regulatory options

Scenario 1: (Option 1)	No change to the status quo.
Scenario 2: (Options 2 and 5)	Schedule 2 and Schedule 3 entries for codeine (including, but not limited to, cough and cold medicine preparations and codeine containing analgesics) be amended to reduce the pack size to not more than 3 days' supply and include a label warning that codeine can cause addition. *Summary* · Reduce pack size and include warning label for S2 and S3
Scenario 3: (Options 3 and 5)	The current Schedule 2 entries for codeine in cough and cold medicine preparations be up-scheduled to Schedule 3, and then all Schedule 3 entries (i.e. those currently Schedule 3 and those previously Schedule 2) for codeine (including, but not limited to, cough and cold medicine preparations and codeine containing analgesics), be amended to reduce the pack size to not more than 3 days' supply, and include a label warning that codeine can cause addiction. *Summary* · S2 up-scheduled to S3 · Reduce pack size and include warning label for S3
Scenario 4: (Options 4 and 6)	Schedule 2 and Schedule 3 entries for codeine (including, but not limited to, cough and cold medicine preparations and codeine containing analgesics) be up-scheduled to Schedule 4. *Summary* · S2 and S3 up-scheduled to S4

Source: TGA and KPMG workshop 4 August 2016

2.2 The regulatory model

Overview

The development of the regulatory model was undertaken in accordance with OBPR Guidance Note: 'Regulatory Burden Measurement Framework' dated February 2016. In accordance with this framework,

regulatory costs were estimated for administrative compliance costs and substantive compliance costs only. The labour cost formula (price x quantity) (or in its more expanded version: (Time required × Labour cost) × (Times performed × Number of businesses or community organisations × Number of staff)) was used to determine these costs. It is important to note the interrelationship between the inputs in this formula as this explains the variation in the calculated regulatory costs for various compliance activities.

Delay costs (application and approval delays) were determined to be out of scope as it was envisaged that any changes to scheduling for codeine products would incorporate sufficient time for industry to respond with only minimal stock-outs (which occur when existing pharmaceutical stock is withdrawn or exhausted prior to new stock being available) being experienced.

As detailed earlier in this report, a workshop was held with TGA staff to identify the key regulatory compliance processes that would arise from the implementation of each option. Component elements of each of the identified regulatory processes were then broken down into their respective time, cost and frequency components and the value of the respective inputs sourced from previous RISs prepared by TGA, as well as information provided via consultations with industry and peak bodies. As agreed, cost models were developed in Microsoft Excel with the summary for each option also presented in the standard Regulatory Burden Measure (RBM) format.

Consultations

The development of the regulatory cost estimates was informed by targeted consultation with sponsors who currently produce codeine-based products in the OTC market. The target sponsors were Sandoz Pty Ltd, Sanofi-Aventis Australia Pty Ltd, GlaxoSmithKline Consumer Healthcare Pty Ltd, Soul Pattinson Manufacturing Pty Ltd and Johnson & Johnson Pacific. These companies occupy both distinct and overlapping segments of the OTC and prescription market and were able to provide a range of perspectives given the different incentives and risks that are intrinsic to their respective business models.

Sponsors were provided with a list of questions in Attachment G which were subsequently used to structure conversations in meetings and focus on issues directly related to the modelling and implementation implication of different options.

Broadly, the interviews were structured around six topics outlined in the questionnaire:

- product strategy;
- market response;
- labelling;
- packaging;
- updated listing and regulatory approvals; and
- implementation.

A high level summary of industry responses are provided here without direct attribution to specific stakeholders. This is intended to provide an overall picture of the feedback and the key themes that emerged from the meetings and informed the modelling.

Topic 1 - Product Strategy

Sponsors were asked about how they would respond to up-scheduling decisions and what factors would be considered in determining their product strategy. There was a high level of concern by S2 and S3 sponsors about the impact of up-scheduling on their business. Sponsors identified a number of issues that undermine the commercial viability of up-scheduled codeine products. The issues were fundamentally connected to the different distribution and market access models associated with S3 and S4 arrangements, and uncertainty about the level of demand for lower dosage codeine products given the current prescribing habits of GPs.

Key points were:

- S2 sponsors are unlikely to migrate products to S4. It is likely that most S2 sponsors would migrate products to S3 but would materially rationalise their product portfolio and range with generic brands to be most impacted by the reduced range behind the pharmacists counter.
- S3 sponsors would evaluate the commercial viability of moving products to S4, however this would be largely contingent on their expectations about demand and confidence that GPs would change their prescribing habits to account for different dosage options.
- Sponsors with branded products highlighted concerns about the impact of discontinuing products on brand equity and the regulatory barriers to redeploying or reformulating well known and trusted brands which are a source of value for these companies.

Topic 2 - Market Response

Sponsors were asked to provide views on what impact different options would have on the behavior of customers (across different segments) and the level of demand and substitution they would expect to see in the market.

Key themes were as follows:

- The introduction of warning labels and reduced pack sizes would reduce overall revenue slightly, however, overall demand for codeine would largely remain.
- The up-scheduling of S2 to S3 would reduce demand but there would still be a market for codeine-based cough and cold products. However consumers would be presented with less choice and range as products move behind the counter. This would necessitate some degree of product rationalisation.
- The up-scheduling of S2 to S4 would effectively see these product lines discontinued.
- The up-scheduling of S3 to S4 would reduce overall demand for medium dosage codeine products, but that a sizable segment of these existing customers would continue to seek out codeine products and visit a GP to obtain a prescription. Sponsors all considered it was likely that some consumers would visit their GP and receive access to higher dosage products with larger pack sizes which could lead to perverse outcomes (note this factor is specifically addressed in the economic model).
- The S3 market is essentially entirely made up of consumers – hospitals and other institutions do not bulk purchase OTC codeine products (tending to use paracetamol and/or ibuprofen or move to higher strength opioids).

Topic 3 – Reduced Pack Size

Sponsors were asked whether they have existing products or manufacturing arrangements that would readily accommodate the change to a 3-day pack (outer pack and the inner blister packs). There was a mixed response regarding this question, with about half of the sponsors indicating they already produced a 3-day pack or had production lines that could be used to do so, and thus they could accommodate this at essentially no cost. Others would incur costs for retooling machinery to modify the depth of the outer pack or the length of the inner blister pack.

The sponsors interviewed stated that costs appeared to depend on whether the manufacturing was done in Australia or overseas. Retooling in Australia was more expensive (and potentially cost prohibitive) and ranged between $30,000 and $150,000. Retooling overseas is cheaper and ranges from between $10,000 and $30,000. The sponsors also expressed an opinion that implementation in local facilities could be executed more quickly (6 months) whilst changes to overseas facilities would take longer (12 months).

Topic 4 – New Warning Labels

Sponsors were asked to describe the steps involved in adding new labels, and the costs associated with these steps. Broadly, the steps identified were the development of artwork and design, internal review, quality assurance and implementation. The range of costs provided by sponsors was between $2,000 and $6,500.

Sponsors noted they would look for opportunities to roll label updates into others which were already in the pipeline. Updates would typically occur once every 3 years.

Implementation timeframes were between 6 and 12 months. Similar to packaging, overseas production arrangements required longer lead-times as there was less flexibility in scheduling updates into manufacturing change windows.

Topic 5 – Updated listings

Sponsors were asked to comment on time or cost of regulatory forms and other compliance processes connected to the various options. Key points were

- C1/C2 forms were considered relatively straight forward. With sponsors indicating time required to complete, undertake internal review and submit forms being between 4 – 10 hours of effort.
- Sponsors indicated updating Product Information (PI)/Consumer Medicines Information (CMI) documents would also be straightforward. In the event a new PI/CMI had to be created (such as S2 up-scheduling to S3) sponsors would not seek to create one from scratch but leverage a model PI already being used in that schedule.
- Sponsors did not anticipate up-scheduling to S4 (if they were currently in S2 or S3) would cause any difficulties with respect to GMP conformity. The sponsors consulted were all confident their facilities were GMP compliant and also noted those facilities were already manufacturing other S4 products.
- In their responses, sponsors indicated that based on precedent, they would expect the TGA to grandfather S2 and S3 products into S4. They cited the standard registration process for a prescription medicine as a material cost and time delay that could require up to 24 months subject to the scope of the application requirements.

Topic 6 – Implementation timeframes

Implementation timeframes were discussed with sponsors throughout each of the topics to understand the minimum and ideal timeframes connected with different change processes. The purpose of this topic was to understand any other implementation considerations pertinent to industry.

Several sponsors expressed concerns about the lack of certainty concerning the implementation timeline and arrangements that would accompany a decision to up-schedule. They noted the critical importance of implementation timeframes in enabling business to reposition themselves in the event of an adverse outcome. They also noted that a short implementation timeframe would potentially increase costs and also make it difficult to reposition themselves in the market without significant losses in revenue. In this respect, sponsors emphasized the engagement of the TGA would be critical towards assisting their planning.

Broadly, sponsors indicated a reasonable end-to-end implementation timeframe would at a minimum be between 18 to 24 months.

Sponsors noted their concerns that an 18 to 24 month timeframe may be perceived as being at odds with the safety/risk rationale of the interim decision and that the TGA would be presented with a moral dilemma in balancing the two.

Other key themes were as follows:

- Pharmacies generally hold between 1 to 2 month(s) worth of stock depending on their location.

- Most manufacturers do not hold large amounts of produced stock but make to order. However they do make bulk purchases of components and materials and these can take between 4 and 9 months to turn over.
- Shelf life of codeine products is 24 months. Sponsors were concerned a short implementation timeframe may require some residual products to be recalled from shelves which would be a costly exercise and involve reverse logistics and associated costs.
- The minimum timeframes to comply with an up-scheduling decision appears to be around 9 months. However sponsors noted this assumes that there is no business case development or evaluation of commercial viability to up-schedule which they considered to be unreasonable. They further expressed a view that a longer timeframe is needed to enable this to be undertaken in an orderly way.
- Sponsors indicated time is also needed for GPs to be educated about the changes (in the event of an up-scheduling) to ensure their prescribing habits adapt to the new situation, and that medium dosage codeine products (at 12.5mg) are prescribed when appropriate. Sponsors also sought clarity as to whether Government or industry would be expected to fund the costs of GP education.

2.3 The health economic model

Data limitations and key assumptions

The health economic model sought to project the changes to a range of costs to the Commonwealth and individual consumers, deaths prevented and changes in quality of life as a consequence of all three scenarios; only Scenario 4 was expected to have quality of life benefits. Most of the parameters that could influence the projected results were identified during consultation and review of available materials. The model sought to include as many of these parameters as possible. Where input data was available and/or the parameter was assessed as potentially influencing the results, it was included in the model. There were a number of key assumptions regarding both baseline parameters (e.g. the proportion of consumers who are dependent on low dose codeine medicines) and projection parameters (the proportion of dependent users whose health outcomes will improve)) that have limited supporting evidence. There were many other parameters for which minimal data and information was available. By using the most appropriate model structure, conservative assumptions and sensitivity analysis it was possible to generate robust results relating to the direction of any net effect of the projected costs and benefits of each scenario.

The only OTC low dose codeine medicines specific data available to use as an economic model input was IMS data (volume data) for sales of codeine-based products (24 months to September 2013). This data needed to be extrapolated for the base year of sales (2017). Some externally sourced inputs (such as categorisation and fee structure for MBS GP consultations and the discount rate) were not specific to the options being modelled but rather relate to the broader health system or to specific requirements of this regulatory assessment process. Initial assumptions were formed for the remaining inputs and then, in the absence of data or relevant literature, they were 'sense-checked' in interviews with peak bodies (i.e. expert opinion was sought). The key assumptions underpinning the economic analysis are:

- 99% of people who used low dose codeine medicines at least once are using it for therapeutic purposes (the remaining 1% is for non-therapeutic use).
    - Of all users, 80% are using it therapeutically for acute conditions.
    - Of the 19% using it therapeutically for chronic conditions, 20% are dependent on low dose codeine medicines.
    - In the absence of reliable data to inform these parameters, these reasonable values were selected and tested in the sensitivity analyses.
- If S2 low dose codeine medicines are up-scheduled to S4 then the prescribing behaviour of GPs will be to provide zero repeats as appropriate for cough and cold medicines. Only 20% of consumers will continue

to use this option and for only 30% of these patients will the visit they make to the GP be in addition to visits they would have made anyway in the absence of the regulatory change. Some consumers will switch to cough and cold medicines without codeine.

- If S3 low dose codeine medicines are up-scheduled to S4 then the model assumes the prescribing behaviour of GPs will be to provide up to 5 repeats if they assess that it is appropriate for this patient to continue with this pharmacotherapy, given the patient's symptomology and medical history. Not all patients are expected to continue and this is accommodated in the model.
- Of current therapeutic acute users of S3 low dose codeine medicines, 25% are assumed in the base case to continue to use low dose codeine medicines. In the absence of reliable data to inform these parameters, this reasonable value was selected and tested in the sensitivity analyses. Some will switch to OTC ibuprofen and/or paracetamol and others to cough and cold medicines without codeine.
- Chronic therapeutic users are assumed in the base case projections to follow one of a number of potential pathways, only one of which is ongoing use of low dose codeine medicines. The potential pathways were identified through stakeholder consultations and a review of the available literature. In the absence of reliable data to inform these proportions of consumers who would follow potential, reasonable 'base case' assumptions were made in the model and then tested in the sensitivity analyses.
- The projected number of prevented deaths per year from up-scheduling S2/S3 low dose codeine medicines to S4 is 5 per year. This is a conservative estimate based on the cited 229 codeine related deaths in which OTC codeine products were recorded over the 14 year period of the study.[18] These deaths are not necessarily entirely attributable to OTC codeine medicine use and hence a very conservative estimate of the deaths prevented was used in the base case assumptions of the model.
- Health benefits as shown in the model will only be realised from improved therapeutic pathways taken by patients who would otherwise be chronic therapeutic users of S3 low dose codeine medicines.[19] For this improved therapeutic pathway to be realized the key enabler was a visit to a GP, which will not be likely to occur under options that keep low dose codeine medicines as an OTC medicine, regardless of pack size or whether up-scheduled from S2 to S3. The potential pathways were identified through stakeholder consultations and a review of the available literature. In the absence of reliable data to inform these proportions of consumers who would follow potential, reasonable 'base case' assumptions were made in the model and then tested in the sensitivity analyses.
- Most current higher dose codeine medicines are limited in the number of repeats that can be provided, often to no repeats if this prescription is dispensed under PBS. This limit does not apply to current users of high dose codeine medicines if they use a private rather than PBS script. Stakeholders indicated that many current users of high dose prescription codeine medicines use private scripts and have up to 5 repeats. The assumption used in this model is that a patient will be provided up to 5 repeats of low dose codeine medicines, if the prescriber assesses this is appropriate. This assumption is considered reasonable for the following reasons.

[18] The MJA article noted that the study (2000-2013) is limited in '… inferences that can be drawn about the likely impact of reducing OTC codeine availability on the prevalence of codeine-related mortality'. Amanda Roxburgh, Wayne D Hall, Lucinda Burns, Jennifer Pilgrim, Eva Saar, Suzanne Nielsen and Louisa Degenhardt. 'Trends and characteristics of accidental and intentional codeine overdose deaths in Australia', *Medical Journal of Australia,* 2015, Volume 203, Issue 7, viewed 6 September 2016, < https://www.mja.com.au/journal/2015/203/7/trends-and-characteristics-accidental-and-intentional-codeine-overdose-deaths>.

[19] In the base case, only chronic therapeutic users of low dose codeine medicines have been included for the modelling of health benefits. It was raised in peak body consultations that some acute therapeutic users of low dose codeine (e.g. migraine sufferers) may also benefit from improved therapeutic pathways; however, because this was assessed to be a low proportion of current acute users so this was not modelled in the base case.

- Stakeholders indicated that pharmaceutical companies are unlikely to seek PBAC approval for PBS listing of low dose codeine medicines; the cost of listing could be high compared to potential impact on the volume of sales.
- If they were to be listed, the option for patent to use private scripts with up to 5 repeats would remain available if the prescriber assessed that this was an appropriate number of repeats.
- There would be no incentive for a general beneficiary (non-concessional) patient to seek a PBS script rather than a private script because the price of low dose codeine medicines is currently below the general beneficiary co-payment.

- Concessional patients are already purchasing OTC low dose codeine medicines at a price that is only a few dollars above the concessional copayment. If a concessional patient is currently using more than two packs a year then there is little incentive to save a few dollars on each script if it requires one GP consultation for every script.
- Paracetamol and/or ibuprofen medicines as alternative to low dose codeine medicines are cheaper than existing S2 and S3 low dose codeine medicines and are also available at supermarkets (which introduces further price competition).

The baseline case

The economic modelling for all options uses a baseline case (current use) that was developed for five groups of patients. Characteristics of these patients groups, including their annual pattern of codeine use (low/high dose, packs and expenditure) are detailed in Annex E, which provides a discussion of the economic model. A key distinction is that all use of Schedule 2 products is assumed to be for acute use, whereas Schedule 3 product use is spread across all five patient groups.

How the economic model works

The economic model works in five main steps, as follows:

Step 1: Simulation. The simulation is based on holding constant the total amount of codeine currently used by the five groups of consumers (though possibly in different pack sizes) and then adjusting the following variables to reflect the post-regulatory change environment:

- packs of low dose codeine medicines;
- out of pocket cost;
- pharmacy purchases; and
- GP consultations.

Step 2: Plausibility analysis. The next step assesses for each consumer group the plausibility that this change in resource use will occur (holding the consumption of low dose codeine medicines constant) relative to alternative pathways and models accordingly. Each of these alternative pathways have different uses of resources and health outcomes associated with them. Scenario 4 does not add pathways; it removes one and hence changes which of the existing pathways that patients will take. These alternative pathways will often incorporate discussions with both GPs and pharmacists, and include options such as:

- use of paracetamol and/or ibuprofen without codeine;
- non-pharmacotherapy;
- prescribed low or high dose codeine;
- alternative prescribed pharmacotherapy;
- GP or self-referrals to allied health providers; and
- GP referrals to specialist pain clinics.

Step 3. Allocation of population across pathways. This step entails identifying the proportion of consumers in each group (cohort) that will pursue each pathway. This proportion varies across groups and also depends on factors such as the capacity for the existing pain clinics to see additional patients, including those who are referred by their GP and are eligible for a Medicare rebate.

Step 4. Determination of resource use and health outcomes. This step assigns changes in resource use to each cohort, where these changes in resource use and health outcomes are a consequence of changes in behaviour.

Step 5. Project changes over time. The final step projects these changes over the specified ten-year period, taking into account changes in cohorts, the ongoing needs for additional services and the longer term impact on health outcomes.

The benefits: their sources and drivers

The benefits are of three types: (1) deaths prevented; (2) health gains (Quality of Life Year – QALY- gain); and (3) financial savings. Deaths are prevented in option 6 and are a consequence of the removal of access to OTC low dose codeine medicines.[20] Financial savings are a benefit in options 4 and 6, where patients substitute their use of low dose codeine medicines with OTC painkillers such as ibuprofen and paracetamol, which are cheaper.

