



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Extract of Minutes
Medicines Evaluation Committee Meeting
30 July 2009

9.2 Review of cough and cold medicines in the treatment of children aged 2-12 years

The committee was requested to consider a TGA review of the efficacy and safety of OTC cough and cold medicines in children aged 2-12 years. The review proposed changes to the availability, labelling, packaging and scheduling of these products.

Reviews by the regulatory authorities in the USA, Canada, the United Kingdom, New Zealand and Australia of the safety and efficacy of OTC cough and cold medicines have each concluded that these products should not be used in children under 2 years of age. The US, Canadian and UK regulatory authorities have subsequently undertaken extensive independent reviews of the use of cough and cold medicines in children aged 2-12 years. Health Canada's Therapeutic Products Directorate (TPD) and the UK's Medicines and Healthcare products Regulatory Agency (MHRA) have each concluded that cough and cold medicines should not be used in children under 6 years of age, while the US Food and Drug Administration (FDA) has strongly endorsed voluntary moves by the US pharmaceutical industry to label cough and cold medicines with a warning that they should not be used in children under 4 years of age.

The TGA is currently reviewing the efficacy and safety of OTC cough and cold medicines in children aged 2-12 years. The TGA commissioned an external review of published data and information provided by sponsors of these products, which was conducted by XXXX and XXXX. A TGA Internal Panel comprising senior medical and scientific staff subsequently considered the conclusions and recommendations made in the external review report, together with additional information from TGA records. The TGA Internal Panel's recommendations addressed the safety, efficacy and availability of OTC cough and cold medicines for use in children, as well as packaging, poisons scheduling and public awareness issues. The MEC was asked to consider the internal and external review documents, and to advise on any actions to be taken by the TGA.

The following information was provided to the committee:

- The TGA Internal Panel Report on a review of the safety and efficacy of OTC cough and cold medicines in the treatment of children aged 2-12 years – this report included the recommendations of the TGA Internal Panel;
- Minutes of the TGA Internal Panel's considerations of the TGA's draft report and external review;
- Review of cough and cold medicines in children (external expert report by XXXX and XXXX);
- Tabulated summaries (prepared by the TGA) of clinical trials referred to in the [external expert report by XXXX and XXXX];

- A summary of industry submissions regarding the efficacy and safety of cough and cold medicines in children;
- A summary of actions taken by the TGA and other regulatory agencies in relation to the use of cough and cold medicines in children.

Members noted the scope of the TGA's review. The review considered the following substances, which are included in OTC oral and/or topical nasal cough and cold medicines registered in Australia for use in children:

- *Antihistamines*: brompheniramine, chlorpheniramine, dexchlorpheniramine, diphenhydramine, doxylamine, pheniramine, promethazine, triprolidine;
- *Antitussives*: codeine, dextromethorphan, dihydrocodeine, pentoxyverine, pholcodine;
- *Mucolytics/expectorants*: ammonium chloride, bromhexine, guaiphenesin, ipecacuanha, senega and ammonia;
- *Decongestants*: phenylephrine, pseudoephedrine, oxymetazoline, xylometazoline.

The TGA's review did not consider substances that are not currently used in cough and cold medicines in Australia, analgesic or antipyretic substances (eg. codeine [when intended solely as an analgesic], paracetamol, ibuprofen), or substances that are only used in listed or other complementary medicines. Complications which may be associated with coughs and colds, such as otitis media or pneumonia, were outside the scope of the review.

Discussion

The committee noted the TGA Internal Panel's recommendations, and the scope and outcome of the review. The committee was advised that there will be a public consultation period to allow consideration of the MEC's recommendations.

Briefly, the TGA Internal Panel had made recommendations regarding the efficacy, safety and availability of cough and cold medicines in children, packaging, poisons scheduling and public awareness, as follows:

1. **Efficacy, safety and availability:** The TGA Internal Panel had recommended that OTC cough and cold medicines should not be used in children under 6 years of age, and they should only be administered to children aged 6-12 years on the advice of a doctor or pharmacist. Product labelling for OTC cough and cold medicines should reflect these recommendations. The need for such limitations on use in children should be reviewed if and when better efficacy data become available.
2. **Packaging:** The TGA Internal Panel had recommended that all OTC cough and cold medicines should be marketed in containers with child-resistant closures.
3. **Scheduling:** The TGA Internal Panel had recommended that the NDPSC should be asked to consider including substances used in cough and cold medicines in Schedule 3 when intended for use in children aged 6-12 years, and in Schedule 4 for use in children under 6 years of age.
4. **Public awareness:** The TGA Internal Panel had recommended that these changes should be widely promoted and explained to medical practitioners, pharmacists, parents and caregivers. This would include current evidence that OTC cough and cold medicines have not been shown to be effective, and are potentially harmful in children under 6 years of age.

