FOI 27-3697 - Document 1

Australian Government
Department of Health
Therapeutic Goods Administration

Record of the 31st meeting of the Advisory Committee on Medicines Scheduling

23-24 June 2020

TRIM Reference no. D20-926060

TGA Health Safety Regulation

FOI 27-3697 - Document 1

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FOI 27-3697 - Document 1

Contents

1 Preliminary Matters 4

1.1 Opening of the Meeting 4

1.2 Conflict of Interest 5

1.3 Procedural Matters 5

2 Proposed Changes to the Poisons Standard 6

s.22

2.4 Clotrimazole 13

s.22

3 Other Matters for Consideration 21

4 Next meeting 21

5 Closure 21

1 Preliminary Matters

1.1 Opening of the Meeting

The 31st meeting of the Advisory Committee on Medicines Scheduling ACMS was held via teleconference on 23-24 June 2020.

The meeting was chaired by A/Prof Suzanne Nielsen, who opened the meeting at 9:33 am on Tuesday 23 June 2020 and at 2:00 pm on Wednesday 24 June 2020. Attending members and observers were welcomed and new members were introduced.

Members were informed that the discussions and recommendations of the committee are confidential until the interim decisions are published.

A quorum was present for all decisions. Those present at the meeting were:

ACMS Members

s.47F(1)	Appointed member, Chair
	Appointed member
	Appointed member
	Appointed member
	Appointed member
	Appointed member
	Commonwealth member
	ACT member
	NSW member
	NT member
	QLD member
	SA member
	TAS member (alternate)
	VIC member
	WA member

Specialist Advisors

s.47F(1)	Proposed ACMS Appointed member
	Proposed ACMS Appointed member

Medicines Scheduling Secretariat and Committee Support Unit

s.47E(d)	Commonwealth Department of Health, TGA
	Commonwealth Department of Health, TGA
	Commonwealth Department of Health, TGA
	Commonwealth Department of Health, TGA
	Commonwealth Department of Health, TGA

Observers

s.47E(d)	Commonwealth Department of Health, Medicines delegate
Mr Avi Rebera	Commonwealth Department of Health, TGA
s.47E(d)	Commonwealth Department of Health, TGA
	Commonwealth Department of Health, TGA
	Commonwealth Department of Health, TGA
	Commonwealth Department of Health, TGA
	Commonwealth Department of Health, TGA
	Commonwealth Department of Health, TGA
	Commonwealth Department of Health, TGA
	NSW Ministry of Health
	Proposed ACMS NT member (alternate)

Apologies

- s.47E(d) s.47E(d) (ACMS nominated member for ACT). s.47E(d) attended in place.

1.2 Conflict of Interest

Declared conflicts s.47E(d) were discussed and it was agreed that this member could be present for the Committee discussion.

1.3 Procedural Matters

Members were informed of various housekeeping rules to ensure the smooth running of the meeting via teleconference.

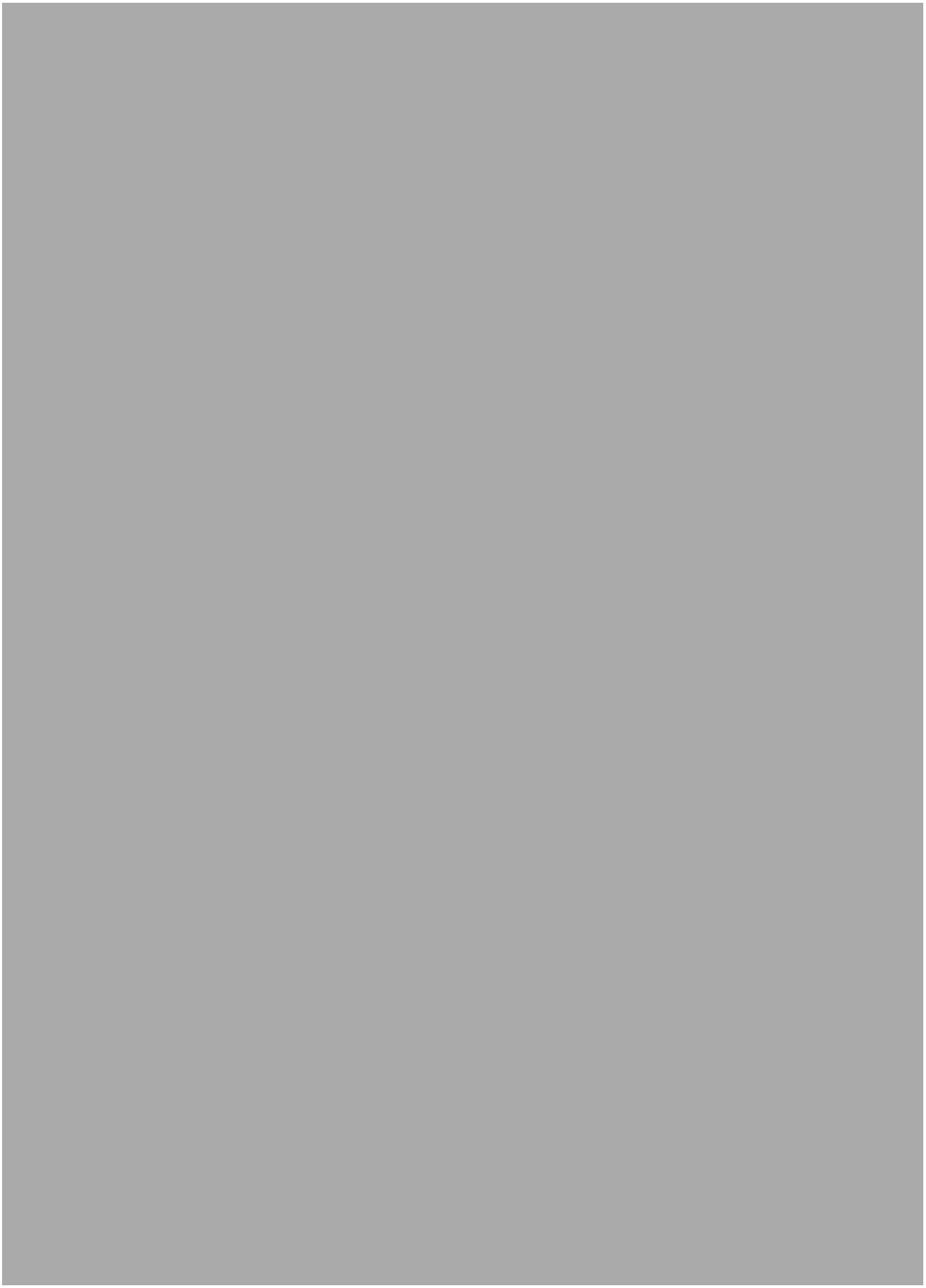
All present were reminded of confidentiality in relation to all matters discussed by the Committee and that all decisions are to remain confidential until they are published along with the delegate's interim decision.