The net health gain requires further explanation. There are several options (of the five specified options to be modelled) where there are no realised health benefits because either (1) there is no change in behaviour or (2) the consumer switches to an alternative therapy that brings the same level of pain relief and might be available at the same or lower cost. For many consumers, clinical trials have demonstrated that they will experience no loss in pain relief if they switch from low dose codeine medicines with paracetamol and/or ibuprofen to either of these two medicines alone.[22] However, stakeholders stated that some patients do benefit from low dose codeine medicines compared to paracetamol or ibuprofen alone, although no references were provided. Stakeholders also stated that while some patients benefit from paracetamol and ibuprofen combination medicines relative to either product alone, this combination product might be contraindicated for use in some patients, for example those with an active gastrointestinal bleed[21]. A small group of patients were assumed to have a loss in pain relief (QALY decrement) which partly offset the QALY gain for patients who participate in improved therapeutic pathways as a consequence of up-scheduling from S3 to S4. While this up-scheduling is expected to result in an increase in the use of paracetamol and/or ibuprofen medicines, it is not expected to result in an increase in the deaths associated with their use compared to the deaths that would otherwise have occurred in the absence of Scenario 4 being enacted. The reason is that consumers who would otherwise have a codeine dependency and used above the maximum recommended daily dose of paracetamol and/or ibuprofen (due to their presence in combination drugs with codeine), are now instead using these medicines for pain relief only and are not consuming above the maximum recommend daily dose.

In summary, the potential health impacts are of the following kinds:

- a reduced level for pain relief for some patients who substitute low dose codeine medicines with OTC paracetamol or/and ibuprofen;

[20] Amanda Roxburgh, Wayne D Hall, Lucinda Burns, Jennifer Pilgrim, Eva Saar, Suzanne Nielsen and Louisa Degenhardt. 'Trends and characteristics of accidental and intentional codeine overdose deaths in Australia', *Medical Journal of Australia,* 2015, Volume 203, Issue 7, viewed 6 September 2016, < https://www.mja.com.au/journal/2015/203/7/trends-and-characteristics-accidental-and-intentional-codeine-overdose-deaths>.

[21] NPS publication: NSAIDs: minimising the risk <https://www.nps.org.au/__data/assets/pdf_file/0006/17079/NSAIDsInsert.pdf>.

- improved quality of life if the patient would benefit more from other pain treatment options that would not otherwise have been used by these patients and they commence using these options;
- prevention of adverse events related to unintentional overdose of paracetamol and/or ibuprofen in combination products also containing codeine; and
- reduced dependence and risk of dependency.

Only the first two of these potential impacts were quantified in the model. The last two are not quantified in the model as there was insufficient information to form initial assumptions.

The costs: their sources and drivers

The main additional costs relate to:

- net out-of-pocket costs to consumer;
- additional costs to MBS due to additional GP and pain consultations; and
- additional costs to the PBS due to additional scripts for PBS listed pain medications.

The additional costs to the MBS are the primary driver of additional costs to government.

Model uncertainty

Modelling has two main types of uncertainty, those associated with inputs (input uncertainty) and structure (systematic uncertainty). Each uncertainty is described below.

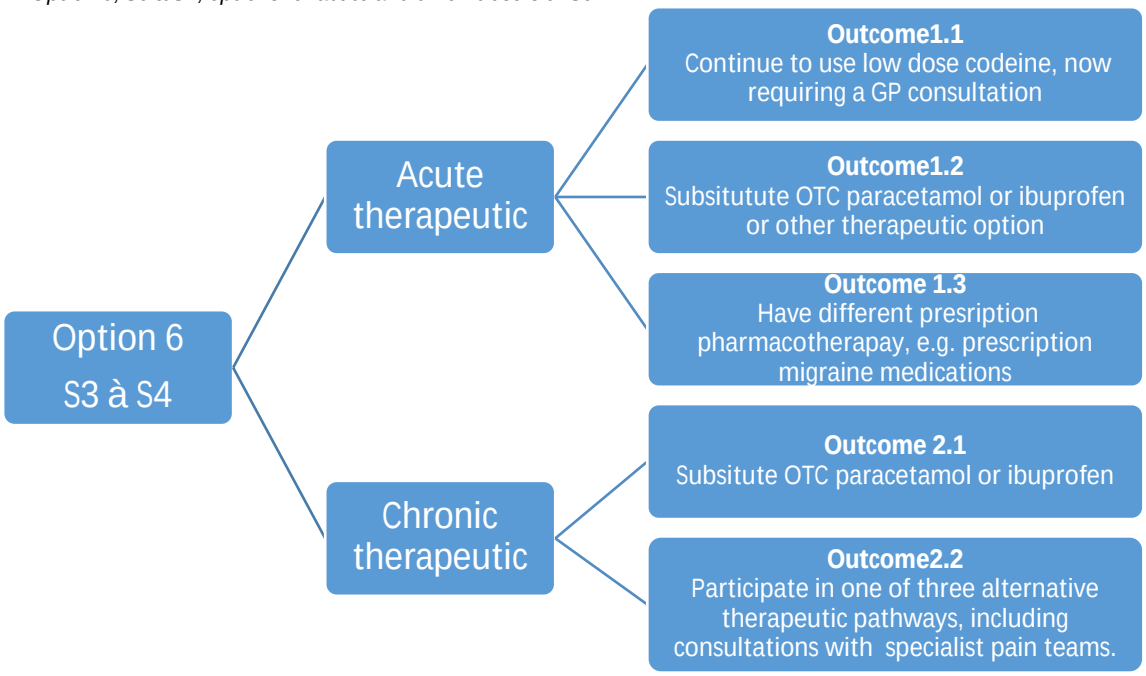
Input uncertainty

There is a paucity of data in relation to many of the inputs needed for this model, particularly in relation to the projected health benefits. The main drivers of input uncertainty related to the benefits in this model are:

- the proportion of consumers that could potentially benefit from changing their pathway;
- the proportion of consumers who will change their pathway in an optimal way;
- the additional health benefits that will be achieved if consumers with the potential to benefit, in fact change their pathway and receive improved treatment; and
- the time period that the benefits are maintained without the need for additional investments in treatment and therapy.

For a discussion of these inputs, as well as the methods that were used to resolve the paucity of data, please see Annex E. The broad options for acute and chronic users of S3 under option 6 are illustrated in Figure 1. Acute users are the only group who are expected to have some users who continue to use low dose codeine medicines at the same rate over the ten years of the model (Outcome 1.1). This assumption is based on discussions with stakeholders, some of whom indicated that it was unlikely that GPs would continue to prescribe low dose codeine medicines for chronic users and instead prescribe higher dose codeine or, more likely, a range of other therapeutic options, including those that arise from diagnoses that would not have been made had the customer continue do use OTC low dose codeine medicines (Outcome 2.2).

Figure 1. Option 6, S3 à S4, options for acute and chronic users of S3



As a general principle, the economic model sought to take conservative approaches to the estimation of health gains, for two reasons.

The first reason for taking a conservative approach was that the health gains arising from the improved therapeutic pathways taken by patients who would otherwise be chronic users of low dose codeine medicines were the primary driver of benefits in the model but also the most contested benefit. There was wide disagreement across the range of stakeholders as to the proportion of current chronic or acute users who would benefit from using different therapeutic pathways, and the extent of this benefit. Stakeholders who were supportive of the up-scheduling highlighted the benefits in terms of patients who would have an improved diagnosis of chronic or acute pain and also a shift to high dose codeine to reduce the risks related to paracetamol and/or ibuprofen use. These stakeholders also referred to the evidence from the Cochrane[22] systematic reviews regarding the evidence of limited effectiveness of low doses of codeine compared to paracetamol and/or ibuprofen alone. However, no stakeholder provided supporting evidence or data, other than the Cochrane reviews, and instead gave specific examples. Stakeholders in favour gave specific examples of patients who was treated by anti-migraine medications or saw their GP and then was referred for non-pharmacotherapy options (hip replacement, weight management clinic). Stakeholders who were not

[22] Cochrane reviews are systematic reviews of primary research in human health care and health policy, and are internationally recognised as the highest standard in evidence-based health care resources. See <www.cochrane.org/whjat-is-cochrane-evidence>. Relevant reviews are: Derry S, Moore RA, McQuay HJ. Single dose oral codeine, as a single agent, for acute postoperative pain in adults. Cochrane Database of Systematic Reviews 2010, Issue 4. Art. No.: CD008099. DOI: 10.1002/14651858.CD008099.pub2. Toms L, McQuay HJ, Derry S, Moore RA. Single dose oral paracetamol (acetaminophen) for postoperative pain in adults. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD004602. DOI: 10.1002/14651858.CD004602.pub2. Derry CJ, Derry S, Moore RA, McQuay HJ. Single dose oral ibuprofen for acute postoperative pain in adults. Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD001548. DOI: 10.1002/14651858.CD001548.pub2. Toms L, Derry S, Moore RA, McQuay HJ. Single dose oral paracetamol (acetaminophen) with codeine for postoperative pain in adults. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD001547. DOI: 10.1002/14651858.CD001547.pub2. Derry S, Karlin SM, Moore RA. Single dose oral ibuprofen plus codeine for acute postoperative pain in adults. Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD010107. DOI: 10.1002/14651858.CD010107.pub3. Derry CJ, Derry S, Moore RA. Single dose oral ibuprofen plus paracetamol (acetaminophen) for acute postoperative pain. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD010210. DOI: 10.1002/14651858.CD010210.pub2.

supportive of the up-scheduling gave examples of patients who could not tolerate ibuprofen and would now have no pharmacotherapy options available to them.

The second reason for taking a conservative approach was that the protocol[23] to be applied to the valuation of a statistical life year is the use of an unconstrained willingness to pay $182,000. This statistical life year is intended to be a year at full health and therefore is also the value of a Quality Adjusted Life Year (QALY). The unconstrained willingness to pay approach is the preferred option under this protocol; however, it results in a much higher value being placed on a QALY compared to that used in health economics and health technology assessment in Australia and internationally.[24]

Avoided deaths were an additional benefit. It was not possible to estimate deaths that could be prevented as a consequence of Option 6, partly because the deaths attributable specifically to low dose codeine could not be estimated. When deaths involving low dose codeine medicine abuse occurred, it was likely that there were multiple influencing factors and changed access to low dose codeine would not necessarily prevent these deaths.[25] The base case assumed five deaths a year would be prevented. Financial saving to patients due to less expenditure on low dose codeine medicines in options 4 and 6 was also included as a benefit.

This approach of taking a conservative estimate of the benefit generates confidence that the true net benefit is unlikely to be lower than that generated by the model. However, the base case of this model will be more likely to underestimate the true net benefit compared to other approaches that use a larger QALY gain for some patients. In the context of this decision, where only the up-scheduling of S2 and S3 low dose codeine medicines to S4 results in health benefits, this approach will not impact on the ranking of options. Given that the decision rule is to prefer the option with the highest net benefit, and options 4 and 6, which are not mutually exclusive, are the only options that result in a net benefit (from the economic model), then having strong confidence that the net benefit is greater than zero is a more appropriate strategy than having a base case net benefit which might be closer to the true net benefit but includes substantive uncertainty. In simple terms, the lower net benefit results in the same ranking of options, but there is less controversy in the assumptions underlying the net benefit.

Systematic uncertainty

Systematic uncertainty can lead to the wrong model structure being adopted and the results might be incorrect (biased), even if all the inputs are clearly correct. The KPMG model was designed to reduce the systematic bias that is inherent in some existing economic models on this issue. The main method to reduce systematic bias was to use five groups of consumers rather than base the model entirely on the 'average' consumer. Refer to Annex E for a discussion of how this reduction in systematic bias was achieved, despite the uncertainty in the inputs.

[23] Office of Best Practice Regulation, 'Best Practice Regulation Guidance Note: Value of statistical life', dated December 2014.
[24] The Pharmaceutical Benefits Advisory Committee does not declare its valuation of A QALY but it is likely to be in the order of $50,000 per QALY. For a discussion of the theory and practice of choice of valuation of a QALY and the use of a shadow price in cost benefit analysis, see Brita A.K. Pekarsky, *The new drug reimbursement game; A regulator's guide to playing and winning*, Springer, 2015.
[25] Amanda Roxburgh, Wayne D Hall, Lucinda Burns, Jennifer Pilgrim, Eva Saar, Suzanne Nielsen and Louisa Degenhardt. 'Trends and characteristics of accidental and intentional codeine overdose deaths in Australia', *Medical Journal of Australia,* 2015, Volume 203, Issue 7, viewed 6 September 2016, < https://www.mja.com.au/journal/2015/203/7/trends-and-characteristics-accidental-and-intentional-codeine-overdose-deaths>.

2.4 Conclusion

As discussed, although annexes C and D present the calculation of the regulatory cost structured along the specified six options for the purpose of inclusion in the RIS, there is a logical grouping of options. Essentially, modification of the regulatory control mechanisms for both S2 and S3 codeine medicines is required simultaneously, otherwise the desired outcomes would largely be negated by consumers shifting from either S2 to S3 (or vice versa) if a single regulatory option was enacted. Regulatory costs projected over ten years are summed (without discounting) and then summarised and reported as an average annual impact (total divided by ten). In contrast, economic costs for a cost-benefit analysis have their impact over the life of the proposed regulation (set at 10 years in this case) monetised and discounted at 7% per annum to obtain present value of the ten years of costs. Noting these differences in calculation methods, Table 3 sums the results of the regulatory costs (the undiscounted ten years summed) and economic modelling (ten years discounted to obtain a predicted net benefit). As discussed in further detail throughout the annexes, only the implementation of Scenario 4 results in a net benefit to society

The economic benefits include the gain in quality of life for additional people who improve treatment, deaths prevented and net financial savings due to the reduction in expenditure on low dose codeine medicines. The economic costs include the additional costs to consumers, MPS and PBS of additional medications, GP consultations and specialist consultations. The gains in quality of life (measured as QALYs) and deaths prevented are monetised at the rates recommended by the OBPR.

Table 3. Summary costs and benefits for regulatory scenarios over the period 2017-26 ($ million)

Element	Scenario 2		Scenario 3		Scenario 4	
	Option 2	*Option 5*	*Option 3*	*Option 5*	*Option 4*	*Option 6*
Regulatory costs (total over ten years (2017-26) not discounted)	*($0.50)*	*($1.30)*	*($101.40)*	*($1.30)*	*($102.40)*	*($22.10)*
Economic costs (PV 2017-26 at 7% discount $M)	*($20.70)*	*($409.87)*	*($14.49)*	*($409.87)*	*($56.03)*	*($209.87)*
Economic benefits (PV 2017-26 at 7% discount $M)	*0*	*0*	*0*	*0*	*$243.95*	*$5,353.17*
Net benefit (option basis) ($M)	*($21.20)*	*($411.17)*	*($115.89)*	*($411.17)*	*$85.52*	*$5,121.20*
Net benefit (scenario basis) ($M)	*($432.37)*		*($527.06)*		*$5,206.72*	

Note: the regulatory costs are undiscounted and the economic costs discounted, as is consistent with OBPR guidelines.
Source: KPMG

3 Annexes

A. Acronyms and Abbreviations

B. Consultation Schedule (external to Department of Health)

C. Impact Analysis for the Regulation Impact Statement

D. Regulatory Costing Section of the Regulation Impact Statement Economic Model

E. Interview Questionnaire for Sponsors

Annex A – Acronyms and Abbreviations

ABS	Australian Bureau of Statistics
ACE	Annual Charge Exemption (Scheme)
ACMS	Advisory Committee on Medicines Scheduling
AMA	Australian Medical Association
ARTG	Australian Register of Therapeutic Goods
ASMI	Australian Self Medication Industry
BAU	Business-as-usual
CMI	Consumer Medicines Information
DoH	Department of Health
GMP	Good Manufacturing Practice
GP	General Practitioner
GSK	GlaxoSmithKline
MBS	Medicare Benefits Schedule
NDPSC	National Drugs and Poison's Committee
OBPR	Office of Best Practice Regulation
OTC	Over-the-counter
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PGA	Pharmaceutical Guild of Australia
PI	Product Information
PSA	Pharmaceutical Society of Australia
QALY	Quality Adjusted Life Year
RASML	Required Advisory Statements for Medicine Labels
RBM	Regulatory Burden Measure
RIS	Regulation Impact Statement
SUSMP	*Standard for the Uniform Scheduling of Medicines and Poisons* (legally known as 'the Poisons Standard')
TGA	Therapeutic Goods Administration

Annex B – Consultation Schedule (external to Department of Health)

Date	Organisation	Stakeholder type	Stakeholder attendee role
15-Aug-16	Sanofi-Aventis Australia Pty Ltd	Product sponsor	Regulatory affairs
18-Aug-16	Australian Medical Association	Peak body	Board Member (and GP)
18-Aug-16	Soul Pattinson Manufacturing Pty Ltd	Product sponsor	Operations
19-Aug-16	GlaxoSmithKline Consumer Healthcare Pty Ltd	Product sponsor	Regulatory affairs
22-Aug-16	Sandoz Pty Ltd	Product sponsor	Regulatory affairs
22-Aug-16	Pharmaceutical Society of Australia	Peak body	Policy and regulatory affairs
24-Aug-16	Australian Self Medication Industry	Peak body	Regulatory affairs
25-Aug-16	Johnson & Johnson Pacific	Product sponsor	Regulatory affairs
13-Sep-16	Pharmacy Guild of Australia	Peak body	Regulatory affairs

Annex C – Impact Analysis

Overview

There are assumptions and limitations underpinning the regulatory impact analysis and the conclusions of the analysis should be regarded as indicative rather than as definitive.

Industry compliance costs have been outlined below and quantified wherever possible. TGA has made assumptions based on general information, ARTG data on existing products, stakeholder feedback, and data provided by the broader Department of Health, specifically the divisions of Medical (MBS) and Pharmaceutical benefits (PBS).

In accordance with OBPR requirements, the costs below have been costed over a 10 year period and presented as an average annual impact.

Table C1. Summary of Regulatory Burden and Cost Offset Estimates for all options (zeroes not shown)

Average annual regulatory costs (from business as usual) ($million)				
Change in costs ($ million)	Business	Community Organisations	Individuals	Total change in cost
Option 1 (status quo)				
Mandatory adoption				
Option 2 (S2 reduced pack size and new label warning)	$0.05			$0.05
Option 3 (S2 to S3, reduced pack size and new warning label)	$6.95		$3.19	$10.14
Option 4 (S2 to S4)	$2.53		$7.71	$10.24
Option 5 (S3 reduced pack size and new label warning)	$0.13			$0.13
Option 6 (S3 to S4)	$0.24		$1.97	$2.21

Option 1 – Status quo

Overview

Option 1 proposes that no changes to the current scheduling of codeine would occur, that a change in pack size would not be enforced and that the inclusion of an additional advisory statement to the label that codeine can cause addition would remain voluntary. The current inconsistencies in the TGA Ingredients Table would remain and these non-harmonised medicine ingredient names would continue to be used in Australia. The health problems associated with this abuse and misuse of codeine would continue (as outlined in Section 2 of the RIS – The problem). Under Option 1 there are no direct compliance costs for industry. However, to establish a baseline, TGA analysed the information it holds on medicine label and product information changes (see Regulatory Costing section in the RIS).

Option 2 – S2 reduced pack size and new label warning

Overview

Under Option 2 the current Schedule 2 entry for codeine in cough and cold medicine preparations would be amended to reduce the pack size to not more than 3 days' supply and include a label warning that codeine can cause addiction.

This option would affect 46[26] ARTG medicine entries (entirely OTC) across 15 sponsors.

Impact on the medicines industry

Annex D outlines the expected costs to industry for Option 2. Current sponsors of S2 products with codeine as the active ingredient would be required to update their labels to reflect the reduced pack size as well as include a new advisory statement that codeine can cause addiction (less those that already contain this advisory statement – currently voluntary). Current sponsors who do not already have a 3 day pack in their production portfolio would need to implement new manufacturing arrangements. All sponsors would need to complete the required documentation to effect the required change to their ARTG listings.

Impact on consumers and healthcare professionals

There is no projected impact on healthcare professionals. Due to the reduction in pack size consumers are expected to spend more to maintain current codeine use. There are no projected gain in health outcomes as there is not expected to be any change in treatment of therapy for those consumers currently abusing low dose codeine medicines.