A member circulated a brief document summarising issues the member considered relevant to the efficacy and safety of OTC cough and cold medicines for use in children. In that document, the member had noted that the TGA Internal Panel's recommendations emphasised safety concerns with the use of cough and cold medicines in children aged under 6 years, and

suggested that more emphasis should be placed on their efficacy. The member contended that relying primarily on the safety of OTC cough and cold medicines could present problems, given their widespread use, with little evidence of substantial harm or deaths following recommended doses or overdosage of most substances, and relatively little information on less severe side effects. The member noted that few studies of the efficacy of cough and cold medicines (in any age group) reach current acceptable scientific standards, and the available evidence suggests a lack of efficacy in relieving coughs or other cold symptoms in children. However, withdrawal from sale of OTC cough and cold medicines intended for use in children may, particularly in the short-term, lead to off-label use of other medicines, or increased use of complementary medicines or alcohol, with the potential for more serious side effects. The member acknowledged that the TGA may not want to be seen to be out of step with the actions taken in other countries.

The committee supported the view that any recommendations against use of OTC cough and cold medicines in children under 6 years of age should emphasise the lack of evidence for efficacy of these products. The committee also agreed that the TGA should take action, in light of overseas actions, particularly in the UK and Canada.

A member commended the TGA's internal and external reviews, and agreed that OTC cough and cold medicines should not be marketed in Australia for use in children under 6 years, consistent with the decisions taken in the UK and Canada. However, the member was concerned that consumers would not realise that products, which had been marketed for many years for use in this age group, were no longer safe. Consequently, consumers may guess the dose for younger children if relevant doses are not included on the labels.

Another member stated that consumers should be educated regarding suitable alternative products or approaches to relieving coughs and colds in young children, for example, non-drug approaches (such as simple comforting of the child) may be used to make the child feel better, other simple approaches such as lemon and honey may help relieve some symptoms, while an analgesic/antipyretic agent may be appropriate for headache or fever. Any changes to poisons scheduling and availability of OTC cough and cold medicines would need to be accompanied by education of doctors and pharmacists, as well as consumers. Deleting doses for young children from product labelling, without an appropriate public awareness campaign, would be insufficient to address the issue. A member commented that consumers (and healthcare practitioners) have, in general, been effectively educated that antibiotics are not an appropriate treatment for uncomplicated coughs and colds, suggesting it is possible to change public attitudes to health issues over time.

A TGA officer noted that the TGA Delegate has to be satisfied in relation to the efficacy and safety of a new product prior to approving its inclusion on the Australian Register of Therapeutic Goods (ARTG). A member noted some difficulties in conducting efficacy studies using cough and cold medicines, since the responsible viruses are heterogeneous, and symptoms generally present sequentially.

Members considered that, while there have been few adverse drug reaction reports to the TGA for cough and cold medicines in children (an average of 3-4 per year since 1981), adverse drug reactions were likely to have been grossly under-reported to the TGA. It was suggested that many side effects would not be reported to the TGA. Instead, many consumers would just not use a product again.

The committee considered the specific recommendations on pages 12-13 of the TGA Internal Panel Report, as follows:

1. *Safety, efficacy and availability:* The TGA Internal Panel had recommended that OTC cough and cold medicines should not be used for the treatment of children under 6 years of age, and should only be given to children aged 6-12 years on the advice of a doctor or pharmacist. Product labels should not include doses for children younger than 6 years, and should advise against use in this age group (or in children younger than the lowest age for which there are doses on the labels, where this is older than 6 years).

A member proposed that the preamble for this recommendation should be amended. The preamble should note that no benefits have been shown with use of these products, and that there is potential harm from use, in children. The member agreed that the TGA should follow the approach taken overseas with regard to the use of cough and cold medicines in children.

Members agreed that most emphasis should be placed on efficacy, and that the heading to this point should be amended to "Efficacy, safety and availability". In addition, references to use of OTC cough and cold medicines in the treatment of children should be amended to refer to use of these products in children (as OTC cough and cold medicines do not treat the condition).

Following further discussion, the committee resolved to support the recommendation that OTC cough and cold medicines should not be used in children under 6 years of age, and that they should only be given to children aged 6-12 years on the advice of a doctor or pharmacist. Some changes were recommended to the wording stated in the TGA Internal Panel's report to address the specific issues noted by members of the committee.

2. *Packaging:* Members noted that the TGA currently requires child-resistant closures for most of the substances considered by the review. The committee endorsed the TGA Internal Panel's recommendation that child-resistant closures should be required for all OTC cough and cold medicines.
3. *Scheduling:* The TGA Internal Panel had recommended that the NDPSC should be asked to consider including substances in Schedule 3 when indicated for use in OTC cough and cold medicines for children aged 6-12 years, and in Schedule 4 when intended for use in children under 6 years of age. Currently, the sedating antihistamines are in Schedule 4 when intended for use (for any indication) in children under 2 years of age, whereas most of the other substances used in OTC cough and cold medicines are in Schedule 2 or unscheduled regardless of the age of the intended user or the indications for use.