2 Proposed Changes to the Poisons Standard

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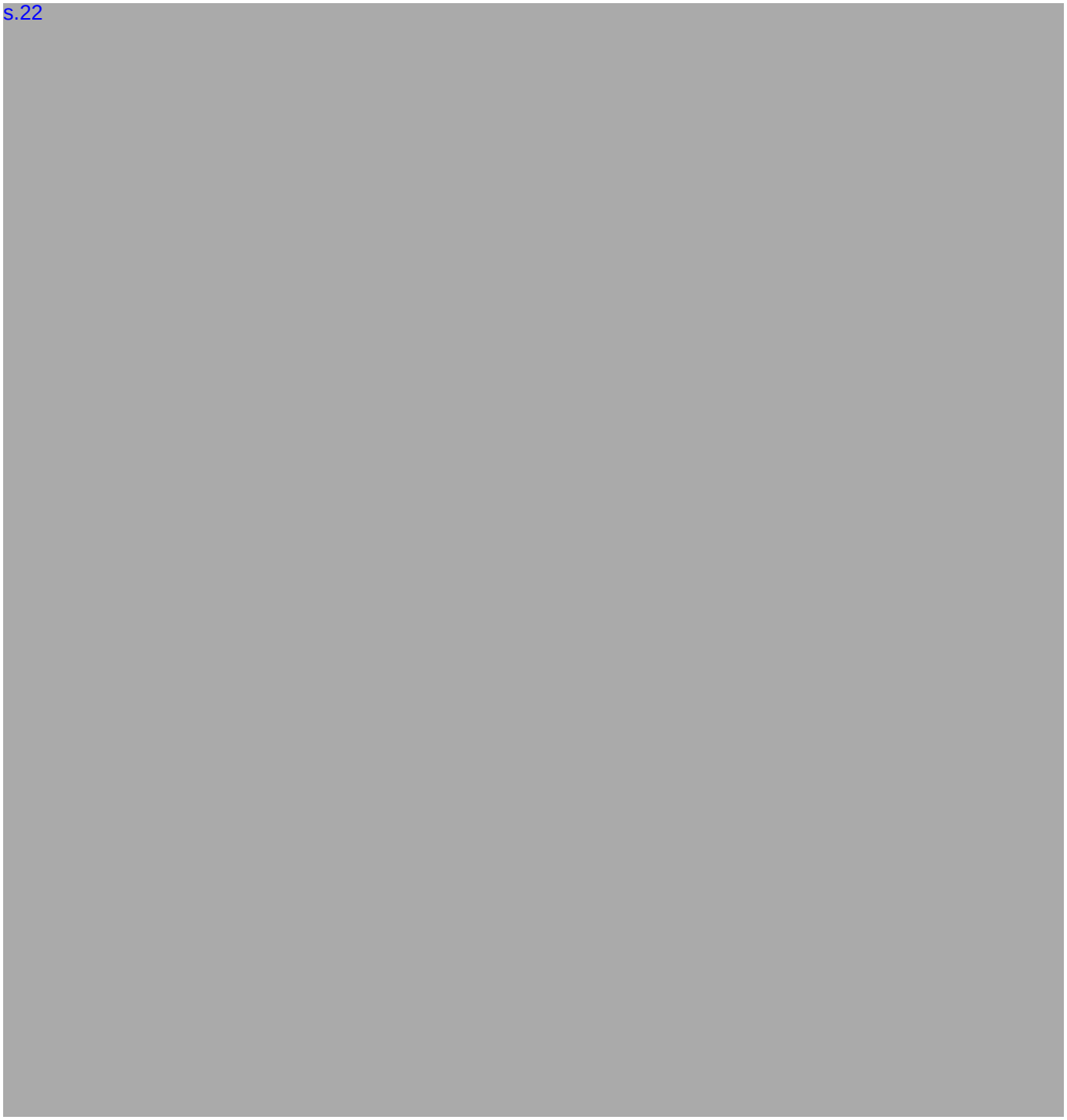


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2.4 Clotrimazole

Advice for the delegate's consideration

The Committee recommends that the current scheduling of clotrimazole in the Poisons Standard remains appropriate.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the and extent of use; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a

substance; and (f) any other matters that the Secretary considers necessary to protect public health.

- The key arguments for down scheduling clotrimazole 1% in preparations for vaginal use are that women can accurately self-diagnose and that labelling on its own is sufficient to prompt women to seek medical advice if unresponsive to treatment.
- In 2018, the delegate made a final decision[1] not to amend the current scheduling of clotrimazole, with the major risks identified as inaccurate self-diagnosis and delayed treatment if the product is used for vaginal infections not caused by *Candida albicans*. These previous concerns regarding misdiagnosis and delayed treatment where a woman self-diagnoses and self-selects a treatment for vaginal symptoms remain unchanged.
- Clotrimazole 1%, does not meet the SPF Scheduling Factors for Schedule 2:
  - Schedule 2 medicines are for minor ailments or symptoms that can easily be self-diagnosed by consumers and are unlikely to be confused with other more serious diseases or conditions. The TAFT project conducted by Tenni *et al* (2005) about treatment of vulvovaginal candidiasis (VVC) concluded that *'women who self-diagnose VVC do so poorly'* and that '*approximately two thirds of patients who self-diagnose vaginal candidiasis are incorrect'*[2]. Another qualitative Australian study of bacterial vaginosis (BV) conducted by Bilardi *et al* (2016) found that women who experienced BV for the first time treated themselves for VVC and '*consequently did not seek medical assistance for up to a few weeks after symptoms first presented, however, sought treatment sooner with subsequent episodes*'[3].
  - The quality use of clotrimazole cannot be achieved by labelling, packaging and/or the provision of other information. The proposed warning statement '*For women who have previously been diagnosed with vaginal thrush*' does not mitigate the risk of inaccurate self-diagnosis and subsequent delay in appropriate treatment.
- The applicant seeks to make clotrimazole vaginal cream available for self-selection on the basis of a survey of 840 Australian women commissioned by the Applicant. The generalisation of the finding that '*most women were recurrent sufferers (82%) with only 18% being first time sufferers*' may be questioned given research into prevalence estimates of VVC and recurrent VVC from seven countries. According to the study by Blostein *et al (2017)*, the estimated probability of VVC by age 50 varied widely by country from 23% to 49% (mean 39%), as did the estimated probability of recurrent VVC after VVC from 14% to 28% (mean 23%)[4].
- The applicant claims that women who have previously had diagnosed vaginal candidiasis are already familiar with the symptoms and that labelling instructions would provide all the necessary information for safe and effective use. However, the US study by Ferris *et al* that

[1] https://www.tga.gov.au/book-page/19-clotrimazole-0

[2] Tenni P, Hughes J, McCloskey J and Hilmi S. (2005) Ensuring the appropriateness of topical over-the-counter antifungal agents for clients with self-diagnosis vaginal thrush (the TAFT Project)Pharmacy of Australia: http://6cpa.com.au/wp-content/uploads/Ensuring-the-appropriateness-of-topical-over-the-counter-antifungal-agents-for-clients-with-self-diagnosed-vaginal-thrush-final-report.pdf