Option 3 – S2 to S3, reduced pack size and new warning label

Overview

Under Option 3 the current Schedule 2 entries for codeine in cough and cold medicine preparations would be up-scheduled to Schedule 3, and the pack size would be reduced to not more than 3 days' supply and include a label warning that codeine can cause addiction.

This option would affect 46[27] ARTG medicine entries (entirely OTC) across 15 sponsors.

Impact on the medicines industry

Annex D outlines the expected costs to industry for Option 3. Current sponsors of S2 products with codeine as the active ingredient would be required to update their labels to reflect the change from S2 to S3, the reduced pack size as well as include a new advisory statement that codeine can cause addiction (less those that already contain this advisory statement – currently voluntary). Current sponsors who do not already have a 3 day pack in their production portfolio would need to implement new manufacturing arrangements and generate a new PI for the S3 medicine. All sponsors would need to complete the required documentation to effect the required change to their ARTG listings.

[26] KPMG has assessed that there will be no rationalisation of ARTG entries if this option is implemented, so all existing entries (46) need to be updated on the ARTG.

[27] The number of ARTG entries under Option 3 is the same as under Option 2. Although some product portfolio rationalisation is likely to occur (50% of products) there are, generally, multiple medicine units (e.g. different pack sizes) per ARTG entry (a planning figure of 2.5 medicines per ARTG entry for OTC medicines has been used). On this basis, KPMG has assumed that no current sponsors will allow existing ARTG listings to lapse if this option is implemented.

Impact on consumers and healthcare professionals

Annex D outlines the expected costs to healthcare professionals for Option 3. The change from S2 to S3 would require customers to speak to a pharmacist prior to making a purchase of codeine-based cough and cold products. Due to the reduction in pack size consumers are expected to spend more to maintain current codeine use. There is no projected gain in health outcomes as there is not expected to be any change in treatment of therapy for those consumers currently abusing low dose codeine medicines.

Option 4 – S2 to S4

Overview

Under Option 4 – The interim decision, current Schedule 2 entries for codeine would be up-scheduled to Schedule 4 and current Schedule 4 and 8 entries for the Poisons Standard would be amended.

This option would affect 46 ARTG medicine entries (entirely OTC) across 15 sponsors.

Impact on the medicines industry

Annex D outlines the expected costs to industry for Option 4. Current sponsors of S2 products with codeine as the active ingredient would be required to update their labels to reflect the change from S2 to S4. All sponsors would need to complete the required documentation to effect the required change to their ARTG listings.

Impact on consumers and healthcare professionals

Annex D outlines the expected costs to consumers and healthcare professionals for Option 4. The change from S2 to S4 would require patients to visit a doctor to obtain a prescription for any product containing codeine. Some of the consultations will be additional; they would otherwise not have occurred. Others would otherwise have occurred; in this case this regulatory change would result in a slight increase in the length of the consultations for doctors to prepare the script. The requirement to see a doctor might generate health gains compared to the existing situation by driving changes in treatment and therapy. However in the case of S2 these health gains are expected to be small and were not quantified in the economic model. There is also projected to be a net reduction in out of pocket expenses (financial benefit - treated as an economic benefit) for the consumer as a consequence of consumers substituting the S2 medicine with another OTC medicine (paracetamol and/or ibuprofen), which is expected to be cheaper. This substitution occurs because although consumers prefer (due to brand loyalty and/or past use) the current low dose codeine S2 product to substitute products, the majority of current consumers are expected to prefer purchasing the ongoing OTC medicines rather than visiting their GP for a prescription for the previous S2 (now S4) medicine. It is assumed that the pharmacological effects of low dose codeine products and substitute products are broadly comparable from the consumer perspective.

Impact on the government

Increased visits to GPs will result in increased costs to MBS, however patients are also expected to incorporate obtaining a prescription with other visits that would otherwise occur.

Option 5 – S3 reduced pack size and new label warning

Overview

Under Option 5 the current Schedule 3 entry for codeine products would be amended to reduce the pack size to not more than 3 days' supply and include a label warning that codeine can cause addition.

This option would affect 168 ARTG medicine entries (entirely OTC) across 22 sponsors.

Impact on the medicines industry

Annex D outlines the expected costs to industry for Option 4. Current sponsors of S3 products with codeine as the active ingredient would be required to update their labels to reflect the reduced pack size as well as include a new advisory statement that codeine can cause addiction (less those that already contain this advisory statement – currently voluntary). Current sponsors who do not already have a 3-day pack in their production portfolio would need to implement new manufacturing arrangements. All sponsors would need to complete the required documentation to effect the required change to their ARTG listings.

Impact on consumers and healthcare professionals

There is not projected to be any impact on healthcare professionals. Due to the reduction in pack size consumers are expected to spend more to maintain current codeine use. There is not projected to be any gain in health outcomes as there is not expected to be any change in treatment or therapy for those consumers currently using low dose codeine medicines when other therapies might be more effective or as effective but with less side effects.

Option 6 – S3 to S4

Overview

Under Option 6 – Current Schedule 3 entries for codeine would be up-scheduled to Schedule 4 and current Schedule 4 and 8 entries for the Poisons Standard would be amended.

This option would affect 168 ARTG medicine entries (entirely OTC) across 22 sponsors.

Impact on the medicines industry

Annex D outlines the expected costs to industry for Option 6. Current sponsors of S3 products with codeine as the active ingredient would be required to update their labels to reflect the change from S3 to S4. All sponsors would need to complete the required documentation to effect the required change to their ARTG listings.

Impact on consumers and healthcare professionals

Annex D outlines the expected costs to consumers and healthcare professionals for Option 6. The change from S3 to S4 would require patients to visit a doctor to obtain a prescription for any product containing codeine. Some of these GP consultations will be additional; they would not otherwise have occurred. Some of the GP visits would have occurred anyway, and the impact of the regulatory change would be a slight increase in the time of that consultations for doctors to prepare the script. The requirement to see a doctor would likely generate health gains (health benefit) compared to the existing situation by driving changes in alternative treatment and therapy, providing better health outcomes for many patients. There is also projected to be a net reduction in out of pocket expenses (financial benefit - treated as an economic benefit) for the consumer as a consequence of consumers substituting the S3 medicine with another OTC medicine (paracetamol and/or ibuprofen), which is expected to be cheaper. This substitution occurs because although consumers prefer (due to brand loyalty and/or past use) the current low dose codeine S3 product to substitute products, the majority of current consumers are expected to prefer purchasing the ongoing OTC medicines rather than visiting their GP for a prescription for the previous S3 (now S4) medicine. It is assumed that the pharmacological effects of low dose codeine products and substitute products are broadly comparable from the consumer perspective.

Impact on the government

Increased visits to GPs will increase MBS costs, but for some patients there will be a health gain if they access cost effective therapies, including more suitable prescription medicines, specialist referrals for pain management, or other non-pharmacological treatment options.

Regulatory options combined into scenarios

This section has presented the calculation of the regulatory cost structured along the specified six options. However, there is a logical grouping of these options. Essentially, modification of the regulatory control mechanisms for both S2 and S3 codeine medicines is required simultaneously, otherwise the desired outcomes would largely be negated by consumers shifting from either S2 to S3 (or vice versa) if a single regulatory option was enacted. The table below details the regulatory cost per scenario.

Table C2. Summary table for scenarios ($ million)

Element	Scenario 2		Scenario 3		Scenario 4	
	Option 2	*Option 5*	*Option 3*	*Option 5*	*Option 4*	*Option 6*
Regulatory cost (average annual)	$0.05	$0.13	$10.14	$0.13	$10.24	$2.21
Net regulatory cost	$0.18		$10.27		$12.45	

Annex D – Regulatory Costing Section of the Regulation Impact Statement

Option 1 – Status Quo

Option 1 – No Change. The current scheduling of codeine remains appropriate.

Poisons are classified according to the schedules in which they are included in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP), which is also known as the Poisons Standard, an extract of which is provided below.

Table D1. Overview of poisons classifications

Schedule 2	Pharmacy Medicine – Substances, the safe use of which may require advice from a pharmacist and which should be available from a pharmacy or, where a pharmacy service is not available, from a licensed person.
Schedule 3	Pharmacist Only Medicine – Substances, the safe use of which requires professional advice but which should be available to the public from a pharmacist without a prescription.
Schedule 4	Prescription Only Medicine, or Prescription Animal Remedy – Substances, the use or supply of which should be by or on the order of persons permitted by State or Territory legislation to prescribe and should be available from a pharmacist on prescription.
Schedule 8	Controlled Drug – Substances which should be available for use but require restriction of manufacture, supply, distribution, possession and use to reduce abuse, misuse and physical or psychological dependence.

Source: Poisons Standard July 2015

The status quo represents the business as usual scenario and therefore has no change in regulatory impact. Nonetheless, it is useful to summarise the current regulatory requirements as set out in the Poisons Standard. A key assumption is that the formulation of the existing codeine-based products will not change as a result of any up-scheduling (that is, if S2 and S3 are up-scheduled to S4 then S4 will be amended to incorporate low dose and high dose codeine products).

Table D2. Current requirements for codeine in the Poisons Standard

Schedule	*Dosage unit*	*Maximum daily dose*	*Pack Size*	*Type*
S2 (Pharmacy Medicine)	10 mg or less[28]	60mg	6 days	Cough and cold
S3 (Pharmacist Only Medicine)	12 mg or less	100mg	5 days	Analgesics
S4 (Prescription Only Medicine)	30 mg or less	Not prescribed	Not prescribed	

[28] References to the dosage unit of codeine in this document refer to anhydrous codeine. This can be multiplied by 1.33 to convert to codeine phosphate. This is important to note because dosages set out in ARTG listings refer to concentrations of codeine phosphate, whereas dosages in the Poisons Standard refer to anhydrous codeine.

Baseline assumptions

Number of codeine products entered on the ARTG (as at August 2016)

- Table D3 (following page) details the distribution of codeine products across the S2, S3, S4 and S8 schedules.
- 73 ARTG entries for codeine phosphate products are currently at Annual Charge Exemption (ACE) status, which means they have $0 turnover and are not being actively marketed in Australia. These entries have been excluded from those shown in Table D3.
- As some ARTG entries cover more than one medicine unit (e.g. different pack sizes), a multiplier has been applied to ARTG entries for each of the following types of medicines:
    - Prescription (S4) – 2.3 medicines per ARTG entry; and
    - OTC (S2 and S3) – 2.5 medicines per ARTG entry.

    The result of applying this multiplier are detailed in the respective 'adjusted' columns in Table D3.
- The ARTG data indicates the majority of products with codeine as an active ingredient are in the S3 category. Furthermore, an analysis of sponsors with a product presence in multiple categories finds that:
    - all 15 sponsors with S2 products also have products in the S3 category;
    - of the 15 sponsors with S2 products, three also have products in the S4 and/or S8 categories;
    - of the 22 sponsors with S3 products, five also have products in the S4 and/or S8 categories; and
    - no sponsors have products across all four categories.
- For many medicines, there is more than one label associated with a product. For example, a medicine in a blister pack is assumed to be associated with two labels (the backing of the blister pack and the outside carton). Based on an analysis of ARTG entries, a multiplier is applied to the number of medicine products to estimate the number of associated labels:
    - Prescription – 1.89 labels per medicine product; and
    - OTC – 1.85 labels per medicine product.

Table D3. ARTG data (actual and adjusted) for codeine phosphate entries (note not all columns will sum due to rounding)

Sponsor	S2	S2 (adjusted)	S3	S3 (adjusted)	S4	S4 (adjusted)	S8	#ARTG listings
Alphapharm Pty Ltd	1	2.5	5	12.5	1	2.3		7
Amneal Pharma Australia Pty Ltd			3	7.5				3
Apotex Pty Ltd	9	22.5	30	75				39
Arrow Pharma Pty Ltd	2	5	7	17.5			1	10
Aspen Pharma Pty Ltd			14	35	4	9.2	1	19
Aspen Pharmacare Australia Pty Ltd					1	2.3		1
Aurobindo Pharma Australia Pty Ltd			4	10				4
Bayer Australia Ltd	2	5	1	2.5				3
Biotech Pharmaceuticals Pty Ltd	1	2.5	3	7.5			1	5
Care Pharmaceuticals Pty Ltd			2	5				2
Cipla Australia Pty Ltd	2	5	12	30				14
Generic Health Pty Ltd	2	5	7	17.5				9
GlaxoSmithKline Consumer Healthcare Australia Pty Ltd	2	5	7	17.5				9
Johnson & Johnson Pacific Pty Ltd	5	12.5	1	2.5				6
Orion Laboratories Pty Ltd T/A Perrigo Australia	1	2.5	5	12.5				6
Pharmacare Laboratories Pty Ltd	5	12.5	12	30				17
Pharmacor Pty Ltd			6	15				6
Phebra Pty Ltd							1	1
Reckitt Benckiser Pty Ltd			3	7.5				3
Sandoz Pty Ltd	2	5	3	7.5				5
Sanofi-Aventis Australia Pty Ltd			8	20	4	9.2		12
Sigma Company Limited	4	10	11	27.5				15
Soul Pattinson Manufacturing Pty Ltd	4	10	10	25				14
Symbion Pty Ltd	4	10	14	35				18
Total ARTG entries	46		168		10		4	228
Total products (adjusted)		115		420		23	4	562
% of ARTG entries	20%		74%		4%		2%	
o. of sponsors (n=24)	15		22		4		4	
% of sponsors	63%		92%		17%		17%	

Source: ARTG extract 1 August 2016

Business-as-usual (BAU) variations to existing medicines

- There is high variability between how often sponsors change an aspect of their product (e.g. update label, PI etc.). Some sponsors vary their ARTG entry regularly (even more than once a year), whereas other

sponsors will not vary their products for several years. The majority of ARTG variation applications are for prescription products.

- A 2014 survey of industry revealed that companies will update their labels as part of BAU, on average, every 3 years.[29] Therefore, with an assumed 18 month implementation timeframe which also aligns with the RASML implementation cycle, it is assumed that should there be a change to the scheduling of codeine resulting in changes packaging at least half of the affected sponsors will have the opportunity to roll the labelling changes into already scheduled updates.

- Consultations with sponsors and manufacturers have identified the cost of implementing a minor labelling change ranges between $2,000 and $6,500 per product. This incorporates the costs of artwork and internal processes to quality assure and implement the change on the production line. For the purposes of the costing, drawing from the TGA RIS on General Requirements for Labels for Medicines, the average cost to implement a labelling change (per OTC product) is estimated at $4,171.[30] We have assumed that this incorporates the aspects of multiple labels per product.

- These minor label change costs include pre-production costs (such as label redesign and approval, artwork and proofing) and production costs (new printing plates for conventional printing processes, changes to the digital printing process). The costs also cover any potential changes to the PI/CMI.

- A minor label change is defined as a small change to the phrasing of text on a label that does not necessitate a change to, or rearrangement of, other label graphics.

Costs associated with transition

General costs

- The compliance costs for stock recalls has not been estimated as the assumed implementation timeframe should provide adequate time for turn-over of stock across the supply chain.

- A default FTE wage rate of $37.40 per hour and an on-cost multiplier of 1.75 has been adopted to account for non-wage labour on-costs as per OBPR guidance.[31] This results in a scaled up rate of $65.45 per hour.

- An individual's time has been costed at $29.00 per hour as per OBPR guidance. A pharmacists wage has been estimated at $35.90 per hour[32] (therefore $62.83 per hour when the on-cost multiplier of 1.75 is applied). A doctor's wage has been estimated at $97 per hour[33] (therefore $169.75 per hour when the on-cost multiplier of 1.75 is applied).

- The amendment of current Schedule 4 and 8 entries in the Poisons Standard will have internal to Government impact only (legislative change) but will not have any impact from a regulatory cost perspective on businesses, community organisations or individuals.

Implementation considerations

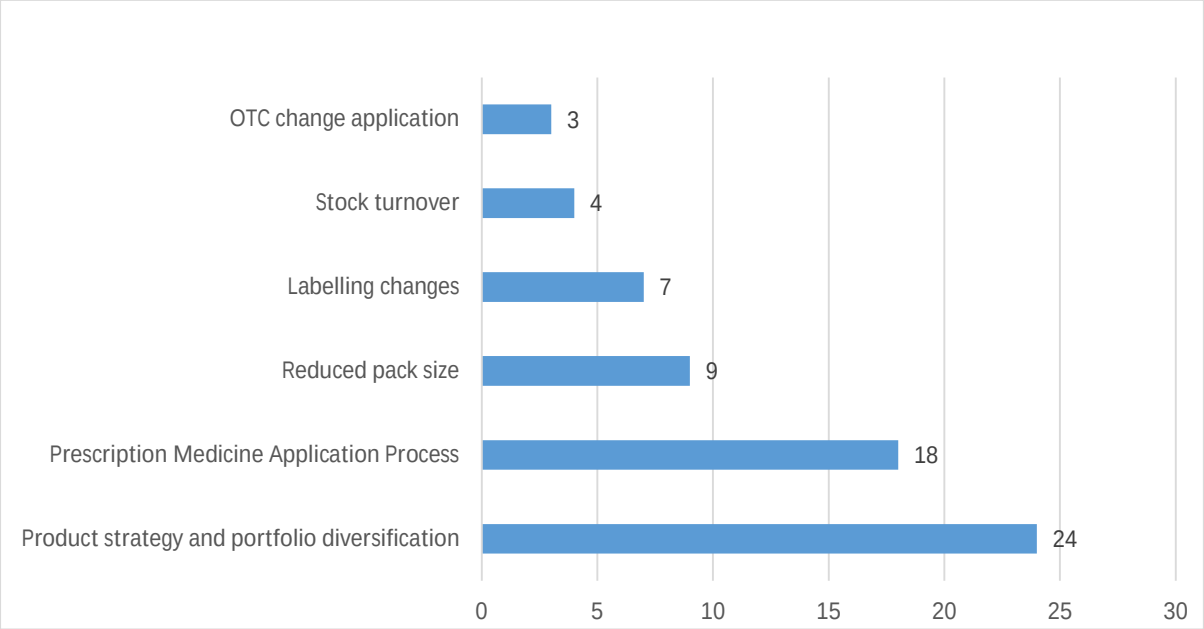
- The implementation timeframe for any decision that impacts on labelling, pack size or up-scheduling has the potential to increase regulatory costs. The cost estimates outlined in the reminder of this section assume an implementation timeframe of 18 months. However, it is important to note that a change in timeframe would impact the estimated costs. For example, a short implementation timeframe may mean

[29] TGA, Regulation Impact Statement: General Requirements for labels for medicines, https://ris.govspace.gov.au/files/2016/08/General-requirements-for-labels-for-medicines-RIS.pdf, July 2016.
[30] TGA, Regulation Impact Statement: General Requirements for labels for medicines, https://ris.govspace.gov.au/files/2016/08/General-requirements-for-labels-for-medicines-RIS.pdf, July 2016, p.32.
[31] Office of Best Practice Regulation, 'Guidance Note: Regulatory Burden Measurement Framework', dated February 2016, p.18
[32] www.open.edu.au/careers/healthcare-medical-pharmaceuticals/pharmacists, Based on average salary of $70,000.
[33] http://www.payscale.com/research/AU/Job=General_Practitioner/Salary (click on 'Show hourly rate' link).

that sponsors cannot make the necessary changes in time (or obtain the necessary approvals), which, in an extreme case, could require products to be removed from the shelves, or may mean that revised products cannot come to market by the time existing products are withdrawn. A longer implementation timeframe may enable a greater proportion of compliance activities (such as a labelling update) to be rolled into other scheduled changes thereby reducing the compliance burden, while also enabling sponsors who are adversely impacted to reposition themselves to adjacent markets.