The committee resolved that the NDPSC should be asked to consider including substances in OTC cough and cold medicines in Schedule 3 when intended for use in children aged 6-12 years, and in Schedule 4 for use in children under 6 years of age.

Members noted that rescheduling could be complex, as many of the substances are also used for conditions other than coughs and colds.

A member queried the merit of including substances that were considered to lack efficacy in Schedule 4 for prescribing by medical practitioners.

4. *Public awareness:* The committee supported the TGA Internal Panel's recommendation that the proposed changes would need to be widely promoted and explained to medical practitioners, pharmacists, parents and caregivers. Members suggested further organisations (in addition to those listed in the TGA Internal Panel's report) that could assist in promoting public awareness of the changes.

The committee considered that its recommendations should apply to topical preparations, such as oxymetazoline and xylometazoline nasal decongestants, in addition to cough and cold medicines for oral administration. Topical medicines can have systemic side effects and the TGA's external review had noted that there is very little evidence of efficacy of these products in children for relief of symptoms of the common cold.

The committee's agreed recommendations were as follows:

Efficacy, safety and availability

Health authorities in Australia, the UK and Canada have recently fully considered the efficacy and safety data for cough and cold medicines intended for use in children. It is currently believed that there is a lack of evidence that these medicines are effective in treating cough and cold symptoms in children. It is recognised also that there are potential dangers associated with use of these medicines, although these have rarely been seen in Australia. Action was previously taken in Australia advising that these medicines should not be used in children aged less than 2 years. The following further actions are now proposed:

It is recommended that over-the-counter cough and cold medicines should not be used in children under 6 years of age, and they should only be administered to children aged 6-12 years on the advice of a doctor or pharmacist.

To this end, it is recommended that:

- **the labelling of over-the-counter cough and cold medicines should not include dosage instructions for children under 6 years of age;**
- **if doses are included for children aged 6-11 years, the labelling must include:**
 - a) **a statement advising against use in children younger than the lowest age specified in the directions for use; and**
 - b) **a statement advising that the product should only be administered to children between the lowest specified age and 12 years on the advice of a doctor or pharmacist; and**
- **the labelling of all over-the-counter cough and cold medicines with dosage specified only for adults and/or for those aged 12 and above should contain a statement specifically advising against their use in children under 12 years of age.**

This approach would bring the regulation of cough and cold preparations in Australia into line with measures in place in the UK and Canada. The need for such limitations on use in children should be reviewed if and when better efficacy and safety data become available.

Packaging

The current requirements under TGO 80 are for most, but not all, of the substances in OTC liquid cough and cold medicines to be in child-resistant packaging. In the interests of consistency and improved safety,

It is recommended that all over-the-counter cough and cold medicines should be marketed in containers with child-resistant closures.

This requirement would bring the packaging of all OTC cough and cold preparations in Australia into line with measures in place in the UK and with recommendations made by the regulators in the USA.

Scheduling

The current scheduling of most cough and cold medicines as Schedule 2 (pharmacy only) medicines ensures that advice is available but does not ensure that such advice is given regarding use in children. Such advice is more likely to be given if these medicines were Schedule 3 (pharmacist only) medicines. For this reason,

It is recommended that the NDPSC be asked to consider including substances used in cough and cold medicines in Schedule 3 when intended for use in children aged 6-12 years, and in Schedule 4 for use in children under 6 years of age.

Public awareness

The changes recommended above would need to be widely promoted and explained to medical practitioners, pharmacists, parents and caregivers. For this reason,

It is recommended that particular efforts be directed towards advising consumers, medical practitioners and pharmacists on the best current care for children with coughs and colds. This would now include:

- **current evidence of the lack of efficacy of OTC cough and cold medicines, including the new recommendations that these products should not be used in children under 6 years of age;**
- **recognition that there are rare potential dangers associated with use of OTC cough and cold medicines in this age group;**
- **simple general measures that can be used by parents or carers to help their child; and**
- **the place for simple medicines, when needed.**

Education campaigns should be directed through organisations such as the National Prescribing Service, professional colleges such as the Royal Australian College of General Practitioners, Australian College of Rural and Remote Medicine and the Royal Australian College of Physicians Paediatrics and Child Health Division, medical schools and other medical training institutions, the Pharmaceutical Society of Australia, Pharmacy Guild, College of Pharmacy Practice, Consumers Health Forum and the pharmaceutical industry.

It was agreed that these recommendations should be circulated to MEC members for comment, before the wording is finalised.

The committee noted that there will be a public consultation period to allow consideration of the MEC's recommendations.