[3] Bilardi J, Walker S, McNair R, Mooney-Somers J, Temple-Smith M, Bellhouse C, *et al.* (2016) Women's Management of Recurrent Bacterial Vaginosis and Experiences of Clinical Care: A Qualitative Study. PLOS ONE11(3): e0151794. https://doi.org/10.1371/journal.pone.0151794

[4] Blostein, F., Levin-Sparenberg, E., Wangner, J. and Foxman, B. (2017) Recurrent vulvovaginal candidiasis. Annals Of Epidemiology Vol 27, Issue 9: 575-582 https://www.sciencedirect.com/science/article/abs/pii/S1047279717302685

was discounted by the Applicant, found that only 34% of women who purchased over the counter antifungal treatment for presumed VVC who were then evaluated by clinical and laboratory tests actually had VVC. The authors concluded '*A history of a previous clinically based diagnosis of vulvovaginal candidiasis and reading the package label do not help women self-diagnose vulvovaginal candidiasis properly. Ready access to these products is associated with wasted financial expenditures, unfulfilled expectations, and a delay in correct diagnosis for a substantial number of women*'[5].

- The Committee notes that both the AMA and the ACD support down-scheduling, while the PGA, the PSA and NSW PIC are opposed.
- The retention of the current Appendix F warning statements for Schedule 2 whilst removing the means to limit sale where any of the situations in the warnings are present, would reduce the effectiveness of such warnings as a risk mitigation strategy. Further, the retention of the warning statement that a woman should seek medical advice before first course of treatment is in line with the SPF Scheduling Factors for Schedule 3.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

Benefits:

– Effective treatment of vulvovaginal candidiasis caused by *Candida albicans*.

Risks:

– Well established safety profile with few risks from use.

b) the purposes for which a substance is to be used and the extent of use of a substance

– For the treatment of vulvovaginal candidiasis caused by *Candida albicans* (clotrimazole 1% for vaginal use).

c) the toxicity of a substance

– Clotrimazole is an imidazole derivative that has low levels of systemic absorption from vaginal administration.

– It is extensively metabolised in the liver to inactive compounds. No carcinogenicity or mutagenicity was observed in animal studies.

– Vaginal clotrimazole is generally well tolerated with the main reported adverse reactions being local irritation (e.g. burning, erythema). Hypersensitivity/allergic reactions are rare.

– Vaginal clotrimazole is considered safe to use in pregnancy (a 1-week course) and in breastfeeding.

d) the dosage, formulation, labelling, packaging and presentation of a substance

– Clotrimazole 10mg/ml (1%) cream to be applied once daily for 6 days.

– Warning statements are already required for clotrimazole vaginal preparations. The effectiveness of the proposed packaging warning statement 'For women who have previously been diagnosed with vaginal thrush' is unclear given there is evidence that

[5] Ferris DG, Nyirjesy P, Sobel JD, Soper D, Pavletic A, Litaker MS: Over-the-counter antifungal drug misuse associated with patient-diagnosed vulvovaginal candidiasis. Obstet Gynecol. 2002, 99: 419-425: https://pubmed.ncbi.nlm.nih.gov/11864668/

women do not read the package information and that reading the label does not improve the accuracy of self-diagnosis.

e) the potential for abuse of a substance

– There is no evidence of dependence or abuse of clotrimazole vaginal preparations, however misuse due to misdiagnosis is probable.

f) any other matters that the Secretary considers necessary to protect public health

– Repeated studies and clinical experience demonstrate that self-diagnosis is inaccurate. Self-misdiagnosis cannot be addressed by labelling, packaging, and the provision of other information alone.

– Use may delay diagnoses so does not meet Scheduling factors for Schedule 2.

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3 Other Matters for Consideration

4 Next meeting

The members noted that the next meeting of the ACMS is scheduled for 3-5 November 2020.

5 Closure

The Chair closed the meeting at 1:00 pm on Tuesday 23 June 2020 and at 4:15 pm on Wednesday 24 June 2020.

Acknowledged by email, 20 July 2020 (D20-3036685)

Associate Professor Suzanne Nielsen Date 20 July 2020

Chair

31st Meeting of the Advisory Committee on Medicines Scheduling

SPEAKER'S NOTES AND RECOMMENDATION

ACMS MEETING #31

JUNE 2020

AGENDA ITEM 2.4: CLOTRIMAZOLE

First Speaker: s.47F(1)

Main Discussion Points:

- The scheduling proposal is to create a new Schedule 2 entry for low concentration clotrimazole products for vaginal use where products contain 1 per cent of less of clotrimazole. A current product that would fall into this proposed Schedule is a 1% cream requiring 6 days treatment. Clotrimazole vaginal products of higher strengths would remain in Schedule 3, that is, pessaries, a 2% cream for 3 days treatment and a 10% cream for a single day treatment. The current warning statements in Appendix F, Part 3 would apply to both Schedule 3 and Schedule 2 vaginal preparations.
- Clotrimazole is an imidazole derivative that has broad spectrum antifungal activity. It is used topically as it is practically insoluble in water and has poor absorption from the gastrointestinal tract. There are low levels of systemic absorption from vaginal administration.
- Clotrimazole products for human use are in schedules 2, 3, and 4 and products for the treatment of tinea pedis are unscheduled. Dermal and nail preparations are S2 while vaginal preparations are S3 with an Appendix H entry and Appendix F warning statements to be used. For external treatment of animals clotrimazole is in schedule 6. The RASML warning statements required for vaginal preparations are:

  54. Seek medical advice before first course of treatment.
  63. See a doctor if you are pregnant or diabetic.
  64. See a doctor if no better after (Insert number of days as per approved Product Information) days.
  66. See a doctor if problem returns

- The applicant's reason for the proposal is to make a 1% clotrimazole vaginal cream directly available to consumers from pharmacies without the need to consult a pharmacist or a doctor because the consumers were embarrassed or uncomfortable about speaking with a pharmacist which deters them from seeking treatment. Because of the embarrassment and a quoted 76% confidence in the ability to self-diagnose and treat thrush, consumers wanted to self-select a product directly. The applicant cited a 2016 survey commission by the applicant as the basis for this position. The survey of 840 women was conducted in 2013, had been included in the 2017 application considered by the Committee.
- The applicant stated that women who have previously had diagnosed vaginal candidiasis were already familiar with the symptoms and that labelling instructions would provide all the necessary information for safe and effective use.