- There are several categories of changes which are impacted by implementation timeframes:
  - time to implement labelling changes (compliance);
  - time to reduce pack sizes (compliance);
  - TGA approval timeframes (approvals);
  - stock recall (compliance); and
  - product strategy and portfolio diversification (business).
- The figure below illustrates indicative implementation timeframes for each of these categories.

Figure D1. Implementation timeframe (months)



- Labelling changes. Consultation has identified that the implementation of labelling changes will take between 6-8 months. The component steps involve the development of artwork, internal approvals, regulatory approvals and implementation. This falls within the 18 month transition window provided by the TGA for recent RASML updates.[34]
- Stock turnover. Consultation with manufacturers has identified stock turnover timeframes of between 6 weeks and 4 months. Different parts of the supply chain will hold different levels of stock. Codeine based products have a shelf life of 24 months, although this is not anticipated to be a constraint, given the level of turnover.

[34] www.tga.gov.au/publication/required-advisory-statements-medicine-labels-rasml

- Product strategy and diversification. In response to a decision, manufacturers and retailers who currently have a market share of codeine-based products will have a planning and investment timeline to reposition their product portfolio. Some sponsors may require registration of new ARTG listings that have a 12-month lead time. Following this, manufacturers may require up to an additional 6-12 months to assemble the production line and source materials. This will vary depending on whether production is local (increased flexibility) or overseas (less flexibility). An 18 month timeframe would be ideal to allow impacted manufacturers (and to a lesser degree sponsors) to reposition, and therefore maintain, their market share.

- Reduce pack size. Manufacturers who do not have existing production lines that can accommodate a reduced outer pack, or inner blister pack, will need to make changes to their production line. Discussions with manufacturers have indicated this would take 9 months from procurement to implementation. In the event that this is not commercially viable, sponsors could seek an alternative manufacturing site. Although in the event that the alternative site does not have GMP certification this may be a lengthier process.

- OTC C1/C2 level applications. The anticipated timeframes for approval of C1/C2 change applications are approximately three months.

- Applications to register a prescription medicine (S4). TGA has advised that the up-scheduling of S2 and S3 medicines to S4 would not require the registration of new prescription medicine as codeine is not a new ('novel') chemical entity. In the case of S3 medicines up-scheduled to S4, the processes for minor variations to registered prescription medicines would be followed. This would entail the submission of a Category 3 application (with an associated processing timeframe of 45 working days). Specifically a '9D(3) Category application to vary an ARTG entry' would be used' with the existing PI and CMI submitted with the application. For S2 medicines up-scheduled to S4 a new PI and CMI would need to be produced (though these could leverage existing PIs and CMIs for medicines with codeine as an active ingredient). This would be considered a Category J variation ('Changes to product information requiring the evaluation of data'), with a maximum processing timeframe of 255 working days (Category 1 application). TGA has advised, however, that as this application does not relate to a new chemical entity or a new indication(s) that the actual processing time (and associated data requirements) is likely to be considerable less than this.

Table D4. Summary table of implementation timeframes

Option	Minimum implementation timeframes	Desired timeframes by industry
2 - Add warning label and reduce pack size on S2 products	9 months Constraint: packaging changes (overseas)	12 months
3 - Up-schedule S2 to S3, and add warning label and reduce pack size	9 months Constraint: packaging changes (overseas)	12 to 18 months Driver: product strategy and repositioning
4 - Up-schedule S2 products to S4	12 months Constraint: regulatory approval	18-24 months Driver: product strategy and repositioning
5 - Add warning label and reduce pack size on S3 products	9 months Constraint: packaging changes	12 months
6 - Up-schedule S3 to S4	12 months Constraint: regulatory approval	18-24 months Driver: product strategy and repositioning

Option 2 – Reduce pack size of S2 products and add warning label

Option 2 – The current Schedule 2 entry for codeine in cough and cold medicine preparations be amended to reduce the pack size to not more than 3 days' supply and include a label warning that codeine can cause addition.

This option would affect 46 ARTG medicine entries (entirely OTC) across 15 sponsors. The same baseline assumption has been used as outlined under Option 1.

Table D5. Regulatory impacts of Option 2

Option 2	Current	Proposed change	Impact
Distribution model	Schedule 2	Schedule 2	Nil
Label	Advisory statement for addiction not required	New advisory statement	Update label
Pack Size	6 days' supply	3 days' supply	Reduce pack size
Dosage	10 mg per dosage unit 60 mg per day	No formulation change	Nil
ARTG, CI and PI	Registered	Update ARTG entry	Updated ARTG entry

Regulatory cost assumptions

- Several sponsors have recently implemented advisory warnings against codeine addiction as part of industry initiatives, however some additional labelling changes would likely be required as a result of the reduced pack size. Based on the baseline assumptions, 115 OTC medicine products[35] currently marketed in Australia are likely to be affected.
- As noted in the BAU costs, it is estimated that half of the product label updates can be rolled into already planned updates reducing the per product cost by 50% for that segment, therefore the carry forward figure is 58 labels will need to be updated in addition to BAU labelling activities.
- Based on BAU costs outlined in Option 1, the label pre-production and production costs are estimated to be $0.24m.
- Consultations have identified that approximately 50% of codeine sponsors already produce 3 day packs or have a production line that could accommodate this change across their impacted product portfolio, provided the implementation timeframe is sufficient. These sponsors will not need to implement new manufacturing arrangements for either the outer carton (apart from the printing) or inner blister pack. It is estimated that approximately 8 sponsors will incur costs to change their pack size.
- For the impacted sponsors, it is estimated from industry consultations that up-front costs to implement the required packaging changes is $30,000 per sponsor. This could include retooling to modify blister pack lengths or reduce packaging depth. It should be noted, however, that these costs can vary depending on the location of the manufacturing facility being used. For example, changes can be implemented more quickly in domestic facilities but are more expensive, whereas changes in overseas facilities can be implemented at lower cost, but are subject to longer delays due to competing priorities.
- Based on BAU costs outlined in Option 1, and the factors listed above, packaging transition costs are estimated to be $0.24m.

[35] Number of existing S2 entries x multiplier to account for ARTG entries covering for more than one medicine unit.

- The required changes fall under a C1 application level, based on a review of the applicable forms, and consultation with sponsors, it is estimated that 4 hours will be required to prepare and submit the relevant form. The cost of completing the required form is estimated to be $0.012m.
- Note that the estimated regulatory compliance costs do not account for the application fees sponsors would have to pay (roughly $1,500 per listing update) as direct financial costs are outside the scope of the Regulatory Burden Measurement (RBM) framework.[36] Similar exclusions also apply to the other 4 options.

When averaged over ten years the total regulatory cost for Option 2 is $0.05m per annum. The tables below summarise the regulatory costing.

Note that the following cell colour coding is used for the tables showing regulatory cost calculations.

Legend for cells				
Calculation	Check Cell	*Explanatory*	Linked Cell	Note
Output	Warning text			

Table D6. Regulatory cost calculation for Option 2

Inputs	
Scaled up hourly wage rate	$65.45
No. of Schedule 2 products impacted	58
No. of Schedule 2 entries impacted	46
One-off cost to implement labelling changes per OTC product	$4,171.00
Number of sponsors who do not have 3 day packs (50%)	8
One-off cost to implement pack size changes per sponsor	$30,000.00
Hours required per ARTG application (C1 level)	4.00
Outputs	**Result**
Total up-front cost to implement labelling changes	$241,918.00
Total up-front cost to implement package size changes	$240,000.00
Total one-off cost to update ARTG entries	$12,042.80
Total RBM compliance cost (over 10 years)	$493,960.80
RBM compliance cost (annualised)	$49,396.08

Table D7. RBM Table for Option 2

Average annual regulatory costs (from business as usual)				
Change in costs ($ million)	Businesses	Community organisations	Individuals	Total change in costs
Total, by sector	$0.05	$0	$0	$0.05

Benefits

- As detailed in the economic model, no health benefits will be realized by the implementation of this option. As noted earlier in the report, the only projected health benefits factored into the economic model arose from improved therapeutic pathways taken by patients who would otherwise be chronic

[36] OBPR, Regulatory Burden Measurement (RBM) guidance note, https://www.dpmc.gov.au/sites/default/files/publications/005-Regulatory-Burden-Measurement-Framework.pdf, February 2016

users of low dose codeine medicines. For this improved therapeutic pathway to be realized the key enabler was a visit to a GP, which will not occur under this option.[37]

Option 3 – Reschedule S2 to S3, reduce pack size, and add warning label

Option 3 – The current Schedule 2 entries for codeine in cough and cold medicine preparations be up-scheduled to Schedule 3, and that the pack size be reduced to not more than 3 days' supply, and include a label warning that codeine can cause addiction.

This option would affect 46 ARTG medicine entries (entirely OTC) across 15 sponsors. The same baseline assumption has been used as outlined under Option 1.

Table D8. Regulatory impacts of Option 3

Option 3	Current	Proposed change	Impact
Distribution model	Schedule 2	Schedule 3	Consumer must now speak with pharmacist
Label	Advisory statement for addiction not required	New advisory statement	Update label
Pack Size	6 days' supply (S2)	3 days' supply	Reduce pack size
Dosage	10 mg per dosage unit 60 mg per day	No formulation change	Nil
ARTG, CI and PI	Registered	Update ARTG entry	Updated ARTG entry) including new CMI and PI

Regulatory cost assumptions

- As part of industry initiatives, several sponsors have recently implemented advisory warnings against codeine addiction. However, some additional labelling changes would likely be required as a result of the reduced pack size. Based on the baseline assumptions, 115 OTC medicine products currently marketed in Australia will be affected.
- It is estimated all S2 sponsors will migrate their products to S3, but with a rationalisation of their product portfolio by 50% to reflect the reduced range which would be expected as products move behind the pharmacists' counter which faces stronger competition for space. Therefore, the carry forward total into the model is 58 medicine products. As noted in the BAU costs it is estimated that half of the product label updates can be rolled into already planned updates reducing the per product cost by 50% for that segment, therefore the carry forward figure is 29 labels will need to be updated in addition to BAU labelling activities.
- Based on BAU costs outlined in Option 1, the label pre-production and production costs are estimated to be $0.12m.
- Consultations have identified that roughly 50% of codeine sponsors already produce 3 day packs or have a production line that could accommodate this change across their impacted product portfolio (provided the implementation timeframe is sufficient). These sponsors will not need to implement new manufacturing arrangements for either the outer carton (apart from the printing) nor inner blister pack. It is estimated that approximately 8 sponsors will incur costs to change their pack size.

[37] No data was able to be sourced by KPMG that would enable the modelling of health benefits arising from smaller pack sizes or additional advisory warnings. While such changes might, conceivably, have some impact on the low dose codeine medicine use by acute therapeutic users this population grouping is not responsible for the arising health costs from codeine medicines abuse/misuse. In relation to the chronic therapeutic population group, particularly the dependent sub-group, which likely accounts for the majority of the health costs from low dose codeine abuse/misuse, in the absence of specific data to the contrary, it is assessed that they will modify their buying habits to maintain their codeine use, thereby negating any projected health benefits.

- It is estimated from industry consultations that up-front costs for the impacted sponsors to implement the required packaging changes is $30,000 per sponsor. This may include retooling to modify blister pack lengths or reduce packaging depth. It should be noted, however, that these costs can vary depending on the location of the manufacturing facility being used. For example, changes can be implemented more quickly in domestic facilities but are more expensive, whereas changes in overseas facilities can be implemented at lower cost, but are subject to longer delays due to competing priorities.

- Based on BAU costs outlined in Option 1, and the factors listed above, packaging transition costs are estimated to be $0.24m.

- The required changes fall under a C2 application level, based on a review of the applicable forms, and consultation with sponsors, it is estimated that 12 hours will be required to prepare and submit the relevant forms (including the creation of PI and CMI documentation). This estimate assumes that current S2 sponsors will adopt the efficient practice of replicating the PI documentation of a generic product already in the market. It is also possible that a core PI would be created to assist industry with an efficient migration of these products which would further reduce costs. The cost of completing the required form and provision of supporting materials is estimated to be $0.036m.

- The rescheduling of S2 products to S3 will now require individuals to speak with a pharmacist prior to making a purchase of codeine-based cough and cold products. In the absence of data it has been estimated this will consume an additional two minutes of time for both the individual and the pharmacist.

- Current sales data indicates roughly 4.4 million packets of codeine-based S2 cough and cold products are sold every year in Australia. In the absence of data to forecast the market responses to Option 3, it is estimated aggregate demand for S2 products would drop by 25% if rescheduled to S3. It is therefore estimated there will be an additional 3.3 million S3 transactions/conversations per year in response to the S2 to S3 rescheduling.

When averaged over ten years the total regulatory cost for Option 3 is $10.14m per annum. The tables below summarise the regulatory costing.

Table D9. RBM calculations for Option 3

Inputs	
Scaled up hourly wage rate	$65.45
No. of Schedule 2 products impacted	29
No. of Schedule 2 entries impacted	46
One-off cost to implement labelling changes per OTC product	$4,171.00
Number of sponsors who do not have 3 day packs (50%)	8
One-off cost to implement pack size changes per sponsor	$30,000.00
Hours required per ARTG application (C2 level)	12.00
Outputs	**Result**
Total up-front cost to implement labelling changes	$120,959.00
Total up-front cost to implement package size changes	$240,000.00
Total one-off cost to update ARTG entries	$36,128.40
Total RBM compliance cost (over 10 years)	$397,087.40
RBM compliance cost (annualised)	$39,708.74

Inputs (for consumers and pharmacists)	
Labour cost per hour (consumers)	$29.00
Scaled up labour cost per hour (pharmacists)	$62.83
Estimated additional S3 transactions per year	3,300,000
Additional time (minutes) for pharmacist to speak with consumer	2
Outputs (for consumers and pharmacists)	**Result**
Total annual compliance costs for consumers	$3,190,000.00
Total annual compliance costs for pharmacists	$6,911,300.00
RBM compliance cost (annualised)	$10,101,300.00

Table D10. RBM summary table for Option 3

Average annual regulatory costs (from business as usual)				
Change in costs ($ million)	Businesses	Community organisations	Individuals	Total change in costs
Total, by sector	$6.95	$0	$3.19	$10.14

Benefits

- As detailed in the economic model, no health benefits will be realized by the implementation of this option. As noted earlier in the report, the only projected health benefits factored into the economic model arose from improved therapeutic pathways taken by patients who would otherwise be chronic users of low dose codeine medicines. For this improved therapeutic pathway to be realized the key enabler was a visit to a GP, which will not occur under this option.

Option 4 – Reschedule S2 to prescription only (S4)

Option 4 – Up-schedule the current Schedule 2 entries for codeine to Schedule 4 and amend the current Schedule 4 and 8 entries.

This option would affect **46 ARTG medicine entries** (entirely OTC) across **15 sponsors.** The same baseline assumptions have been used as outlined under Option 1.

Table D11. Regulatory impacts of Option 4

Option 4	Current	Proposed change	Impact
Distribution model	Schedule 2	Schedule 4	Consumer must see doctor for prescription
Label	Advisory statement(s) as per RASML	Insertion of 'prescription only' medicine	Update of label
Pack Size	6 days' supply	Not prescribed	Nil
Dosage	10 mg per dosage unit 60 mg per day	No formulation change	Nil
ARTG, CI and PI	Registered OTC medicine on ARTG	Register prescription medicine on ARTG	ARGPM: category application (Type G/J) including new PI/CMI + GMP conformity assessment (if required for sponsor)

Regulatory cost assumptions

- There are no packaging or supply restrictions prescribed for S4 products.
- Up-scheduling S2 products to S4 will require sponsors to apply to register a prescription medicine. Consultations have identified significant commercial and practical barriers to migrating low dose codeine products to a prescription-only market. Further, is not clear whether there is a market for former S2 products in this scenario. For this reason, it is estimated only 15% of current S2 sponsors would seek to migrate their products to S4. It is estimated S2 sponsors will rationalise their portfolio to two products per sponsor given the challenging commercial realities of the prescription only market. As there are currently 15 sponsors of S2 products, the total number of products to be carried forward into the model is therefore 4 medicine products (15% of 15 sponsors (2 sponsors) and 2 products per sponsor) which will incur costs to update labels. It has been assumed that each product to be up-scheduled relates to a separate ARTG listing.[38]
- Based on BAU costs outlined in Option 1, the label pre-production and production costs are estimated to be $0.017m.
- The required changes fall under a major variation (Category 1 application – maximum processing time of 255 days) level but TGA have advised that as these applications do not relate to a new chemical entity or a new indication(s) then the actual processing time (and associated data requirements) is likely to be considerable less than that required for a standard Category 1 application. Based on a review of the applicable forms, it is estimated that 12 hours will be required to prepare and submit the relevant forms (including the creation of PI and CMI documentation). This estimate assumes that current S2 sponsors will adopt the efficient practice of replicating the PI documentation of a generic product already in the market. It is also possible that a core PI would be created to assist industry with an efficient migration of these products which would further reduce costs. The cost of completing the required form and provision of supporting materials is estimated to be $0.003m.

[38] In actuality, the two products for each sponsor might be able to be incorporated into a single ARTG entry but we have left this as each product up-scheduled from S2 to S4 requires a separate ARTG entry to avoid understating the regulatory burden.

- This analysis has not accounted for reformulation in response to Option 4 as consultation has indicated, due to costs and potential regulatory barriers to the redeployment of branding, there should be no reformulation.

- Registered prescription (S4) medicines have the site of manufacture of the active pharmaceutical ingredient(s) (API) recorded in the ARTG. Moving to S4 will require more detailed ARTG records for the products, with the addition of the site of manufacture of the active pharmaceutical ingredient(s). This is a minor administrative process which can be combined with any other application type (e.g. an application to amend the labels).

- For new prescription medicine, evidence of Good Manufacturing Practice (GMP) at API manufacturing site is assessed by the TGA. S2 sponsors currently self-certify they are compliant with GMP principles; subsidiary GMP requirements encompass supplier (e.g. API) qualification. The TGA can seek evidence of GMP compliance from sponsors of medicines at any time. Sponsors who already have a related S4 medicine containing codeine made at the same medicine manufacturing site are assumed to be compliant with API GMP requirements and possess all the necessary GMP evidence (it is noted that this applies to 3 of the current 15 S2 sponsors). For other products, where S2 medicines are converted to S4 medicines on the ARTG due to the up-scheduling of codeine, the TGA may seek GMP evidence. It is estimated the engagement of GMP professionals, development of documentation, and implementation of staff and managerial processes would cost $34,500 per impacted sponsor.

- Similarly for new prescription medicines, the manufacturing process and controls for the API(s) are reviewed. Any up-scheduling is a change to a currently supplied medicine: the extent of review at the time of up-scheduling is a matter of judgment. The TGA might require assurances from the sponsor that no changes have been made to the existing S2 products that would move to S4, including the drug substance manufacturing site(s). If a sponsor changes API details for these products in the future, the required documentation to demonstrate compliance will be required. As detailed previously, it is estimated that 2 sponsors will need to undertake this process. The upfront cost of demonstrating GMP compliance is estimated to be $0.069m.