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- The applicant states that clotrimazole vaginal creams are safe and effective with low potential toxicity and low potential for abuse and therefore meet the Scheduling Factors for Schedule 2.
- Information is provided about the safety of clotrimazole vaginal preparations based on Australian and international experience and that these products are available for general sale in several countries, notably the UK and the USA.
- Clotrimazole products for vaginal use were first down-scheduled to Schedule 3 in 1994 with the current warning statements. Applications for an S2 entry for clotrimazole vaginal preparations were made in 1996, 2006 and 2007 and in 2017. The 2017 application was not supported due to risks related to inaccurate self-diagnosis and delayed treatment of other conditions.
- The applicant argues that the reasons given for the 2017 decision based on the studies cited in that interim decision are not justified on the basis that.
  - For the risk of mis-diagnosis, the published studies which compared presumptive diagnosis with laboratory confirmed diagnosis were old (published 2002-2010). The generalisation of these studies to the current Australian context was questioned because, apart from the Tenni study, the studies were conducted overseas in places that have different legislation and labelling requirements. It is hard to see how this is relevant to studies looking at the accuracy of self-diagnosis.
  - For delayed treatment, that if symptoms did not get better, women would seek treatment, and that the proposed labelling would say this.
  - For the study that found that women did not read labels, the study was conducted among US military women and that labelling in the context of over-the- counter purchase in Australia and increased access to information on the internet so that the relevance of the study was questionable.
- The applicant has not presented new information. The 2005 Australian study (Tenni, 2005) was again included as evidence in support of a claim that consumers could accurately self-diagnose vaginal candidiasis (the rate was 47%) or that in the case where the consumer did not actually have vaginal candidiasis (42%) that at least unnecessary treatment with clotrimazole would not have been harmful.
- There are currently 92 non-prescription clotrimazole products on the ARTG. Products include composite packs that combine clotrimazole vaginal cream with oral fluconazole.
- Five public submissions were received, two in support, one with reservations and two opposed. The Australasian College of Dermatologists supported the proposal and the AMA did not oppose the proposed change. The NSW Poisons Information Centre did not consider a change to schedule 2 would increase poisoning risk however an increased potential for therapeutic misuse was raised.
- The PSA and the Pharmacy Guild did not support the proposal. There were concerns about inappropriate use due to inaccurate self-diagnosis. The same findings of the Tenni study were expressed as 53% of women seeking to purchase a topical antifungal for presumed vulvovaginal candidiasis were confirmed to have another infectious cause or that symptoms were not secondary to infection. Interaction with a pharmacist could help minimise the risk of mis-diagnosis and delay in treatment of other health conditions. Unnecessary treatment with an anti-infective agent was also not consistent with antimicrobial stewardship; increasing resistance of Candida species to azole antifungals has been found. PSA also

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identified that a Schedule 2 entry would not allow self-selection by women in Western Australia and Queensland as Schedule 2 medicines are kept behind the counter.

Evaluation:

- The previous concerns about misdiagnosis and delayed treatment where a woman self-diagnoses and self-selects a treatment for vaginal symptoms remain.
- Making a clotrimazole product available for self-selection in some States and Territories that must be used for 6 days to find out whether treatment was ineffective rather than Schedule 3 product requiring only 3 or 1 day treatment does not reduce the risk of incorrect self-diagnosis and would delay treatment further compared to the Schedule 3 products.
- The US study by Ferris that was discounted by the applicant found that only 34% of women who purchased over the counter antifungal treatment for presumed vulvovaginal candidiasis (VVC) who were then evaluated by clinical and laboratory tests actually had VVC. The authors concluded 'A history of a previous clinically based diagnosis of vulvovaginal candidiasis and reading the package label do not help women self-diagnose vulvovaginal candidiasis properly. Ready access to these products is associated with wasted financial expenditures, unfulfilled expectations, and a delay in correct diagnosis for a substantial number of women' (Ferris DG, Nyirjesy P, Sobel JD, Soper D, Pavletic A, Litaker MS: Over-the-counter antifungal drug misuse associated with patient-diagnosed vulvovaginal candidiasis. Obstet Gynecol. 2002, 99: 419-425.)
- Clotrimazole vaginal treatments have been available over-the-counter in the US since the 1990s. An earlier study by Ferris found that only 11% of women completing a questionnaire designed to test their knowledge of different vaginal conditions accurately diagnosed common causes of vaginitis after reading classic case scenarios. Women with a prior VVC diagnosis did somewhat better, but still poor (34.5%)(Ferris D.G., Dekle C., Litaker M.S.: Women's use of over-the-counter antifungal medications for gynecologic symptoms.J Fam Pract 1996; 42: pp. 595-600)
- The study by Tenni (2005) also found no association between the 'history of the same symptoms diagnosed as VVC' and culture-proven VVC in the current episode. Tenni found that 53% of women seeking antifungals for presumed VVC did not have VVC and would not have gained relief from use of a vaginal antifungal. A more recent study from the US found a similar poor relief rate of 57% among women who reported they self-diagnosed and self-medicated with over-the-counter products https://link.springer.com/article/10.1186/s12905-019-0748-8
- A more recent Swedish study of women seeking treatment for presumed VVC found 66% had VVC confirmed by yeast cell culture (Bullarbo M, Andersch B, Samuelson E, Lindgren A, Kondori N, et al. (2017) Self-diagnosis of Vulvovaginal Candidiasis is Poor – A Comparison of Diagnostic Methods Introducing β -Glucan as a Complement. Reprod Syst Sex Disord 6: 202.)
- Another qualitative Australian study of bacterial vaginosis (BV) found that women who experienced BV for the first time treated themselves for VVC and 'consequently did not seek medical assistance for up to a few weeks after symptoms first presented, however, sought treatment sooner with subsequent episodes' (Bilardi J, Walker S, McNair R, Mooney-Somers J, Temple-Smith M, Bellhouse C, et al. (2016) Women's Management of Recurrent Bacterial

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Vaginosis and Experiences of Clinical Care: A Qualitative Study. PLoS ONE11(3): e0151794. https://doi.org/10.1371/journal.pone.0151794).

- The applicant seeks to make a clotrimazole vaginal cream available for self-selection on the basis of a survey of 840 Australian women commissioned by the applicant. Unfortunately, the application does not include sufficient detail of the subject selection and survey methodology to assess the quoted findings. The generalisability of the finding that 'most women were recurrent sufferers (82%) with only 18% being first time sufferers' may be question given research into prevalence estimates of VVC and recurrent VVC from 7 countries (https://www.sciencedirect.com/science/article/abs/pii/S1047279717302685). The estimated probability of VVC by age 50 varied widely by country (from 23% to 49%, mean 39%), as did the estimated probability of RVVC after VVC (from 14% to 28%, mean 23%). The findings of the survey presented in the executive summary and used in the application are presented in a way that overstates the level of discomfort of respondents in in talking with a pharmacist about their symptoms. The application says 70% reported being slightly or very uncomfortable but equally the results could have been presented as 78% of respondents were not at all bothered or slightly uncomfortable (38% slightly uncomfortable).
- The effectiveness of the proposed packaging warning statement 'For women who have previously been diagnosed with vaginal thrush' to direct women with not previous diagnosis to speak with the pharmacist is not certain given the findings of a 5 country survey study (Johnson, SR; Griffiths, H; Humberstone, FJ. Attitudes and Experience of Women to Common Vaginal Infections. Journal of Lower Genital Tract Disease: October 2010 – 14(4)287-294. doi: 10.1097/LGT.0b013e3181d85bb7). The study included women from the UK and Sweden where these products are general sale – 16% of UK respondents had never been examined. The authors also stated that although bacterial vaginosis is the most common vaginal infection that most respondents thought they had experienced VVC only.
- Note: The proposed carton shown on page 76 of the application is for a 1 day pessary and cream combination pack containing a 500mg clotrimazole pessary and a 10g tube of 1% clotrimazole cream.

Delegates Questions:

1. Noting this was previously been seen in ACMS in 2017 are there reasons to change the previous advice? Then the major risk identified was inaccurate self-diagnosis, or delayed treatment if the product is used to treat other vaginal infections not caused by Candidia albicans.

Advice: No. The proposal to make an S2 product that must be used for 6 days before determining it is ineffective potentially increases the delay in effective treatment.

2. Is it appropriate to be accessed without direct pharmacist intervention?

Advice: No. The study by Tenni (2005) proposed a diagnostic flowchart to assist pharmacists to ensure appropriate use of over the counter antifungals and appropriate referral that to improve 'the rate of identifying those with microbiologically proven VVC to an expected rate of at least 60%" compared to 47% of correct self-diagnoses, and to aid prompt referral of those women with potentially more serious medical conditions (13% of women in that study)

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3. If so, noting the strength requested to down schedule is this appropriate or should it also cover stronger preparations?

Advice: Not applicable

Recommendation:

Retain the existing scheduling.

The concerns regarding misdiagnosis and delayed treatment that were concerns in 2017 remain.

The rationale to make a lower strength product available for self-selection by women who are uncomfortable or embarrassed to interact with a pharmacist is flawed on two counts:

- In Queensland and Western Australia, Schedule 2 products are behind a counter – a woman must ask for the product.
- The 1% product must be used for 6 days rather than the 3 or 1 day clotrimazole treatments that remain in Schedule 3, before treatment failure identifies the likelihood of mis-diagnosis. This proposal would delay correct treatment compared to the remaining Schedule 3 products.

The retention of the current Appendix F warning statements for Schedule 2 while removing the means to limit sale where any of the situations in the warnings are present would reduce the effectiveness of such warnings as a risk mitigation. The retention of the warning statement that a woman should seek medical advice before first course of treatment is in line with the criterion for schedule 3.

A copy of this section must be sent to the Scheduling Secretariat (medicines.scheduling@health.gov.au) at least 5 business days before the meeting **23 June 2020**.

52E Table

Please ensure that you provide clear and concise reasons in the 52E Table below in **dot point** form. These reasons will be presented as a starting point to the committee for discussion; we therefore ask that only salient points are provided.

52E(1) Considerations	*Reasons*
a – the risks and benefits of the use of a substance	Clotrimazole vaginal preparations are effective treatments for vulvovaginal candidiasis. The risks associated with their use are related to misdiagnosis and delayed treatment for the actual cause, as well as the financial impact of purchasing an ineffective product.
b – the purposes for which a substance is to be used and the extent of use of a substance	Clotrimazole vaginal preparations are used for vuvovaginal candidiasis. The estimated probability of VVC by age 50 varied widely by country (from 23% to 49%, mean 39%) in research drawn from 7 countries.
c – the toxicity of a substance	Clotrimazole is an imidazole derivative that has low levels of systemic absorption from vaginal administration. It is extensively metabolised in the liver to inactive compounds. No carcinogenicity or mutagenicity was observed in animal studies. Vaginal clotrimazole is considered safe to use in pregnancy (a 1-week course) and in breastfeeding. Vaginal clotrimazole is generally well tolerated with the main reported adverse reactions being local irritation (e.g. burning, erythema). Hypersensitivity/allergic reactions are rare.
d – the dosage, formulation, labelling, packaging and presentation of a substance	Warning statements are already required for clotrimazole vaginal preparations. The effectiveness of the proposed packaging warning statement 'For women who have previously been diagnosed with vaginal thrush' is unclear given there is evidence that women do not read the package information and that reading the label does not improve the accuracy of self-diagnosis.
e – the potential for abuse of a substance	There is no evidence of dependence or abuse of clotrimazole vaginal preparations, however misuse due to misdiagnosis is probable.
f – any other matters that the Secretary considers	Consideration should be given to strengthening the required warning statements if a Schedule 2 entry for clotrimazole is made

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FOI 27-3697 - Document 2

necessary to protect public health	

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SPEAKER'S NOTES AND RECOMMENDATION

ACMS MEETING #31

JUNE 2020

AGENDA ITEM 2.4: CLOTRIMAZOLE

Second Speaker: s.47F(1)

Main Discussion Points:

- Proposal by Bayer Australia to down schedule clotrimazole 1% in preparations for vaginal use from schedule 3 to schedule 2.
- The difference between this proposal compared to the 2017 proposal is that it is limited to clotrimazole 1% and not all the vaginal preparations currently in schedule 3.
- The key argument for down scheduling clotrimazole 1% in preparations for vaginal use is that women can accurately self-diagnose but feel too embarrassed to ask pharmacists for the treatment. A Bayer sponsored consumer survey was supplied to support this claim.
- Applicant claims labelling on its own is sufficient to prompt women to seek medical advice if unresponsive to treatment.
- The same risks remain as in 2017– inaccurate self-diagnosis risk is not mitigated by labelling.
- The TAFT project conducted by Tenni et al concluded that "women who self-diagnose VVC do so poorly" and that "approximately two thirds of patients who self-diagnose vaginal candidiasis are incorrect".
- This observation is supported by the research of Ferris et al 2002 and Schwiertz et al 2006.
- AMA and ACD supportive, PSA, Guild and NSW PIC opposed
- Proposal does not satisfy the scheduling factors for Schedule 2, namely the criteria:
  - The quality use of the medicine can be achieved by labelling, packaging, and/or provision of other information;
  - The use of the medicine at established therapeutic dosage levels is not likely to mask the symptoms or delay diagnosis of a serious condition.

Delegates Questions:

1. Noting this was previously been seen in ACMS in 2017 are there reasons to change the previous advice? Then the major risk identified was inaccurate self-diagnosis, or delayed treatment if the product is used to treat other vaginal infections not caused by Candidia albicans.

Advice: No

2. Is it appropriate to be accessed without direct pharmacist intervention?

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Advice: No

3. If so, noting the strength requested to down schedule is this appropriate or should it also cover stronger preparations?

Advice: N/A

Recommendation:

Scheduling remains appropriate

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52E Table

Please ensure that you provide clear and concise reasons in the 52E Table below in **dot point** form. These reasons will be presented as a starting point to the committee for discussion; we therefore ask that only salient points are provided.