- The reclassification of S2 products to S4 will require patients to visit a doctor to obtain a prescription for any product containing codeine. This will increase the compliance burden on individuals. The costs to the healthcare system, in the form of GP payments via MBS, are outside the scope of RBM as they are considered a direct financial cost and not a compliance cost. These are instead considered in the economic modelling. It is estimated that consumers will require 15 minutes (each way) to drive to their local doctor (therefore a total of 30 minutes). It is also estimated, based on consumer behaviour survey data,[39] that individuals will spend an average of 30 minutes in a waiting room before being able to see their doctor and that they will have a standard 15 minute consult. It is assumed that the patient would proceed immediately to the pharmacy to process the script and that the pharmacy is located close-by to the GP's office. It is estimated that the consumer will spend 5 minutes in the pharmacy (including wait time for the script to be processed and discussing the medicine with the pharmacist).[40] Therefore the total time to visit the GP and get the resulting script for codeine processed is 80 minutes (1.33 hours)). It is also assumed doctors spend an additional 30 seconds to process the prescription for these new visits. The time taken for the pharmacist to process the script and talk to the consumer regarding the prescription medicine is estimated to be 2 minutes (please note that no adjustment was made in relation to the

[39] www.wsmi.org/wp-content/uploads/2015/06/CONSUMER-BEHAVIOUR-FACT-BOOK_MARCH-2015.pdf

[40] This estimation of time spent by the consumer in obtaining S4 medicines from a pharmacist takes into account that many pharmacies are located adjacent to other shops and that if a wait time of greater than a couple of minutes is indicated for the processing of a script, a consumer is likely to leave the pharmacist to undertake other tasks (e.g. purchase of groceries) and then return when the script has been processed. As the expenditure of this time is no longer directly related to the obtaining of a script it has been excluded from the time calculation to determine the regulatory burden.

estimated pharmacist wage rate for whether the processing of the script is undertaken by a pharmacist's assistant rather than the pharmacist as not all pharmacies will have this business model).

- Based on the economic modelling undertaken for this RIS it is estimated this option would generate an additional average of 200,000 GP appointments per annum over the next ten years. This estimate accounts for the modelled behaviour of consumers in these scenarios (demand side), factors in supply side assumptions, and assumes no repeats due to S2 codeine medication being for cough and colds. In addition, the economic modelling shows that there are 599,000 per annum existing visits to GPs (that is, would have occurred in the absence of any regulatory change) where a script for codeine would be requested. For the latter category it is assessed that this does not increase the time taken to visit the GP by consumers (as they were undertaking a GP visit anyway) but does result in a slight incremental increase in the duration of the consultation because the GP now needs to prepare a script for codeine (it is assessed that no additional time is required by GPs compared to the average consultation for the writing of script for codeine for the additional GP appointments). The increase in the time taken by pharmacists to respond to the regulatory change is the net of the two populations (additional GP appointments plus existing GP appointments with a codeine script requested).

When averaged over ten years the total regulatory cost for Option 4 is $10.24m per annum. The tables below summarise the regulatory costing.

Table D12. RBM calculations for Option 4

Inputs (for Schedule 2 sponsors)	
Scaled up hourly wage rate	$65.45
No. of Schedule 2 sponsors impacted	2
No. of Schedule 2 products impacted	4
One-off cost to implement labelling changes per OTC product	$4,171.00
Proportion of sponsors who will need to change packs	0%
Hours required per ARTG application (Category 1 level)	12.00
Cost to demonstrate GMP compliance per Sponsor	$34,500.00
Proportion of S2 sponsors migrating their products to S4	15%
Outputs (for Schedule 2 sponsors)	**Result**
Total up-front cost to implement labelling changes	$16,684.00
Total up-front cost to implement package size changes	$0.00
Total one-off cost to register Prescription medicine	$3,141.60
Total up-front cost to demonstrate GMP compliance	$69,000.00
RBM compliance cost (over 10 years)	$88,825.60
RBM compliance cost (annualised)	$8,882.56

Inputs (for consumers and doctors) - Option 4	
Labour cost per hour (consumers)	$29.00
Scaled up labour cost per hour (doctors)	$169.75
Scaled up labour cost per hour (pharmacists)	$62.83
Additional S4 prescriptions visits to doctors per year (S2-->S4)	200,000
Existing visits to doctors where codeine script requested	599,000
Incremental time in hours to visit doctor (additional visits) and obtain script	1.33
Time in minutes for doctor to write prescription	0.5
Time in minutes for pharmacist to process script and discuss with consumer	2
Outputs (for consumers and pharmacists)	**Result**
Total annual compliance costs for consumers	$7,714,000.00
Total annual compliance costs for doctors	$847,335.42
Total annual compliance cost for pharmacists	$1,673,372.33
RBM compliance cost (annualised)	$10,234,707.75

Table D13. RBM summary table for Option 4

Average annual regulatory costs (from business as usual)				
Change in costs ($ million)	Businesses	Community organisations	Individuals	Total change in costs
Total, by sector	$2.53	$0	$7.71	$10.24

Benefits

- As detailed in the economic model, some health benefits will be realized by the implementation of this option. The requirement to see a doctor would likely generate health gains compared to the existing situation by driving changes in treatment and therapy.

Option 5 – Reduce pack size of S3 and add warning label

Option 5 – The current Schedule 3 entries for codeine (including, but not limited to codeine containing analgesics) be amended to reduce the pack size to not more than 3 days' supply and include a label warning that codeine can cause addiction.

This option would affect 168 ARTG medicine entries (entirely OTC) across 22 sponsors. The same baseline assumptions have been used as outlined under Option 1.

Table D14. Regulatory impacts of Option 5

Option 5	Current	Proposed change	Impact
Distribution model	Schedule 3	Schedule 3	Nil
Label	Advisory statement for addiction not required	New advisory statement	Update label
Pack Size	5 days' supply	3 days' supply	Reduce pack size
Dosage	12 mg per dosage unit 100 mg per day	No formulation change	Nil
ARTG, CI and PI	Registered OTC medicine on ARTG	Update ARTG OTC entry	Updated ARTG entry

Regulatory cost assumptions

- As part of industry initiatives, several sponsors have recently implemented advisory warnings against codeine addiction. However, some additional labelling changes would likely be required as a result of the reduced pack size. Based on the baseline assumptions, 420 OTC medicine products currently marketed in Australia will be affected.
- As noted in Option 2, it is estimated that half of the product label updates can be rolled into already planned updates reducing the per product cost by 50% for that segment. Therefore the carry forward figure is 210 labels will need to be updated in addition to BAU labelling activities.
- Based on BAU costs outlined in Option 1, the label pre-production and production costs are estimated to be $0.88m.
- Consultations have identified that roughly 50% of codeine sponsors already produce 3 day packs or have a production line that could accommodate this change across their product portfolio (provided the implementation timeframe is sufficient). These sponsors will not need to implement new manufacturing arrangements for either the outer carton (apart from the printing) nor inner blister pack. It is estimated that approximately 11 sponsors will incur costs to change their pack size.
- It is estimated from industry consultations that up-front costs for the impacted sponsors to implement the required packaging changes is $30,000 per sponsor. This may include retooling to modify blister pack lengths or reduce packaging depth. It should be noted, however, that these costs can vary depending on the location of the manufacturing facility being used. For example, changes can be implemented more quickly in domestic facilities but are more expensive, whereas changes in overseas facilities can be implemented at lower cost, but are subject to longer delays due to competing priorities.
- Based on BAU costs outlined in Option 1, and the factors listed above, packaging transition costs are estimated to be $0.33m.
- The required changes fall under a C1 application level, based on a review of the applicable forms, and consultation with sponsors, it is estimated that 6 hours will be required to prepare and submit the relevant form (including updates to the PI and the CMI). The cost of completing the required form is estimated to be $0.066m.

When averaged over ten years the total regulatory cost for Option 5 is $0.13m per annum. The tables below summarise the regulatory costing.

Table D15. RBM calculations for Option 5

Inputs	
Scaled up hourly wage rate	$65.45
No. of Schedule 3 products impacted	210
No. of Schedule 3 listings impacted	168
One-off cost to implement labelling changes per OTC product	$4,171.00
Number of sponsors who do not have 3 day packs (50%)	11
One-off cost to implement pack size changes per sponsor	$30,000.00
Hours required per ARTG application (C2 level)	6.00
Outputs	**Result**
Total up-front cost to implement labelling changes	$875,910.00
Total up-front cost to implement package size changes	$330,000.00
Total one-off cost to update ARTG entries	$65,973.60
Total RBM compliance cost (over 10 years)	$1,271,883.60
RBM compliance cost (annualised)	$127,188.36

Table D16. RBM summary table for Option 5

Average annual regulatory costs (from business as usual)				
Change in costs ($ million)	Businesses	Community organisations	Individuals	Total change in costs
Total, by sector	$0.13	$0	$0	$0.13

Benefits

- As detailed in the economic model, no health benefits will be realized by the implementation of this option. As noted earlier in the report, the only projected health benefits factored into the economic model arose from improved therapeutic pathways taken by patients who would otherwise be chronic users of low dose codeine medicines. For this improved therapeutic pathway to be realized the key enabler was a visit to a GP, which will not occur under this option.

Option 6 – Reschedule S3 to prescription only (S4)

Option 6 – Up-schedule the current Schedule 3 entries for codeine to Schedule 4 and amend the current Schedule 4 and 8 entries.

This option would affect 168 ARTG medicine entries (entirely OTC) across 22 sponsors. The same baseline assumptions have been used as outlined under Option 1.

Table D17. Regulatory impacts of Option 6

Option 6	Current	Proposed change	Impact
Distribution model	Schedule 3	Schedule 4	Consumer must see doctor for prescription
Label	Advisory statement(s) as per RASML	Insertion of 'prescription only' medicine	Update of label
Pack Size	5 days' supply	Not prescribed	Nil
Dosage	12 mg per dosage unit 100 mg per day	No formulation change	Nil
ARTG, CI and PI	Registered OTC on ARTG	Register prescription medicine on ARTG	ARGPM Category application (Type J) + GMP conformity assessment (if required for sponsor)

Regulatory cost assumptions

- There are no packaging or supply restrictions prescribed for S4 products.
- Up-scheduling S3 products to S4 will require sponsors to apply to register a prescription medicine. It is estimated 50% of current S3 sponsors would seek to migrate their products to S4. Further, it is estimated S3 sponsors will rationalise their portfolio to two products per sponsor given the challenging commercial realities of the prescription only market. As there are currently 22 sponsors of S3 products, the total number of products to be carry forward into the model is therefore 22 medicine products (50% of 22 sponsors (therefore 11 sponsors) and 2 products per sponsor) which will incur costs to update labels. It has been assumed that each product to be up-scheduled relates to a separate ARTG listing.[41]
- Based on BAU costs outlined in Option 1, the label pre-production and production costs are estimated to be $0.092m.
- The required changes fall under a minor variation (Category 3 application) level. Based on a review of the applicable forms it is estimated that 4 hours will be required to prepare and submit the relevant form. The cost of completing the required form is estimated to be $0.005m.
- This analysis has not accounted for reformulation as consultation has indicated there will be no reformulation in response to Option 6 due to costs and potential regulatory barriers to the redeployment of branding.
- As outlined in Option 4, a prerequisite to submitting an application to register a prescription medicine is for the sponsor to have GMP certification for the manufacturing facility. S3 sponsors currently self-certify they are compliant with GMP principles. Moving to S4 will require those sponsors to produce documentation to demonstrate compliance and also be subject to inspections. Sponsors who already have an S4 product are assumed to be compliant with GMP requirements and possess all necessary

[41] In actuality, the two products for each sponsor might be able to be incorporated into a single ARTG entry but we have left this as each product up-scheduled from S2 to S4 requires a separate ARTG entry to avoid understating the regulatory burden.

certification (it is noted that this applies to 3 of the current 22 S3 sponsors). In addition, 14 of the remaining 22 S3 sponsors also have a product in S2. To avoid double counting with Option 4, it is assumed that only 3 sponsors[42] will incur costs to obtain GMP certification from the TGA.

- It is estimated the engagement of GMP professionals, development of documentation, and implementation of staff and managerial processes would cost $34,500 per impacted sponsor. As detailed above, 3 sponsors are estimated to undertake this process. The upfront cost of demonstrating GMP compliance is estimated to be $0.104m.

- The reclassification of S3 products as S4 will require patients to visit a doctor to obtain a prescription for any analgesic product containing codeine. This will increase the compliance burden on individuals. As noted in Option 4 this will require 1.33 hours to travel to and from a doctor's, attend an appointment, and then visit a pharmacy to obtain the medicine. As per Option 4, it is also assumed doctors spend an additional 30 seconds to process the prescription for these new visits and that pharmacists will take an additional 1 minute to process the script and talk to the consumer when providing them the medicine.

- Based on the economic and social impact modelling undertaken for this RIS it is estimated this option would generate an additional average of 51,000 GP appointments per annum over the next ten years. This estimate accounts for the modelled behaviour of consumers in these scenarios (demand side), factors in supply side assumptions, and assumes a maximum of five repeats (therefore up to 6 packs per script). In addition, the economic modelling shows that there are 152,000 existing visits to GPs (that is, would have occurred in the absence of any regulatory change) where a script for codeine would be requested. For the latter category it is assessed that this does not increase the time taken to visit the GP by consumers (as they were undertaking a GP visit anyway) but does result in a slight incremental increase in the duration of the consultation because the GP now needs to prepare a script for codeine (it is assessed that no additional time is required by GPs compared to the average consultation for the writing of script for codeine for the additional GP appointments). As this option relates to up-scheduling S3 to S4 there is assessed to be no additional time required by pharmacists (assuming a 2 minute time interaction for the processing of S3 transactions).[43]

When averaged over ten years the total regulatory cost for Option 6 is $2.21m per annum. The tables below summarise the regulatory costing.

[42] The figure was calculated as follows: Currently 22 S3 sponsors. 3 of these sponsors also have S4 products (carry-forward figure is 19). 14 of the remaining S3 sponsors also have S2 drugs (and so are picked-up in Option 4 calculations) which leaves 5 remaining sponsors. If we assume that the 50% of S3 sponsors indicated by industry consultations that are likely to migrate products from S3 to S4 are wholly contained within this group then this leave a maximum of 3 sponsors.

[43] This assessment of time spent by the pharmacist (and their staff) for Option 6 takes into account additional time spent by the pharmacy staff in preparing a label and updating any required dispensing recording systems and for the pharmacist to talk to the consumer to explain any specific usage requirements and any known side effects. This is counterbalanced by the time previously taken by the pharmacist when dispensing S3 codeine medicines to talk to the consumer to determine the appropriateness of the requested product, noting this matter is now largely addressed in the GP/patient consultation

Table D18. RBM calculations for Option 6

Inputs (for Schedule 3 sponsors)	
Scaled up hourly wage rate	$65.45
No. of Schedule 3 sponsors impacted	3
No. of Schedule 3 products impacted	22
One-off cost to implement labelling changes per OTC product	$4,171.00
Proportion of sponsors who will need to change packs	0%
Cost per ARTG application (Category 3 level)	4.00
Cost to demonstrate GMP compliance per Sponsor	$34,500.00
Proportion of S3 sponsors migrating their products to S4	50%
Outputs (for Schedule 3 sponsors)	**Result**
Total up-front cost to implement labelling changes	$91,762.00
Total up-front cost to implement package size changes	$0.00
Total one-off cost to register Prescription medicine	$5,759.60
Total up-front cost to demonstrate GMP compliance	$103,500.00
RBM compliance cost (over 10 years)	$201,021.60
RBM compliance cost (annualised)	$20,102.16

Inputs (for consumers and doctors) - Option 6	
Labour cost per hour (consumers)	$29.00
Scaled up labour cost per hour (doctors)	$169.75
Scaled up labour cost per hour (pharmacists)	$62.83
Additional visits to doctors per year (S3-->S4)	51,000
Existing visits to doctors where codeine script requested	152,000
Incremental time in hours to visit doctor (additional visit) and obtain script	1.33
Time in minutes for doctor to write prescription	0.5
Outputs (for consumers and pharmacists)	**Result**
Total annual compliance costs for consumers	$1,967,070.00
Total annual compliance costs for doctors	$215,016.67
RBM compliance cost (annualised)	$2,182,086.67

Table D19. RBM summary table for Option 6

Average annual regulatory costs (from business as usual)				
Change in costs ($ million)	Businesses	Community organisations	Individuals	Total change in costs
Total, by sector	$0.24	$0	$1.97	$2.21

Benefits

- As detailed in the economic model, substantial health benefits will be realized by the implementation of this option. The requirement to see a doctor would likely generate health gains compared to the existing situation by driving changes in treatment and therapy.

Regulatory options combined into scenarios

This annex has presented the calculation of the regulatory cost structured along the specified six options. However, there is a logical grouping of these options. Essentially, modification of the regulatory control mechanisms for both S2 and S3 codeine medicines is required simultaneously, otherwise the desired outcomes would largely be negated by consumers shifting from either S2 to S3 (or vice versa) if a single regulatory option was enacted. The table below details the regulatory cost per scenario.

Table D20. Summary table for scenarios ($ millions)

Element	Scenario 2		Scenario 3		Scenario 4	
	Option 2	*Option 5*	*Option 3*	*Option 5*	*Option 4*	*Option 6*
Regulatory cost (average annual)	$0.05	$0.13	$10.14	$0.13	$10.24	$2.21
Net regulatory cost	$0.18		$10.27		$12.45	

Annex E – Economic Model

Aim

Scenarios 2, 3, and 4 are expected to have an impact on the purchase and use of low dose codeine and, in the case of Scenario 4, on the decisions to seek treatment for both dependence and the conditions such as chronic pain that consumers are currently treating with OTC low dose codeine combination medicines.

The aim of the economic model is to estimate the projected costs and benefits of each scenario in relation to both of these broad consequences.

Overview of model and the interpretation of its results

Scenarios 2, 3, and 4 are intended to achieve public health outcomes relating to codeine misuse and abuse; however, these gains could come at a cost to the majority of consumers, who do not misuse low dose combination codeine and who will be required to attend a GP to obtain a script or substitute with other OTC analgesics. This comparison of the expected consequences, both costs and benefits is routinely assessed as part of economic and social models that support regulatory impact assessments.

However, part of the expected health benefits (improved quality of life) are not the result of the Scenario 4 *per se*. Instead, they are the result of additional treatment options being pursued by patients if OTC low dose codeine combination medicines were not available. Patient behaviour has to change and other costs have to be incurred to achieve these intended and expected health consequences. The benefits are available to a broader range of consumers other than the small group who might misuse or abuse OTC low dose codeine combination medicines, including those whose migraines or chronic pain could be treated more effectively with prescription only medicines or by specialised pain centres. This assessment of the costs of additional treatment compared to the health gains is conventionally addressed through health economic models such as those used routinely by the Pharmaceutical Benefits Advisory Committee (PBAC) and the Medical Services Advisory Committee (MSAC). The economic model has a health economic component in addition to the conventional economic and social impact component to ensure that it accommodates both the costs and benefits of the expected health gains.

The economic and social net benefit of the each scenario is reported as a net benefit. This net benefit represents the sum of additional costs (negative figure) and benefits (positive figure) derived from the economic model, where these additional costs and benefits are an aggregation of the consequences for:

- the 'improved treatment' group;
- the same treatment group who continue to use prescription low dose codeine combination drugs; and
- those consumers who switch to other OTC medications including paracetamol and/or ibuprofen.

Key results

The net economic benefits of each option and scenario are presented in Table E1. The economic benefits include the gain in quality of life for additional people who improve treatment, deaths prevented and net financial savings due to reduction in expenditure on low dose codeine medicines. The economic costs include the additional costs to consumers, MBS and PBS of additional medications, GP consultations and specialist consultations. The gains in quality of life (measured as QALYs) and deaths prevented are monetised at the rates recommended by OBPR.[44] Gains in quality of life and deaths prevented are experienced only in Scenario 4. The net economic benefit remain positive for Scenario 4 under a full range of sensitivity analyses.

[44] Office of Best Practice Regulation, 'Best Practice Regulation Guidance Note: Value of statistical life', dated December 2014.

Table E1. Summary costs and benefits for regulatory scenarios over the period 2017-26 ($ million)

Element	Scenario 2		Scenario 3		Scenario 4	
	Option 2	*Option 5*	*Option 3*	*Option 5*	*Option 4*	*Option 6*
Economic costs (PV 2017-26 at 7% $M)	*($20.70)*	*($409.87)*	*($14.49)*	*($409.87)*	*($56.03)*	*($209.87)*
Economic benefits (PV 2017-26 at 7% $M)	*0*	*0*	*0*	*0*	*$243.95*	*$5,353.17*
Net benefit (option basis) ($M)	*($20.70)*	*($409.87)*	*($14.49)*	*($409.87)*	*$187.92*	*$5,143.30*
Net benefit (scenario basis) ($M)	*($430.57)*		*($424.36)*		*$5,331.22*	

Structure of this annex

This annex first sets out the reasoning behind the economic model, with clear illustrations of the potential sources of bias in the analysis and how these were resolved.

Next, the document steps through the economic model, summarising each of the key components: the model's levers and assumptions; the first year analysis; the projections, and the results. Model levers are the model inputs that can be changed in order to explore the results under a range of scenarios. These inputs relate to baseline use of low dose codeine medicines, changes in behaviour in response to each option, and the consequences of these changes. Levers are essential in this model where there is limited evidence and data as well as limited agreement across the range of stakeholders in relation to their actual value. These levers ensure that the base case can easily be respecified in response to different stakeholders understanding of the base case and the impact on the net benefit re-assessed.

Sources of complexity – interdependency and data paucity

The *first source* of complexity in developing this model relates to the interdependency between the responses by the three main stakeholder groups (consumers, GPs and pharmacists) to Scenario 4. In summary, potential actions by these groups are:

- Consumers. Will need to decide whether they go to their GP, consider the treatment options provided by the GP, and/or use OTC non-codeine analgesic such as paracetamol and/or ibuprofen.
- GPs. Will have a new patient group for whom they can suggest a range of additional options (appropriate for the patient), including referring patients to specialist pain units or allied health providers; providing scripts of low or high dose codeine or other prescription only medicines; and/or suggesting OTC pain relief medications.
- Pharmacists. Will continue to interact with consumers who are seeking pain relief, such as those who require prescription medications, some of which will be new to the consumer, and consumers continuing to attend the pharmacy seeking pain relief without any prescriptions for medications.

The *second source* of complexity was the paucity of data that could inform the estimate of the key benefit of Scenario 4; that being the proportion of current users of OTC low dose codeine will experience a health gain, including preventing deaths, as a consequence of this change. KPMG was unable to obtain any data to inform the following estimates:

- the number of people who are currently dependent on low dose codeine medicines (note high dose medicines specifically excluded);
- the number of adverse events attributable to low dose codeine medicines(excluding high dose codeine medicines); and

- the number of people who use low dose codeine medicines chronically and, while currently not dependent, are at risk of dependence.[45]

The critical issue in developing the economic model is the combined effect of these two complexities (interdependency between responses and paucity of estimate data). Unless there are changes in treatment (the cumulative result of changes in activity and/or decisions made by the three groups identified above) there will be very limited changes in health outcomes. Scenario 4 in itself will not produce the expected benefits; rather, it will be the changes in people's activity and behaviour that realises the benefits.

Discussion of the model design

Complexity of this model

The complexity of the model is primarily driven by the use of five separate consumer groups, rather than relying on the concept of an 'average' consumer. This segmentation of the population allows the plausibility of responses to the proposed rescheduling to be assessed more meaningfully and also reduces sources of unintentional systematic error that result from working with a model based on the characteristics of an 'average' consumer. However, this approach does increase the number of required assumptions, an important consideration in this data-poor area. A possible consequence of these additional assumptions is that, when these assumptions are all varied between base, worst and best cases, a very wide range for any resultant metric, such as a net benefit, emerges. The model incorporates a set of analyses that identify the most plausible combinations of these parameters, before conducting the sensitivity analyses, hence addressing this risk.

The third feature of this model is its conservative approach to estimating the size of the projected benefits of Scenario 4. (See discussion in Section 2.3 on input uncertainty.) This approach entails ensuring that the base case parameters for estimating these benefits is conservative, and that the key mechanisms by which this gain is achieved, as articulated by stakeholders, is clearly explained. Potential offsets to these gains, also identified by stakeholders, are also incorporated into the model.

The five main considerations

Listed below are five key considerations that the model addresses and which, collectively, reduce the systematic bias that may arise from a simpler model. These considerations are:

- Why is the concept of an 'average' consumer potentially misleading?
- At what point does using an 'average' response model for Scenario 4 produce a biased estimate of the increase in GP visits?
- What are the five consumer groups and what are their differences?
- What are the drivers of the model's benefits?
- How are the model's key parameters determined?

A pre-modelling exercise was performed to explore these issues, using hypothetical data. In the following sections, the results of this pre-modelling exercise are presented and the implications of these results for the model developed for this regulatory change are discussed.

[45] Compared to occasional users of low dose combination medicines, a higher risk of adverse events due to paracetamol and/or ibuprofen is expected in consumers who are using combination products for longer periods than recommended and/or with greater frequency than the maximum recommended dose for the combination product. These events, and a reduction in their occurrence, are not quantified as part of the model. This leads to an underestimate of the health benefits that are projected to result from Scenario 4.

The average consumer

Table E2 provides a hypothetical example of a market with 14 million sales and 1.1 million consumers. It is straightforward to calculate the average use per consumer; 12.7 packs per year. In this case, if 9% of current consumers stop using low dose codeine medicines post up-scheduling, and the remainder continue their use, then there is a reduction in volume of sales of 9%. However, if it assumed that there are two types of consumers: those with an average of two packs per year, and those with an average of 120 packs per year (two to three packs a week). The latter group is 9% of the market, but represent 86% of the sales.

Table E2: Consumer share of market and share of sales by different consumer groups (hypothetical data)

	Low use consumers	High use consumers	Total use
Number of consumers	1,000,000	100,000	1,100,000
Packs per consumer per year	2	120	12.7
Packs per year	2,000,000	12,000,000	14,000,000
% of consumers	91%	9%	100%
% of packs	14%	86%	100%

The implications of the above calculations (using hypothetical data) are as follows:

- While there are only a low percentage of consumers (9%) with potential misuse or abuse concerns, they account for the majority of the overall use (86%).
- For consumers using 2 packs per year, one would expect a different response to the shift from S3 to S4 when compared to the second type of consumer that use 120 packs per year.
- The demand for codeine containing medicines by low use consumers is more likely to be price elastic; they are likely to respond to the introduction of an additional cost to obtain the product by reducing their demand for that product, and substituting it with less expensive alternatives. They may reduce use if required to pay to see a GP in addition to the cost of the medicines.
- The demand for codeine containing medicines by high use consumers is more likely to be price inelastic; they will be less likely to reduce their demand in response to a price increase. However, it would also be infeasible for them to visit a GP every week (or multiple visits per week) if they had to obtain a script for each pack used. Therefore, their principal constraint is their time; although they may be willing to visit a GP 12 times a year, they are far less likely to make 50 visits per year. (This pre-modelling exercise initially assumes that scripts have no repeats and hence there is one GP consultation per script.)
- The health benefits are most likely to accrue in the smaller group of high use consumers.
- Problem users might use several pharmacies for supply and hence (in the absence of a tracking system) no single pharmacy has an accurate picture of their overall use.

The average response calculation

A pre-modelling exercise was undertaken to assess the potential limitations of using an 'average patient' approach as a basis for the model's structure. This approach was used in the Cadence report[46] concerning the financial implications of Scenario 4. Noting the absence of additional data to inform the calculation of the number of additional GP visits arising from the Scenario 4, if it is assumed, for the purpose of this pre-modelling exercise, that: 1) annual sales are 14 million packs, and 2) a consumer will only go to their GP to

[46] Cadence Economics Pty Ltd, 'Fiscal Impact of Codeine Changes: Report for the Pharmacy Guild of Australia', dated 6 November 2015, viewed 24 August 2016, <http://www.auspharmacist.net.au/images/cad.pdf>.

obtain a script for codeine 40% of the time, then this would lead to an additional 5.6 million trips to the GP and the total volume of sales would be 40% of the original value (see Table E3).

Table E3: Predicting additional GP consultations using an average response (Hypothetical data)

Variable	Value
Packs per year	14,000,000
% of occasions where the consumer go to the GP	40%
Additional trips to the GP	5,600,000

Given this result, some reasonable assumptions about Scenario 4 are:

- the GP will be able to provide up to five repeats (based on the level of repeats associated with current S4 codeine containing medicines for private scripts); the 'no repeats' scenario is unlikely to apply;
- not all trips to the GP will be solely for the purpose of obtaining a prescription for codeine as some patients will request a script as part of a consultation that would otherwise have occurred;
- different consumers will respond differently to the change, depending upon whether they have acute or chronic pain; and
- GPs will also respond to the actions of their patients; if their patients come every two weeks, for example, for an additional supply then they may refer them to an alternative service such as a pain management clinic.[47]

Table E4 shows that, by incorporating these reasonable assumptions the volume of additional GP visits is reduced to 540,000 from the original estimate in Table E3 (5,600,00). It should be noted that the same base numbers are used as for the previous table. It should also be noted that the assumption that five repeats[48] will be available (rather than zero repeats) is not the only driver of the lower number of GP visits. If only one repeat (or zero repeats) were available, this approach would identify that the high use group would require an implausible number of annual trips to the GP and hence this would act as a constraint on both their volume of scripts and the number of additional GP visits as a response to Scenario 4. The average response approach does not identify this.

[47] If a patient is referred to a pain clinic by their GP this attracts a rebate via the MBS (MBS items 2801 2806).
[48] While 5 repeats is the maximum number of repeats that can be given, GPs have discretion to provide a lower number (or even zero) repeats based on the patient's symptomology and medical history.

Table E4: Predicting the additional GP consultations using a disaggregated approach with more realistic assumptions. (Hypothetical data)

Category/Input	Hypothetical Value	Assumptions/Comments - illustrative only
Low use consumer		
Pre changes to scheduling		
Number of people	1,000,000	
Packs per person per year	2	
Post changes to scheduling		
% of consumers who get a script	20%	Most people will use OTC paracetamol and/or ibuprofen instead of low dose codeine medicines
Consumers who get a scripts	200,000	
Packs in year per person	2	For those who continue, the same number of packs a year are used
Additional GP visits per person	0	Most of the population has at least 2 visits to a GP a year and this would be absorbed into existing visits
High use consumer		
Pre changes to scheduling		
Number of consumers	100,000	
Packs per year	120	
Post changes to scheduling		
% of consumers who get a script	90%	Most of these consumers will continue to use low dose codeine medicines. The continued use of low dose codeine as the only option other than OTC pharmacotherapy is consistent with the Cadence modelling. (In the actual economic model, it is assumed that some of these consumers will have high dose codeine medicines and others will have other pharmaco-therapy and specialist pain care. This is consistent with the advice from stakeholders who supported the up-scheduling.)
No. of consumers who get a script	90,000	
Maximum additional visits		
Additional GP visits (0 repeats)	120	If there were no repeats, then this would result in 120 visits to a GP a year, which is implausible.
Additional GP visits (5 repeats)	20	With 5 repeats, the patients could go 20 times a year, but that would still mean they were a very frequent user of GP services.
Additional GP visits (max with 5 repeats)	6	It is more reasonable to assume they would limit themselves to 6 additional visits a year.
Plausible additional visits		
Max per year	6	
Plausible packs per year		
Total GP visits	12	Assuming that they would otherwise have had 6 visits, they now have 12 visits a year. This means that half of their visits when they obtain a script are visits that would otherwise have occurred.
Packs - with 5 repeats	72	Consumers could have 6 additional visits a year, 12 in total, and then a script with 5 repeats at each occasion which is a total of 72 packs (12 visits x 6 packs (5 repeats + 1 pack – original dispensing))
Total population - the combined effect of the two		
% of consumers who get a script	26%	The combined effect is that 26% of consumers continue as patients (290,000/1,100,000)
No. of consumers who get a script	290,000	(200,000 (low use consumer) + 90,000 (high use consumer))
Packs per year per consumer	23.7	The average packs per patient is now 23.7 (6880000/290000), which is

Category/Input	Hypothetical Value	Assumptions/Comments - illustrative only
		higher compared to the average preceding the scheduling change. This is a consequence of two factors. First the identification of two different groups of consumers allows group to change their use at a different rate. Second, the denominator (the number of people who continue to consume) is reduced.
Total packs per year	6,880,000	
As % of previous packs	49%	The volume is now 49% of the previous volume
Additional GP visits total	540,000	There are 540,000 additional GP visits

The average response approach and consistency check against the results of the Cadence Economics Report – Fiscal Impact of Codeine Changes[49]

KPMG reviewed the methods and results of the Cadence Economics report, which predicts an additional 8.7 million GP consultations each year as a consequence of the proposed up-scheduling of codeine to S4.[50] There are two key differences between the KPMG and Cadence economic modelling approaches: one methodological the other relating to a key assumption. The key methodological difference is the Cadence model uses an 'average' consumer concept, while the KPMG model used a segregated population (refer to Figure E1). The differing key assumption was that the Cadence model assumed no repeats while KPMG has assumed 5 repeats. These two key differences were assessed to be the primary drivers of the different results produced by the two models.

The five groups of consumers

The five groups of consumers are set out in Figure E1. Codeine use can be either therapeutic or non-therapeutic. Therapeutic use can be for acute pain and consumers might purchase only one or two OTC packs a year and use it in a way consistent with the product advice: i.e. for no more than three days in a row without seeing their GP and no more than eight tablets a day.[51] Therapeutic use for chronic conditions such as chronic pain can lead to dependence. In the model, dependent consumers use more than the recommended maximum dose each day, whereas non-dependent consumers use the maximum recommended dose each day. All chronic users use the low dose codeine medicines for the majority of days in a year, which in the base case we assume to be 250 days. They are also assumed to be more likely to use the largest pack size (40 tablets) compared to acute users. Consequently, a regulatory change that restricts pack size to three days' supply will impact on this group of consumers more so than acute users.

Chronic therapeutic use is more likely to result in adverse events such as gastrointestinal bleeds as a consequence of the use of ibuprofen for longer periods and at higher daily doses than recommended. They are also more likely to have an accidental death due to an overdose of codeine, although this is considered to be a very rare event. Consumers who use therapeutic low dose codeine medicines for chronic pain are at greater risk of becoming dependent in comparison to users that self-treat acute conditions.

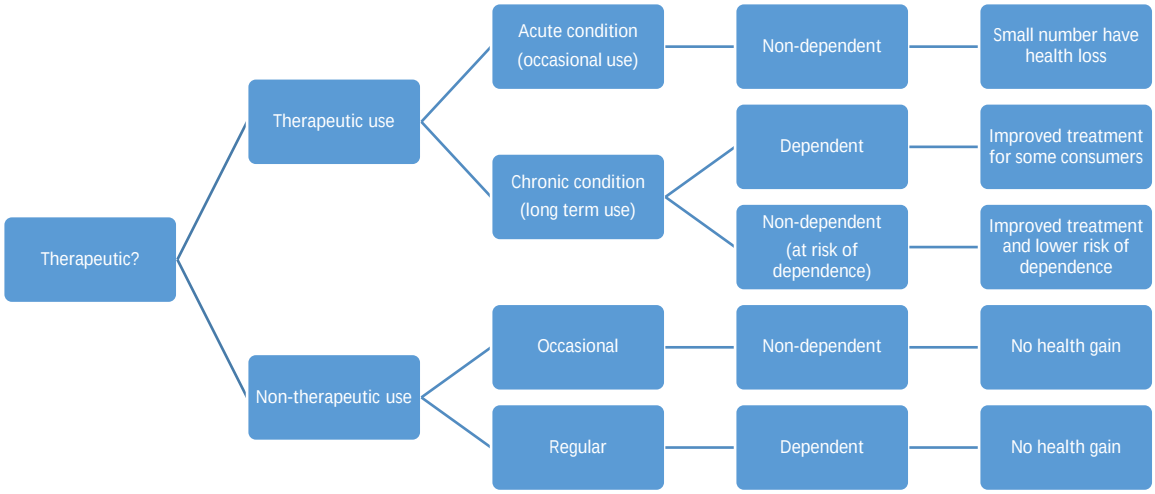
[49] The following public domain document included an estimate of the fiscal impact of the proposed rescheduling of codeine. Cadence Economics Pty Ltd, 'Fiscal Impact of Codeine Changes: Report for the Pharmacy Guild of Australia', dated 6 November 2015, viewed 24 August 2016, <http://www.auspharmacist.net.au/images/cad.pdf>.

[50] ibid., p. 10.

[51] "Do not take more than a few days at a time unless your doctor tells you to." Source: Mersyndol DayStrength Caplets Consumer Medicines Information "Developed by the pharmaceutical company responsible for this medicine in Australia, according to TGA regulations." <http://www.nps.org.au/medicines/pain-relief/combination-simple-pain-relievers/paracetamol-codeine/mersyndol-daystrength-caplets>, accessed 24 August 2016.

While non-therapeutic use is often referred to in the media[52], it is likely to be only a very small proportion of consumers in this group. KPMG has taken a conservative approach and included this group to account for the total volume of sales. However, we do not account for any benefits that might result from the proposed rescheduling for this group. KPMG does assume that their use of low dose codeine medicines will be limited substantially if they are required to go to a GP to obtain a script. However, we have assumed that they are likely to substitute this with other forms of recreational drug use.

Figure E1: Patient/consumer groups used in the health economic modelling



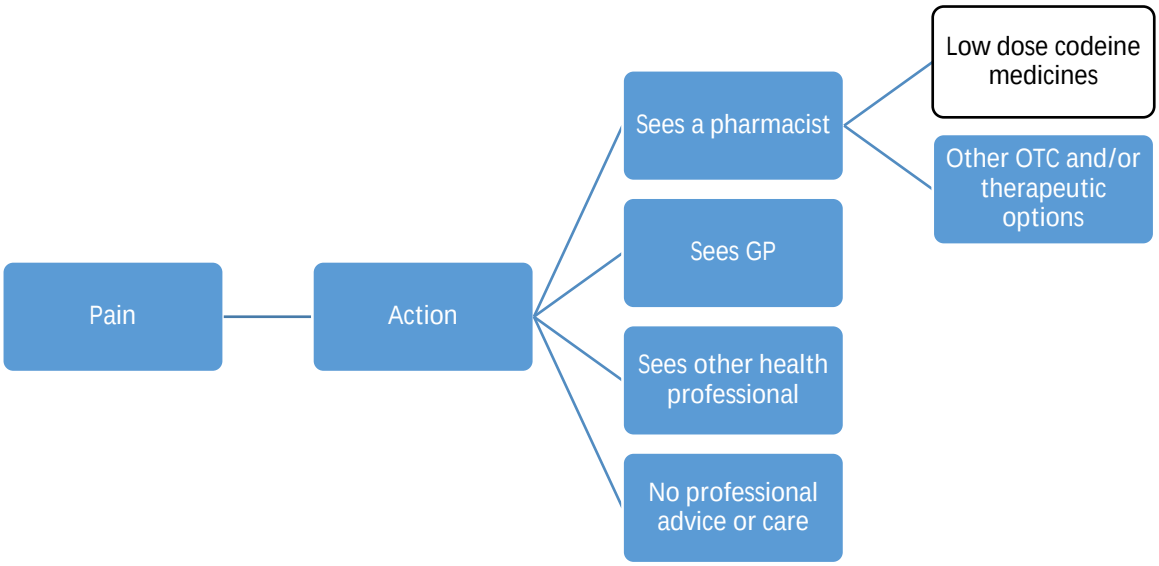
The drivers of gains in health outcomes

If low dose codeine medicine is only available by prescription, then the health gains compared to the existing situation (low dose codeine OTC medicines) are driven by changes in treatment and therapy. This change could arise because they discuss alternative treatment options with their pharmacist or, alternatively, they visit their GP, who then either maintains their current use of low dose codeine medicines or changes their therapy (Figure E2). This change may include an alternative analgesic medicine that is more suitable, or a diagnosis of their condition resulting in treatment and ultimately reducing the need for analgesic use. There are also other treatment options that include non-pharmacological options, referrals to allied health professionals or specialist pain clinics. If patients are referred to these services by their GPs, then in many situations, patients will be able to obtain a Medicare rebate for the service. However, there are currently waiting lists for pain clinic services, so capacity constraints must also be considered.