52E(1) Considerations	***Reasons***
a – the risks and benefits of the use of a substance	Risks - Self-misdiagnosis & self-mistreatment - Potential of masking more serious underlying conditions including bacterial vaginosis, UTI, STI and undiagnosed or uncontrolled diabetes and delaying appropriate treatment Benefits - More ready access a safe and effective treatment of vulvovaginal candidiasis caused by Candida albicans without pharmacist intervention/consultation (removes embarrassment seeking treatment)
b – the purposes for which a substance is to be used and the extent of use of a substance	For the treatment of vulvovaginal candidiasis caused by Candida albicans (clotrimazole 1% for vaginal use)
c – the toxicity of a substance	Low toxicity
d – the dosage, formulation, labelling, packaging and presentation of a substance	Labelling on its own does not mitigate risk of self-misdiagnosis or delay seeking treatment of more serious underlying condition. Evidence of women who do not read the label and that reading the label does not improve accuracy of self-diagnosis.
e – the potential for abuse of a substance	Low potential for abuse
f – any other matters that the Secretary considers necessary to protect public health	

A copy of this section must be sent to the Scheduling Secretariat (medicines.scheduling@health.gov.au) at least 5 business days before the meeting **23 June 2020**.

FOI 27-3697 - Document 3

A copy of this section must be sent to the Scheduling Secretariat (medicines.scheduling@health.gov.au) at least 5 business days before the meeting **23 June 2020**.

SUGGESTED GUIDELINES FOR CONTENT OF PRESENTATION

- Scheduling Application
  - Accuracy (or otherwise) of applicant's claims
  - Additional note: Some applications include justifications based on proposed product labelling/presentation (e.g. label warning statements, label design/differentiation, product name, packaging) – where this has not been evaluated by the TGA, it could support suggestions for RASML or other label warnings, but is not appropriate for a 52E justification for a decision.

- Evaluation of applicant's Proposal (where applicable)
  - Evaluator's consideration and conclusions – main points
  - Applicant's comments on evaluation
  - Response to applicant's comments from evaluator
  - Does evaluator support rescheduling proposal – with reasons for support/opposition.

- Pre-meeting submissions
  - View on submissions.

- RASML statements (where applicable)
  - Currently applying to substance and/or that apply to similar OTC substances
  - Suggested by applicant and/or evaluator and/or presenter.

- Questions from delegate to ACMS (as applicable)
  - Question 1 and presenter's response
  - Question 2 and presenter's response
  - Question 3 and presenter's response etc.

- Advice, comments and suggestions from the speaker.

ACMS MEETING #31

24 June 2020

AGENDA ITEM 2.4

Clotrimazole

Referred scheduling proposal

The medicines scheduling delegate is seeking advice from the Advisory Committee on Medicines Scheduling (ACMS) on a scheduling proposal, received on March 2020, to amend the Poisons Standard with respect to clotrimazole.

Applicant's scheduling proposal and reasons for the proposal

An application (Attachment A) was submitted by Bayer Australia to amend the Poisons Standard with respect to clotrimazole. The application proposes to amend the Schedule 2 entry for clotrimazole.

The applicant's proposed amendments to the Poisons Standard are:

Schedule 6

CLOTRIMAZOLE for the external treatment of animals.

Schedule 4

CLOTRIMAZOLE except:

a) when included in Schedule 2, 3 or 6; or

b) in preparations for dermal use for the treatment of tinea pedis.

Schedule 3 – Amend Entry

CLOTRIMAZOLE in preparations for vaginal use **except** when included in Schedule 2.

Schedule 2 – Amend Entry

CLOTRIMAZOLE for human use:

a) in preparations for vaginal use containing 1 per cent or less of clotrimazole; or

b) in dermal preparations; and

c) for application to the nails.

except in preparations for the treatment of tinea pedis.

Appendix F, Part 3

Poison	Warning statements	Safety directions
CLOTRIMAZOLE in vaginal preparations when included in Schedule 2 or Schedule 3.	54,63,64,66	

The applicant's reasons for the proposal are:

- The applicant proposes to make clotrimazole 1% vaginal cream directly available to consumers from pharmacies without the need to consult a pharmacist or doctor.
- Vaginal candidiasis is a common occurrence with 12.5% of Australian women experiencing at least one episode in the last 12 months. Of these women:
  - 82% were repeat sufferers;
  - 76% were confident of their ability to self-diagnose and treat thrush;
  - 70% were uncomfortable about speaking with a pharmacist about thrush, 70% wanted the option to self-select and only 2% preferred to speak with a pharmacist rather than self-selecting;
  - the 42% of participants who had not treated their thrush reported finding it 'very uncomfortable' to speak with a pharmacist;
  - 30% of those who believed asking for help is 'very embarrassing' purchased the Canesten regular antifungal cream inappropriately for vaginal use.
- Canesten vaginal creams are a safe and effective first-line treatment for vulvovaginal candidiasis. They have low potential toxicity and a low potential for abuse.
- Products are clearly labelled to provide all the information that is needed to ensure the quality use of the medicine including an instruction to consult a health care professional "if you have not had thrush before".
- A 2005 Australian study (Tenni 2005) found a self-diagnostic accuracy rate for vaginal candidiasis of 47% with a further 42% having 'normal' vaginal flora. The combined 'do no harm' scenario for these consumers (i.e. successful treatment + no treatment required) was 89%.
- Women who have had vaginal candidiasis previously diagnosed by a doctor will already be familiar with the symptoms. Other vaginal infections will usually have different symptoms as described on the pack with a prompt to seek healthcare professional advice if no improvement in 4 days.
- This application is limited to the lowest strength clotrimazole 1% (6 day) vaginal cream. No change is proposed to the current Schedule 3 entries covering pessaries and the 3 day 2% and 1 day 10% creams.
- The proposed SUSMP entry for clotrimazole 1% vaginal cream meets all of the SPF criteria for Schedule 2.

For full 52E reasons, see the application at Attachment A.

For consideration of the Scheduling Factors see the Scheduling Policy Framework.[1]

Current scheduling status

Schedule 6

CLOTRIMAZOLE for the external treatment of animals.

Schedule 4

CLOTRIMAZOLE except:

a) when included in Schedule 2, 3 or 6; or

b) in preparations for dermal use for the treatment of tinea pedis.

Schedule 3 – Amend Entry

CLOTRIMAZOLE in preparations for vaginal use.

Schedule 2 – Amend Entry

CLOTRIMAZOLE for human use in dermal preparations and for application to the nails **except** in preparations for the treatment of tinea pedis.