The critical point here is that the same treatment options are available to the consumers before and after Scenario 4 is enacted. The impact of the up-scheduling to Schedule 4 does not introduce the other treatment options but does make the existing treatment options more likely to be explored. The potential health impact is to increase the chance that a patient, who would have better treatment option in comparison to low dose codeine medicines, explores these options with their pharmacist or their GP as a consequence of Scenario 4 being enacted.

[52] See, for example, "Codeine addiction a growing problem as Aussies abuse over-the-counter pain medication" Leisa Scott QWeekend The Courier-Mail August 31, 2013 http://www.couriermail.com.au/news/queensland/codeine-addiction-a-growing-problem-as-aussies-abuse-overthecounter-pain-medication/story-fnihsrf2-1226707777107

Figure E2: One option is excluded as a consequence of Scenario 4



Determining key modelling parameters

Four steps are taken to determine the key modelling parameters given available data (sales data from IMS), reasonable assumptions about the number of tablets consumed per day, days of use for each of the five types of consumers, and the share of total consumers in each group. This method is illustrated in Figure E3. These four steps are outlined below, with the inputs to steps 1), 2) and 3) having been informed by discussions with stakeholders:

1) The total number of sales by pack size (dollar value and packs sold) was calculated from the IMS data. The total retail sales value by pack size was calculated by assuming a 44% retail mark up.[53]
2) The number of tablets per consumer, from 6-20 tablets per day over 12-365 days per year depending on the type of consumer:
    a. Therapeutic, acute pain, non-dependent – 8 tablets/day over 12 days/year.
    b. Therapeutic, chronic pain, non-dependent – 8 tablets/day over 250 days/year.
    c. Therapeutic, chronic pain, dependent – 12 tablets/day over 250 days/year.
    d. Non-therapeutic, occasional use, non-dependent –6 tablets/day over 20 days/year.
    e. Non-therapeutic, regular use, dependent –20 tablets/day over 365 days/year.
3) The proportion of consumers in each group:
    a. Therapeutic – 99%:
        i. Therapeutic, acute pain, non-dependent – 80% of all users
        ii. Therapeutic, chronic pain – 19% of all users of whom:
            1. 40% are Therapeutic, chronic pain, non-dependent.
            2. 60% are Therapeutic, chronic pain, dependent.
    b. Non-therapeutic– 1%, of whom:

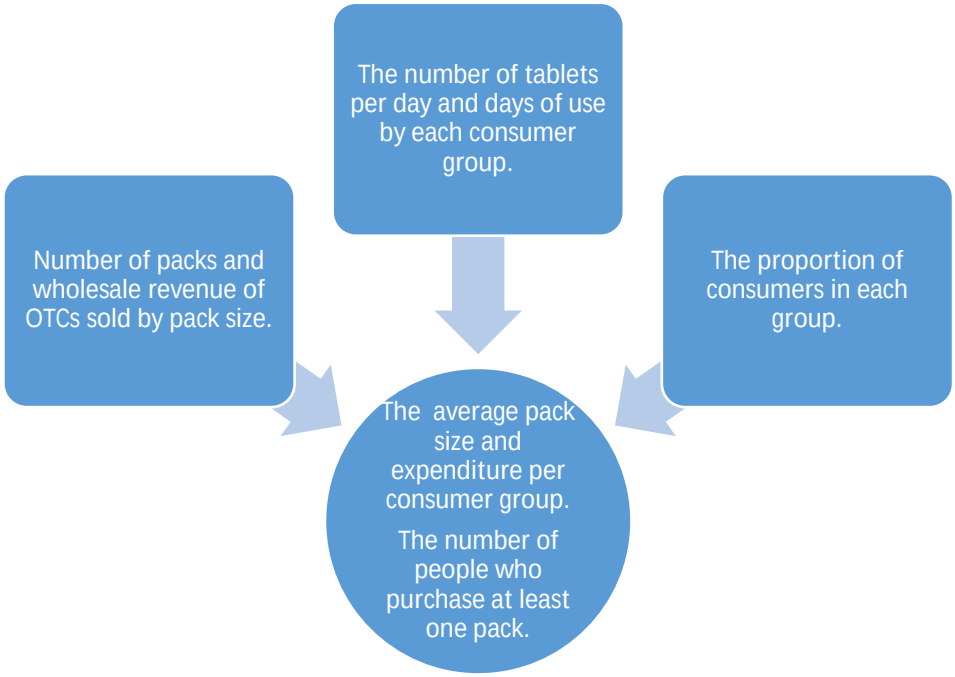
[53] The total sales values and units by pack size were used to estimate the wholesale prices of both IMS S2 and S3 codeine-based medicines. The retail prices of those codeine-based medicines were captured from the retail market in Australia. The retail mark-up is then estimated by employing both wholesale and retail values of codeine-based medicines

i. 10% are Non-therapeutic, regular use, dependent.
ii. 90% are Non-therapeutic, occasional use, non-dependent.

4) The pack sales were then allocated by the model across consumers, starting with the smaller packs allocated to the lower use consumers, and with the maximum pack sizes allocated last to the most frequent users.

This approach allowed the calculation of the average pack size and expenditure per consumer group. In turn, this enabled the assessment of the plausibility of changes to current behaviour based on a more accurate picture of the current pattern of use.

Figure E3: Determining key modelling parameters



Assumptions and levers

The model includes two types of inputs:

1) Administrative inputs, such as the value of a statistical life year ($182,000), which was used to value a Quality Adjusted Life Year (QALY). These inputs are set via a range of protocols detailed in the economic model.
2) A small number of inputs that are set in Analysis Tables 1 to 3, which need to be considered in the context of other information and hence are most appropriately entered in a table.

The input panel at the start of the model provides a range of inputs that can be tested. The details of these are set out in the model.

The model assumes very small gains in QALYs from treatment and, in the base case, only some of the consumers who use low dose codeine medicines for chronic pain are assumed to have active treatment as a consequence of Scenario 4 being enacted.

Consumers who are using low dose codeine medicines for non-therapeutic reasons are assumed, conservatively, to not have any health gains, and are not treated under Scenario 4. As these consumers are assumed to be only 1% of the total users of low dose codeine, this assumption is conservative.

It is reasonable to expect that the medications that are PBS listed for pain are cost-effective, assuming that most of these will have been part of the Pharmaceutical Benefits Advisory Committee (PBAC) process. It is also reasonable to expect that the MBS items for pain clinics also represent cost-effective care. The costs of these additional services to both the consumer and the Commonwealth are included.

Analysis tables

The model comprises one output table and 5 analyses tables, two of which (Analysis Tables 1 and 2) also include inputs relating to current use of low dose codeine medicines per consumer, the proportion that will take each therapeutic pathway, and the resource use and QALY outcome of each pathway. Analysis Table 3 performs projections from 2017 to 2026.

The last two model tables set out the IMS data on sales for S2 and S3 medicines, the projected sales for 2017, the impact of the changes in pack sizes. These tables inform all Options. Option 6 is additionally informed by the assumptions set out in Analysis Tables 1 to 3.

Projections: First year and 2017 – 26 present value

Projections were performed for ten years. QALY and death results were projected for ten years and then the QALYs, and monetised QALYS and deaths were discounted using 7% (in the base case), to ensure consistency with the OBPR guidelines.

The base case assumes a constant rate of reduction in the total costs, and benefits, of treatment due to a decreasing rate of participation in treatment. Some stakeholders noted that the initial increase in the number of people who are additionally treated and experience a health benefit is likely to decline in a few years until the system recalibrates. That is, patients who are currently using low dose codeine medicines and who, following up-scheduling will pursue therapeutic pathways that improve health outcomes, are part of a cohort. They will receive additional treatment and care for the following year, but this additional treatment, compared to what they would otherwise have received, will reduce each year. The model captures this factor by assuming, in the base case, a 30% annual reduction on previous year's treatment and health gains.

Deaths were assumed to be prevented at the same number each year. A conservative assumption[54] was made regarding the changing prevalence of dependence due to accessibility of low dose codeine medicines; it is assumed that there would be no increase in either, the overall use of these medicines, or in the prevalence of codeine dependence under Scenario 1, the current situation.

Results

The overall results are presented in the RIS table in the model (Table ES2 of the Executive Summary). The main result is the net benefit, which is presented using 2 subset results for the first year and tenth year net benefit. These yearly results are further subdivided into: (1) first year benefit, cost and net benefit; and (2) the ten year NPV benefit, cost and net benefit. Option 6 is the only option with a net benefit hence all other options have a net economic cost, driven by additional out-of-pocket costs to consumers as well as the cost attributed to the administrative burden for businesses and individuals.

The following tables (Tables E5 and E6) presents the 2017 costs and benefits included in the economic model disaggregated by broad categories. (More detailed tables are presented in the Executive Summary)

[54] A conservative assumption was made because KPMG was unable to determine whether the prevalence of low dose dependence is increasing due to the paucity of data.

Table E5 Additional economic costs 2017 ($M)

2017	Scenario 2		Scenario 3		Scenario 4	
Economic costs	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6
Additional Out-of-pocket costs to consumers	($2.76)	($54.63)	($1.93)	($54.63)	0	0
Additional costs to MBS	0	0	0	0	($7.47)	($51.97)
Additional treatment related GP consultations ($M)	0	0	0	0	0	($42.86)
Additional Low Dose codeine prescription GP consultations ($M)	0	0	0	0	($7.47)	($1.89)
Additional specialist consultations ($M)	0	0	0	0	0	($7.21)
Additional costs to PBS - for medicines already demonstrated to be cost effective	0	0	0	0	0	($23.06)
Total economic costs	($2.76)	($54.63)	($1.93)	($54.63)	($7.47)	($75.03)

Table E6 Additional economic benefits, 2017 ($M)

2017	Scenario 2		Scenario 3		Scenario 4	
Economic benefits	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6
Improved quality of life (ex. Deaths prevented)						
Total QALY gains	0	0	0	0	0	9,074
Monetised QALY gain	0	0	0	0	0	$1,651.52
Deaths prevented						
Estimated deaths prevented	0	0	0	0	0	5
Monetised deaths prevented ($M)	0	0	0	0	0	$21.00
Net financial savings to consumers	0	0	0	0	$32.51	$40.21
Total economic benefits	0	0	0	0	$32.51	$1,712.73

The following tables (Tables E7 and E8) present the disaggregated costs and benefits as present values over the period 2017 to 2026 discounted at 7%. The ten-year results are not simply the one year results multiplied by ten. The following factors drive the differences in the summary statistics in the following (2017 to 2026) and previous (2017) tables:

- Clinical stakeholders indicated that there would be an initial 'hump' in additional treatment for patients who would otherwise be chronic users (dependent or risk of dependency) but that this would taper off over time. Hence the additional benefits and costs of Option 6 are substantially less than ten times the single year (2017) results; that is, the additional benefits and costs are incurred each year at a reducing rate.
- A 7% discount rate was applied to the monetary values, which is consistent with OBPR guidance.
- The population of ongoing low-dose codeine medicines users is assumed to increase by the same rate as the ABS projected annual population growth (1.66%)

Table E7 Additional economic costs, 2017-26 PV at 7% ($M)

2017-26 present value (7% discount rate)	Scenario 2		Scenario 3		Scenario 4	
Economic costs ($M)	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6
Additional Out-of-pocket costs to consumers ($M)	($20.70)	($409.87)	($14.49)	($409.87)	0	0
Additional costs to MBS ($M)	0	0	0	0	($56.03)	($148.43)
Additional treatment related GP consultations ($M)	0	0	0	0	0	($112.59)
Additional Low Dose codeine prescription GP consultations ($M)	0	0	0	0	($56.03)	($16.56)
Additional specialist consultations ($M)	0	0	0	0	0	($19.27)
Additional costs to PBS- for medicines already demonstrated to be cost effective ($M)	0	0	0	0	0	($61.43)
Total economic costs ($M)	($20.70)	($409.87)	($14.49)	($409.87)	($56.03)	($209.87)

Table E8: Additional economic benefits, 2017-26 PV at 7%

2017-26 present value (7% discount rate)	Scenario 2		Scenario 3		Scenario 4	
Economic benefits ($M)	Option 2	Option 5	Option 3	Option 5	Option 4	Option 6
Improved quality of life (ex. Deaths prevented)						
Total QALY gains (PV at 7%)	0	0	0	0	0	24,173
Monetised QALY gain ($M)	0	0	0	0	0	$4,399.47
Deaths prevented						
Estimated deaths prevented (not discounted)	0	0	0	0	0	50
Monetised deaths prevented (PV at 7%) ($M)	0	0	0	0	0	$147.50
Net financial savings to consumers (PV at 7%) ($M)	0	0	0	0	$243.95	$806.21
Total economic benefits ($M)	0	0	0	0	$243.95	$5,353.17

Table E9 presents the economic costs and benefits for 2017 and for 2017-26 summarised as net benefits.

Table E9: Economic costs, benefits and net benefit 2017 and 2017-26 PV at 7% ($M)

Net economic benefit	Scenario 2		Scenario 3		Scenario 4	
	Option 2	Option 5	Option 3	Option 5	O ption 4	Option 6
2017						
Economic cost ($M)	($2.76)	($54.63)	($1.93)	($54.63)	($7.47)	($75.03)
Economic benefit ($M)	0	0	0	0	$32.51	$1,712.73
Net economic benefit ($M)	($2.76)	($54.63)	($1.93)	($54.63)	$25.05	$1,637.70
For Scenarios ($M)	*($57.38)*		*($56.56)*		*$1,662.74*	
2017-26 (PV, 7% discount rate)						
Economic cost ($M)	($20.70)	($409.87)	($14.49)	($409.87)	*($56.03)*	*($209.87)*
Economic benefit ($M)	0	0	0	0	*$243.95*	*$5,353.17*
Net economic benefit ($M)	($20.70)	($409.87)	($14.49)	($409.87)	*$187.92*	*$5,143.30*
For Scenarios ($M)	($430.57)		($424.36)		$5,331.22	

Sensitivity analyses

Sensitivity analyses can be performed in two ways within this model. The first is a structured approach using the Scenario Manager tool. Seven sensitivity analyses have been programmed and they vary a total of nine key inputs, as set out in Table E10. An alternative approach is to use the input panels at the start of the RIS sheet. Any number of these inputs can be changed and the impact on the net benefit can be tested. Regardless of the variations made via the input panel, the Scenario Manager will always use the base case programmed into the tool, not the prevailing values of the variables.

The input panel was used to test the model as a quality assurance process and also to test the overall robustness of the results. The base case value of assumptions that were varied as part of testing the model are presented in Table E10. The values that were varied in the seven standard sensitivity analyses included in 'Scenario manager' to test the robustness of the final results are also included in Table E10. Other inputs were not tested in the sensitivity analysis as they were assessed to be administrative inputs, for example, the monetary value of a statistical year of life. The results indicate that only in extreme cases does the model predict a net loss with Option 6. An example of an extreme scenario is when the QALY gains from treatment are reduced by 30%, the treatment costs are increased by 30%, the loss in QALYs to a small proportion of consumers is assumed to be high and the treatment activity in the first year is expected to continue at a high rate for the next ten years.

Table E10: Option 6 Base case of all variables tested in the sensitivity analyses and the values of the variables in the sensitivity analyses

Selected Inputs	Base case value	Value in sensitivity analysis	Present value of net benefit (2017 to 2026)	Change compared to base case	Interpretation
Base case value: $ 5,143,299,606 (This is the present value of the annual net benefit over ten years)					
Univariate sensitivity analysis					
Deaths prevented per year	5	20	$5,585,785,243	9%	A study[55] indicate that the deaths potentially attributable to OTC low dose codeine medicines are around 15-30 a year. However given these consumers have multiple complexities, only some of these deaths are assumed in the base case to have been prevented. The net benefit increases as the number of deaths prevented increases.
		50	$6,470,756,517	26%	
Discount rate	7%	10%	$4,705,920,607	-9%	OBPR guidelines require that the base case discount rate is 7% and is varied to 10% and 3% in univariate sensitivity analyses. The net benefit varies in a way that is consistent with expectations.
		3%	$5,857,149,799	14%	
Repeats for a private script of low dose codeine medicines	5	0	$5,072,341,663	-1%	The less repeats in a private script of LD codeine, the more visits to a GP required for a patient to maintain current usage. This only applies to acute users (current S2 and S3) who continue to use these medicines. Some of these visits (75%) are assumed to have occurred without the need for the prescription. The less repeats the higher the cost to the consumer for the co-payment and the higher the cost to MBS. The impact on the net benefits is small because the main driver of the additional MBS costs is the S2 users, who are predicted to only require one pack a year and hence not require a repeat. The Medicare cost for the current S3 users increases by approximately 5 fold, however this is from a low base. The MBS costs for this group are driven by treatment related consultations. And finally, the net benefit is driven by the very high economic benefit relative to the cost.
		2	$5,125,560,120	0.3%	

[55] Amanda Roxburgh, Wayne D Hall, Lucinda Burns, Jennifer Pilgrim, Eva Saar, Suzanne Nielsen and Louisa Degenhardt. 'Trends and characteristics of accidental and intentional codeine overdose deaths in Australia', *Medical Journal of Australia,* 2015, Volume 203, Issue 7, viewed 6 September 2016, < https://www.mja.com.au/journal/2015/203/7/trends-and-characteristics-accidental-and-intentional-codeine-overdose-deaths>.

Selected Inputs	Base case value	Value in sensitivity analysis	Present value of net benefit (2017 to 2026)	Change compared to base case	Interpretation
% of all acute users of LD codeine who continue to use LD Codeine after the shift from S3→S4 at the same rate as they do currently: 5 packs per year	20%	25%	$5,137,897,522	0.1%	These are consumers who continue for the next ten years to use LD codeine for acute pain. The less who continue, the less GP visits, the lower the cost to Medicare and to consumers and the greater the savings from less low dose codeine prescriptions.
Of the consultations for the above group, what% are additional consultations. Assume all patients get maximum repeats, currently 5 packs per year	25%	50%	$5,125,560,120	0.3%	Only some of the consultations for the above group are additional. The greater the proportion that are additional, the higher the additional cost to consumers and Medicare.
% of consumers whose use is for acute pain	80%	90%	$4,829,883,483	-6%	This is the group who are least likely to participate in treatment hence the overall QALY gains are reduced, and the net savings from reduced expenditure are also minimised when this proportion is increased.
		70%	$5,275,835,569	3%	
% of consumers whose use is chronic, who are also dependent	20%	50%	$5,169,648,377	1%	Chronic therapeutic users represent 19% of all users in the model's base case. At 20% of this group, dependent consumers represent 3.8% of all current users of low dose codeine medicines. Chronic dependent users have the greatest potential for a health benefit (have a QALY gain) and will make the highest savings in expenditure on LD codeine. However their treatment costs are also expected to be the highest as they are more likely to require referrals to pain clinics. Hence the net effect on the net benefit of increasing the share of consumers in this group is small.
		10%	$5,098,036,330	-1%	
% of consumers whose use is non-therapeutic	1%	2%	$5,061,830,607	-2%	No therapeutic users are assumed not to participate in the ongoing pathways and so incur neither additional costs nor additional benefits. Hence the larger the share of current consumers in this group, the lower the net benefit because less consumers experience the average net benefit per consumer at baseline, which is maintained.
		0.25%	$5,201,561,529	1%	

Selected Inputs	Base case value	Value in sensitivity analysis	Present value of net benefit (2017 to 2026)	Change compared to base case	Interpretation
% of therapeutic Chronic dependent and non-dependent users who are referred to pain clinics	10% and 5%	1% and 0% (instead have intensive GP management with smaller health gains and lower cost)	$4,960,883,22	-3.5%	Chronic dependent therapeutic users represent 3.8% of all consumers in the model's base case and chronic non-dependent therapeutic users represent 15.2%. Hence, under the base case. 1.4% of all current consumers are expected to be referred to pain clinics. However, pain clinics are likely to have waiting lists. This sensitivity analysis reflects this situation. Instead of going to a pain clinic, these customers are assumed to have multiple GP visits and use a range of prescription pain medications. Hence, there is still an additional health gain, and MBS and PBS cost for these patients. The impact on the overall net benefit is a small reduction.
Annual change in additional treatments (projections)	-30%	0%	$1,423,923,121	-74%	With these benefit minimising and cost maximising assumptions, a net benefit is expected but is substantially reduced.
Change in the average QALY per treatment	0%	-80%			
Change in the average cost per treatment (all costs - consumer, MBS and PBS)	0%	80%			
Deaths prevented per year	5	0			
Repeats for a private script of low dose codeine medicines	5	0			

Discussion

General

The additional health gains are achieved at an additional cost to the system. The comparison of the health gains with the additional costs of achieving these gains is analogous to the PBAC assessment of the additional costs and benefits of a new medicine.

It is noted that:

- Typically, new medicines listed on the PBS come at an additional cost to the health system; however, if it can be demonstrated that the additional costs are justified by the additional benefits then the new medicine will be usually be listed on the PBS.
- Similarly, this proposed change in regulation comes with additional costs (additional visits to the GP, additional out-of pocket costs to the consumer, etc.); however, the additional costs are justified by the additional benefits (i.e. the net benefit is positive)

The economic model indicates that Scenario 4 is broadly 'cost effective'. One way of summarising and assessing the health and financial consequences of Scenario 4 is as a net benefit, where the QALYs and deaths are summarised as monetised values and compared to the costs. This approach is consistent with OPBR guidelines and presented in this report. Another approach, which is used by the Pharmaceutical Benefits Advisory Committee (PBAC) and the Medical Services Advisory Committee (MSAC), is cost effectiveness analysis: a comparison of the additional costs with the additional effects (QALYs) expressed as an incremental cost effectiveness ratio (ICER).

A formal cost effectiveness analysis was outside the scope of this project. It is possible to use the results generated by the economic model to make a broad estimate of the ICER of Scenario 4 compared to Scenario 1 (current practice). Using the results report in previous tables, the additional costs to MBS and PBS from Scenario 4 relative to current practice were compared to the additional QALYs, for both the first year and the present value over ten years and estimates $9,092 per QALY and $11,097 per QALY respectively are reported. (See Table ES16). Although the decision threshold for PBAC is not publicly reported, it is reasonable to conclude that at around $10,000 per QALY that these preliminary results indicate that Scenario 4 is projected to achieve additional QALYs at a cost per QALY that would be considered to be 'cost effective'.

Table E11: A preliminary estimate of the likely cost effectiveness of Scenario 4 relative to current (Scenario 1)

Cost and effect (QALYs) - all sourced form previous tables	2017	PV of 2017-26
Additional MBS low dose codeine prescription consultation costs ($M)	$9.36	$72.60
Additional MBS treatment consultation costs ($M)	$50.08	$134.22
Additional PBS costs ($M)	$23.06	$61.43
Total MBS and PBS costs ($M)	$82.50	$268.25
Additional QALYs (ex. Deaths) (QALYs) (Number)	9,074	24,173
ICER = additional cost/additional QALYS ($)	$9,092	$11,097

The following drivers contribute to the 'cost effectiveness' of Scenario 4.

- Each ongoing pack of low dose codeine combination medicines purchased does not require an additional GP consultation. Specifically:
  - up to 5 repeats are possible for consumers should they continue to use low dose codeine combination medicines resulting in up to 6 scripts per consultation; and
  - for many consumers, this additional script is unlikely to represent an additional GP consultation and will instead form part of a consultation that would otherwise have occurred in the absence of Scenario 4 being enacted.
- For some consumers (namely ongoing low dose codeine medicine users) there is an additional cost but no change in health outcomes. However, the number of additional GP consultations for these consumers are likely to be substantially less than the number of packs they purchase (due to being able to obtain up to 6 scripts per consultation).
- The additional cost for pain clinics and some GP consultations are for treatment that would otherwise not have occurred in the absence of Scenario 4 being enacted. Treatment costs are accepted as a cost effective part of the health system.
- The additional treatment costs to PBS are largely for medicines already shown to be cost effective.
- There is a financial saving without loss of health benefits for most consumers who shift from low dose codeine combination medicines to paracetamol and/or ibuprofen OTC medicines. There is no loss in health outcomes because for most of these consumers, as the evidence indicates, there is no incremental health effect of the use of low dose codeine combination products compared to using these analgesics without codeine.

In many scenarios KPMG tested, there was a net reduction in out-of-pocket costs to the consumer. When this occurs, the model adjusts the resultant saving to be included as a benefit, not a negative cost. This net savings to consumers in Option 6 is the result of a combination of factors, including:

- the reduction in use of low dose codeine medicines;
- the substitution of low dose codeine medicines to cheaper supermarket products such as paracetamol and/or ibuprofen;
- patients who continue with prescription medicines (whether containing codeine or not) in most cases will pay the same or less than their current expenditure on low dose OTC codeine medicines;
- if patients substitute low dose codeine medicine with high dose prescription codeine medicine via script, they can be provided up to five repeats by their GP reducing the need for less visits to their GP;
- the high bulk-billing rate for GP consultations, which reduces the net additional cost to consumers[56], and;
- the rate at which pain-related GP consultations can be accommodated within visits that would otherwise have occurred in the absence of Scenario 4 being enacted.

One issue raised by stakeholders is that the predicted demand for additional consultations at pain clinics is unlikely to be accommodated within existing capacity. A sensitivity analysis that assumes only 0.38% rather than 1.4% of all current consumers will be referred to a pain clinic indicates that there would only be a small reduction in the net benefit if less patients were referred. This result occurs because these patients would instead have intensive pain management provided by their GP and still have health gains at an additional cost to the MBS for treatment (compared to the current situation). However, these gains are assumed to be slightly smaller and the costs slightly lower. (See the results of the sensitivity analysis reported in Table E10.)

Most stakeholders indicated that additional face-to-face education[57] for prescribers and pharmacists was unlikely to be necessary. With an estimated one million people using at least one S3 low dose codeine medicine product a year, the need to invest in an education and awareness campaign, particularly for consumers is apparent. This issue was raised with stakeholders. The question of how an education campaign for consumers would be funded, and what form it might take is still to be determined and is dependent on the regulatory process changes, if any. The cost of this campaign was not included in these costings.

For some consumers, Scenario 4 will result in a reduction in out of pocket costs with no change in health status. Many consumers who currently use low dose codeine combination medicines occasionally (only three days at a time for acute pain) and are expected to substitute this medicine with codeine free alternative that do not require a prescription. Generally these will be at a lower cost to the consumer compared to the expenditure that would otherwise have occurred. However, on average, it is expected that there will be no loss in pain relief for these many of these consumer, as indicated by systematic reviews of clinical trials. Hence there will be financial savings to some consumers as they switch to less expensive medications, without a loss in pain relief.

[56] In 2015/16 83.4% of all GP/GP VR non-referred attendances were bulkbilled. The economic model incorporates this rate in two ways. First, the data provided by Medicare to estimate the cost of additional consultations was developed using Medicare's estimates of the mix of MBS items and the rate of bulkbilling (for the bulkbilling incentive payment). Second, the model assumes a co-payment is paid by 15% of all patients. http://www.health.gov.au/internet/main/publishing.nsf/Content/Annual-Medicare-Statistics

[57] Also known as 'Academic detailing', this is the process of delivering face-to-face education of prescribers by trained health care professionals, typically pharmacists, physicians, or nurses. The goal of academic detailing is to improve prescribing of targeted drugs to be consistent with medical evidence from randomized controlled trials, which ultimately improves patient care and can reduce health care costs.

The additional cost to the PBS (relating to Option 6 (Scenario 4))

Additional PBS items are an expected consequence of Scenario 4 being enacted. Some additional pharmaco-therapies used by patients as prescribed by their clinician as a consequence of their attendance at a GP for acute of chronic pain will incur a PBS subsidy. A key clinical stakeholder contact indicated this additional prescribing would occur and provided examples of the medicines prescribed but did not provide estimated numbers of patients who be prescribed these medicines. Another key stakeholder indicated that there would be additional PBS scripts now dispensed by pharmacies, including for medicines other than low dose codeine, and that pharmacists would need to provide information on these new (to the patient) pharmacotherapies.

The assumptions incorporated into the economic model include:

- that the current S2 and S3 codeine medicines would not be listed on the PBS;
- that a proportion of current consumers of S3 codeine medicines (some acute, mainly chronic) will be provided with alternative pharmacotherapy for chronic pain and acute pain such as migraines;
- the ongoing use of these PBS medicines would taper off);
- that these PBS medicines would be cost-effective for patients and hence the additional costs, while recorded, would be accompanied by an additional health benefit for patients (on average); and
- as there was no data on which to inform the exact mix of these additional medicines an average additional PBS cost was assumed.

These assumptions were generated as a result of discussions with key stakeholders and reasonable base case assumptions were then tested in the sensitivity analysis and the net benefit remained positive.

The additional cost to the MBS (Scenario 4)

As discussed above, the additional treatment options that will be pursued by some acute and most chronic users will require additional consultations.

It was assumed that only some patients who are currently chronic users would go to pain clinics, and the constraint on current resources was identified by a key clinical stakeholder).

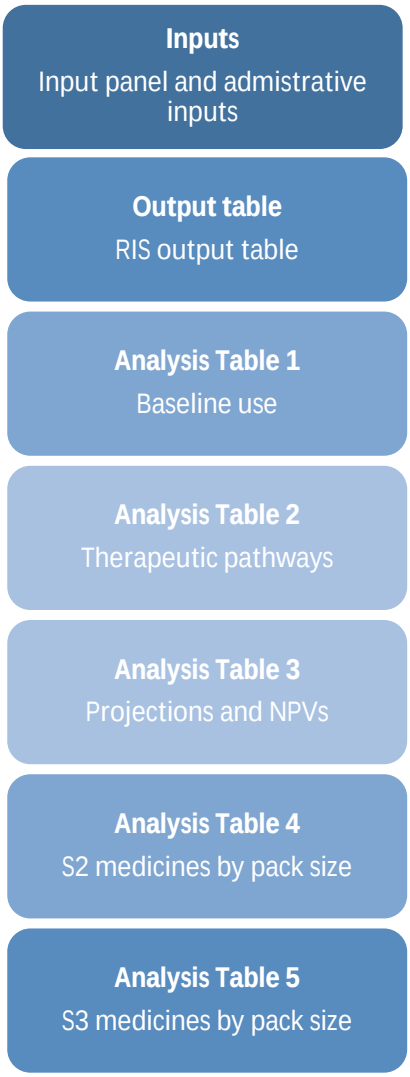
In addition, some consumers will continue to use low dose codeine combination medicines. Although no stakeholders provided an estimate of this number, all stakeholders who commented on this factor indicated that there would be a substantive reduction in volume of low dose codeine combination medicines used. This ongoing use of low dose codeine combination medicines would require additional GP visits and the model's estimate takes into account the number of repeats (up to 5) and the fact that these patients would likely be attending a GP for some of these consultations (in the absence of Scenario 4 being enacted).

The cost per additional MBS visit (specialist and non-referred) was derived using the data provided by Medicare specifically for this project. This took into account a range of assumptions made by Medicare about the share of these patients who would be bulkbilled and the mix of level A, B and C consultations. This actual mix was not provided to KPMG, only the total cost to Medicare for a range of potential volumes of consultations each year.

Output

The structure of the worksheet that presents the economic model is detailed in Figure E4.

Figure E4: Overview of structure of the Economic Model worksheet



Annex F – Interview Questionnaire for Sponsors

Context

On 1 October 2015, the Therapeutic Goods Administration (TGA) published an Interim Decision by the medicines scheduling delegate (the delegate) to adopt the proposal that all medicines containing codeine currently available over-the-counter (Schedule 2 and Schedule 3) be up-scheduled to Schedule 4, prescription-only medicines. See the TGA website for further detail regarding this decision, including the reasons for the decision: https://www.tga.gov.au/book-page/interim-decisions-matters-referred-expert-advisory-committee-11

The TGA undertook a series of public consultations regarding the interim decision, as well as seeking comment on alternative courses of action. Subsequently, on 19 November 2015, the Delegate announced that a final decision on the rescheduling of codeine would be deferred to allow a more thorough consideration of the numerous submissions and broader implications to current products in the market. See the TGA website for more information regarding this decision: https://www.tga.gov.au/book-page/part-final-decisions-matters-referred-expert-advisory-committee-11-14#codei

The TGA will be undertaking a regulatory impact review and producing a Regulation Impact Statement (RIS). To assist with production of the RIS, on 2 August 2016, TGA engaged KPMG to undertake economic, social and regulatory impact modelling on the range of codeine scheduling options as developed through the public submission process. The KPMG modelling will be provided to the TGA in late August 2016 to support the development of the RIS.

KPMG is engaging with codeine sponsors to better understand the potential impacts on industry, understand potential implementation considerations and inform the development of modelling to support the development of a RIS.

Scenarios

Formally, the options being considered for the purposes of constructing the RIS are presented in a step-wise manner, as follows:

Option 1	No change - the current scheduling of codeine remains appropriate.
Option 2	The current Schedule 2 entry for codeine in cough and cold medicine preparations be amended to reduce the pack size to not more than 3 days' supply and include a label warning that codeine can cause addition.
Option 3	The current Schedule 2 entries for codeine in cough and cold medicine preparations be up-scheduled to Schedule 3, and that the pack size be reduced to not more than 3 days' supply, and include a label warning that codeine can cause addiction.
Option 4	To up-schedule the current Schedule 2 entries for codeine to Schedule 4 and amend the current Schedule 4 and 8 entries.
Option 5	The current Schedule 3 entries for codeine (including, but not limited to codeine containing analgesics) be amended to reduce the pack size to not more than 3 days' supply and include a label warning that codeine can cause addiction.
Option 6	To up-schedule the current Schedule 3 entries for codeine to Schedule 4 and amend the current Schedule 4 and 8 entries.

In practice, these options could result in the following scenarios:

Scenario 1 (Option 1)	No change to the status quo.
Scenario 2 (Options 2 and 5)	Schedule 2 and Schedule 3 entries for codeine (including, but not limited to, cough and cold medicine preparations and codeine containing analgesics) be amended to reduce the pack size to not more than 3 days' supply and include a label warning that codeine can cause addition. Summary - Reduce pack size and include warning label for S2 and S3
Scenario 3 (Options 3 and 5)	The current Schedule 2 entries for codeine in cough and cold medicine preparations be up-scheduled to Schedule 3, and then all Schedule 3 entries (i.e. those currently Schedule 2 and those previously Schedule 2) for codeine (including, but not limited to, cough and cold medicine preparations and codeine containing analgesics), be amended to reduce the pack size to not more than 3 days' supply, and include a label warning that codeine can cause addiction. Summary - S2 up-scheduled to S3 - Reduce pack size and include warning label for S3
Scenario 4 (Options 4 and 6)	Schedule 2 and Schedule 3 entries for codeine (including, but not limited to, cough and cold medicine preparations and codeine containing analgesics) be up-scheduled to Schedule 4. Summary - S2 and S3 up-scheduled to S4

Topic 1 – Product strategy

1. How would your product strategy respond to an up-scheduling decision (i.e. Scenarios 3 or 4)?
   1.1. Would you rationalise your codeine portfolio?
   1.2. Would the current S2 and S3 product lines be reformulated?
   1.3. Would you substitute this share of the market with non-codeine containing S2 and S3 products and / or increased production of S4 product lines?

Topic 2 – Market response

2. (Contextual) How is the market for your S2 and S3 codeine products composed; i.e. principally individual patients or does this also include bulk institutional customers?
3. What are the anticipated impacts on demand for your products in the following scheduling scenarios? Consider impacts to individual patients (including different types of patients, i.e. acute / chronic users, dependent / non-dependent etc.), prescribers, institutional customers, and any other relevant demand groups.
   3.1. Scenario 3 (S2 up-scheduled to S3)
   3.2. Scenario 4 (for S2 up-scheduled to S4)
   3.3. Scenario 4 (for S3 up-scheduled to S4)
4. In the case of a rescheduling decision (i.e. Scenarios 3 and 4), what segment of patients currently consuming your codeine-containing S2 and S3 product lines do you anticipate will substitute these for other, non-codeine containing S2 and S3 products (rather than seek a prescription for the S4 products?)
5. Are there any other market responses that you are anticipating?

Topic 3 – Reduced pack sizes

6. (Contextual) How are changes to your packaging (outer and inner) implemented for your products?
7. In terms of physical pack sizes, what would be required to conform with a decision regarding limiting pack sizes to no more than three days' supply?
   7.1. Does this differ for types of packaging for all codeine containing products, i.e. blister pack inserts and boxes, liquid preparations, tablet bottles etc.?
   7.2. Do you have product lines currently in production that would meet the reduced pack size requirements, i.e. through placing a reduced number of blister pack inserts in existing boxes?
   7.3. What upfront costs would be incurred to implement changes in outer or blister packs per ARTG listing? (Either in dollar terms or FTE resources.)
8. What are the timeframe involved in making these changes?

Topic 4 – New warning labels

9. (Contextual) How are changes to labelling (outer and, where required, inner) implemented for your products?
10. What would be required to conform with a decision regarding mandatory warning labels?
    10.1. Consider for all types of packaging for all codeine containing products, i.e. blister pack inserts and boxes, liquid preparations, tablet bottles etc.
    10.2. Consider all key steps in the process (i.e. design, manufacture, printing etc.), including which of these are managed internally and which are outsourced.
    10.3. What upfront costs would be incurred? (Either in dollar terms or hours of FTE resources.)
11. What are the timeframes involved in making these changes?

Topic 5 – Updated listings

12. How many hours or FTE resources would usually be required to complete and submit an ARTG change application to the TGA?
13. If required under the decision made, would you anticipate creating a new PI/CMI (i.e. 'from scratch') or copying and modifying an existing PI/CMI as needed?
    13.1. How many hours or FTE resources would usually be required to undertake this task?
14. What are the timeframe involved in making these changes?
15. If S2 and S3 product lines were up-scheduled to S4 (i.e. Scenario 4), would you seek reimbursement under the PBS?
    15.1. If so, what costs would be incurred as a result? (Either in dollar terms or FTE resources.)

Topic 6 – Implementation timeline

(Contextual) Consideration has already been given (above) to timeframes required for changes to pack size, labelling, and updating listings.

16. Please indicate any other key considerations in relation to a projected implementation timeline.