Appendix F, Part 3

Poison	**Warning statements**	**Safety directions**
CLOTRIMAZOLE in vaginal preparations when included in Schedule 3.	54,63,64,66	

Appendix H

CLOTRIMAZOLE

Index

CLOTRIMAZOLE

Schedule 6
Schedule 4
Schedule 3
Schedule 2

[1] Scheduling Policy Framework https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals

Appendix F, Part 3
Appendix H

Scheduling history

Clotrimazole was first scheduled in August 1977. Clotrimazole has an extensive scheduling history since 1985. The scheduling history relevant to vaginal preparations have been presented below.

The August 1977, the Drugs and Poisons Schedule Standing committee (DPSSC) included clotrimazole in Schedule 4.

In April 1994, the National Drugs and Poisons Schedule Committee (NDPSC) agreed to down-schedule preparations of clotrimazole for vaginal use to Schedule 3 to give its current entry. Following out-of-session consideration, the committee also agreed to include the current warning statements in Appendix F for clotrimazole when included in Schedule 3.

In November 1996, the NDPSC considered a submission to reschedule clotrimazole for vaginal use to Schedule 2. The committee did not support the rescheduling application.

In February 1997, the NDPSC considered the post-meeting comment concerning the November 1996. The committee agreed that the November 1996 decision remained appropriate and that clotrimazole for vaginal use should remain in Schedule 3.

In August 1998, the NDPSC considered a submission to include miconazole in Appendix H, and decided to allow other antifungals currently included in Schedule 3 to be advertised by including them in Appendix H. These substances were clotrimazole, econazole, miconazole and nystatin.

In February 2006, the NDPSC considered a submission to reschedule clotrimazole for vaginal use to Schedule 2. After consideration of the new data presented, the committee agreed that the current scheduling of clotrimazole remained appropriate. The committee noted that maintaining mandatory pharmacist involvement in the sale of clotrimazole was needed to fully address the committee's concerns, particularly the risk of repeated clotrimazole use masking an underlying serious condition.

In February 2007, the NDPSC considered a submission to reschedule clotrimazole for vaginal use to Schedule 2. The committee agreed that the current scheduling of clotrimazole for vaginal use remained appropriate. Maintaining mandatory pharmacist involvement in the sale of clotrimazole was needed to fully address the committee's concerns, particularly the risk of repeated clotrimazole use masking an underlying serious condition without referral to a pharmacist or doctor or being used incorrectly on non-fungal vaginal infections or conditions.

In November 2017, the Advisory Committee on Medicines Scheduling (ACMS#22) considered an application to amend the Schedule 2 and Schedule 4 entries and to delete the Schedule 3 and Appendix H entries for clotrimazole. The intent of the amendment was to allow vaginal preparations to be considered as Schedule 2 medicines. The delegate made a final decision not to amend the current scheduling of clotrimazole, with the major risk being inaccurate self-diagnosis, or delayed treatment if the product is used to treat other vaginal infections not caused by Candidia albicans.

Australian regulations

As of March 2020:

- There are 94 medicines currently active on the Australian Register of Therapeutic Goods (ARTG)[2] that list clotrimazole as an active ingredient (Attachment B). These include 1 prescription, 92 non-prescription medicines and 1 export-only medicine. Clotrimazole is available in the following formulation types: cream, capsules, topical solution and pessaries. Clotrimazole can be found in 10 mg/g, 20 mg/g and 100 mg/g concentrations. Clotrimazole creams for vaginal use are often found in combination with fluconazole which is classed as a Schedule 3 substance in preparations containing 150 mg or less of fluconazole. There are 78 medicines containing only clotrimazole at a concentration of 10mg/g.
- According to the TGA Ingredient Database,[3] clotrimazole is:
  - available for use as an active ingredient in biologicals, export only, over the counter and prescription medicines;
  - available for use as an excipient ingredient in biologicals, devices, prescription medicines; and
  - not available as an equivalent ingredient in any application.
- Clotrimazole is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination[4] No.1 of 2020.
- The TGA prescribing medicines in pregnancy database[5] classifies clotrimazole as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Clotrimazole	A	Drugs used in Dermatology	Topical antifungals, antiseptics (see also antifungal agents)	
Clotrimazole	A	Genitourinary System	Topical vaginal medication	
Category A – Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.				

- The Therapeutic Goods (Medicines Advisory Statements) Specification 2019[6] requires the following warning statements pertaining to clotrimazole to be included on the labelling:

[2] ARTG database https://www.tga.gov.au/artg
[3] TGA Ingredient Database https://www.ebs.tga.gov.au/
[4] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination
[5] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database
[6] Therapeutic Goods (Medicines Advisory Statements) Specification 2019 https://www.legislation.gov.au/Details/F2019L00213

Substance	Conditions	Required Statement(s)
Clotrimazole	In preparations for vaginal use	· Seek medical advice before first course of treatment. · See a doctor if you are pregnant or diabetic. · See a doctor if no better after [*Insert number of days as per approved Product Information*] days. · See a doctor if problem returns.

- The Database of Adverse Event Notifications (DAEN)[7]contains 176 reports of adverse events for products containing clotrimazole as an active ingredient, with 128 reports where clotrimazole was the single suspected medicine. There was 1 report of deaths associated with clotrimazole use (Attachment C).
- There are five products containing clotrimazole listed on the Public Chemical Registration Information System Search (PubCRIS).[8] These include two approved active constituents and three registered products.
- In 2009-2019 the following adverse experiences were recorded for clotrimazole in the APVMA Adverse Experience Reporting Program database (AERP):[9]
  - Five reports, with two reports where clotrimazole was the probable cause and three reports where clotrimazole was a possible cause (2009);
  - Three reports, with two reports where clotrimazole was the probable cause and one report where clotrimazole was a possible cause (2010);
  - Three reports where clotrimazole was a possible cause (2012);
  - One report where clotrimazole was the probable cause (2013);
  - Three reports, with one report where clotrimazole was the probable cause and two reports where clotrimazole was a possible cause (2014);
  - One report on clotrimazole related to crop health (2015);
  - One report on clotrimazole related to animal health (2016); and
  - One report on clotrimazole related to animal health (2017).

International regulations

As of March 2020 the following international regulatory information was available for clotrimazole:

[7] Database of Adverse Event Notifications (DAEN) https://apps.tga.gov.au/Prod/daen/daen-entry.aspx
[8] Public Chemical Registration Information System Search (PubCRIS) https://portal.apvma.gov.au/pubcris
[9] APVMA Adverse Experience Reporting Program database (AERP) https://apvma.gov.au/node/10946

United States (U.S)

According to the United States Food and Drug Administration Approved Drug Products Database (Drugs@FDA)[10] clotrimazole is available as a prescription and over-the-counter medicine in the U.S. Clotrimazole is not identified on the United States Environmental Protection Agency's (US EPA) Office of Pesticides Programs.[11]

Europe

The European Chemicals Agency (ECHA)[12] hazard classification & labelling classifies for clotrimazole is '*Danger! According to the classification provided by companies to ECHA in CLP notifications this substance is very toxic to aquatic life with long lasting effects, is very toxic to aquatic life, is toxic in contact with skin, is harmful if swallowed, causes serious eye irritation, is suspected of damaging fertility or the unborn child, may cause damage to organs through prolonged or repeated exposure and causes skin irritation*.' Clotrimazole is predicted as likely to meet criteria for category 1A or 1B carcinogenicity, mutagenicity, or reproductive toxicity according to ECHA.

The European Commission database for information on cosmetic substances and ingredients database[13] identifies clotrimazole as an ingredient in anti-dandruff and anti-microbial products. Clotrimazole is not included on the European Union Pesticides Database.[14] According to the European Medicines Agency,[15] clotrimazole is available in a number of products with current market approval.

New Zealand (NZ)

Clotrimazole was first included in the New Zealand Inventory of Chemicals (NZIoC)[16] on 1 December 2006. According to the New Zealand Medicines and Medical Devices Safety Authority (MedSafe)[17] clotrimazole is available as follows in NZ:

Ingredient	Conditions (if any)	Classification
Clotrimazole	**except** in medicines for vaginal or external use	Prescription
Clotrimazole	for vaginal use	Restricted

[10] FDA Approved Drug Products Database https://www.accessdata.fda.gov/scripts/cder/daf/
[11] United States Environmental Protection Agency's (US EPA) Office of Pesticides Programs https://iaspub.epa.gov/apex/pesticides/f?p=CHEMICALSEARCH:1:
[12] European Chemicals Agency (ECHA) https://echa.europa.eu/search-for-chemicals
[13] European Commission database for information on cosmetic substances and ingredients database https://ec.europa.eu/growth/tools-databases/cosing/
[14] European Union Pesticides Database https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN
[15]European Medicines Agency https://www.ema.europa.eu/en/medicines
[16] New Zealand Inventory of Chemicals (NZIoC) https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/DatabaseSearchForm/?SiteDatabaseSearchFilters=36&Keyword=acequinocyl&DatabaseType=NZIOC
[17] New Zealand Medicines and Medical Devices Safety Authority (MedSafe) https://www.medsafe.govt.nz/profs/class/classintro.asp

Clotrimazole	for external use **except** in medicines for tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	Pharmacy Only
Clotrimazole	for external use in medicines for tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	General Sale

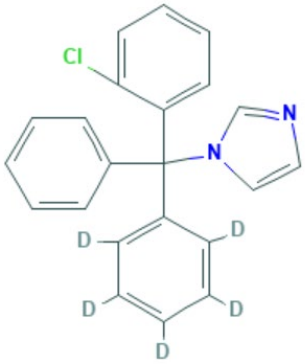
Canada

Clotrimazole is not included in Canada's Pest Management Regulation Agency.[18] According to the Canadian (Health Canada) Drug Product Database[19] clotrimazole is available as a prescription medicine and over-the-counter medicine in Canada.

[18] Canada's Pest Management Regulation Agency https://pesticide-registry.canada.ca/en/active-ingredient-search.html
[19] Canadian (Health Canada) Drug Product Database https://health-products.canada.ca/dpd-bdpp/index-eng.jsp

Substance summary

Table 1: Chemical information for clotrimazole

Property	clotrimazole
Chemical structure	
Molecular formula	$C_{22}H_{17}ClN_2$
CAS numbers	23593-75-1
IUPAC and/or common and/or other names	1-[(2-chlorophenyl)-diphenylmethyl]imidazole (IUPAC);

Pre-meeting public submissions

Public submissions will be uploaded onto GovTeams as a separate attachment.

Internal consultation

The following section at the TGA submitted feedback on the scheduling proposal:

- OTC Medicines Evaluation Section: see Attachment D

Delegate's specific issues and questions to be considered by the ACMS

The medicines scheduling delegate seeks advice from the Committee on the following questions:

1. Noting this was previously been seen in ACMS in 2017 are there reasons to change the previous advice? Then the major risk identified was inaccurate self-diagnosis, or delayed treatment if the product is used to treat other vaginal infections not caused by Candidia albicans.
2. Is it appropriate to be accessed without direct pharmacist intervention?
3. If so, noting the strength re quested to down schedule is this appropriate or should it also cover stronger preparations?

OPTIONS

OPTION 1

The Committee recommends that the current scheduling of clotrimazole remains appropriate.

OPTION 2

The Committee recommends that the current Schedule 2 and Schedule 3 entries for clotrimazole be amended as follows:

Schedule 3 – Amend Entry

CLOTRIMAZOLE in preparations for vaginal use **except** when included in Schedule 2.

Schedule 2 – Amend Entry

CLOTRIMAZOLE for human use:

a) in preparations for vaginal use containing 1 per cent or less of clotrimazole; or

b) in dermal preparations; and

c) for application to the nails.

except in preparations for the treatment of tinea pedis.

OPTION 3

The Committee also recommends the Appendix F entry be amended as follows:

Poison	**Warning statements**	**Safety directions**
CLOTRIMAZOLE in vaginal preparations when included in Schedule 2 or Schedule 3.	54,63,64,66	

IMPLEMENTATION DATE

The Committee is asked to discuss and consider the resolutions with an implementation date of 1 February 2021/1 June 2021/1 October 2021.

RECOMMENDATION FOR OTHER ACTION BY THE DELEGATE

ATTACHMENTS

Attachment A: Application D20-438122

Attachment B: ARTG product list – clotrimazole (retrieved 30 March 2020) D20-435235

Attachment C: DAEN Report - clotrimazole (retrieved 30 March 2020) D20-438271

Attachment D: Internal Consultation D20-720778

Product Name Sponsor Name
CANDACORT MINIPAK clotrimazole 10 mg/g and hydrocortisone 10 mg/g cream tube AFT Pharmaceuticals Pty Ltd
SOUL PATTINSON DUO THRUSH TREATMENT fluconazole 150 mg capsule blister pack & clotrimazole 10 mg/g cream tube composite pack Soul Pattinson Manufacturing Pty Ltd
CANESTEN CLOTRIMAZOLE ANTIFUNGAL TOPICAL SOLUTION clotrimazole 10 mg/mL bottle Bayer Australia Ltd
AMCAL FEM-V PLUS fluconazole 150mg capsule and clotrimazole 10mg/g cream Cipla Australia Pty Ltd
PHARMACY CARE FEMINA V 6 DAY CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
PRICELINE PHARMACY CLOTRIMAZOLE 3 DAY THRUSH TREATMENT clotrimazole 20 mg/g cream tube Cipla Australia Pty Ltd
AMCAL FEM V3 DAY CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
TOPIZOL ANTIFUNGAL CREAM clotrimazole 10mg/g tube Medis Pharma Pty Ltd
PHARMACY SELECT CLOTRIMAZOLE 1% CREAM 10 mg/g tube Cipla Australia Pty Ltd
CANESTEN CLOTRIMAZOLE THRUSH 1 DAY CREAM 500 mg/5 g single dose cream tube Bayer Australia Ltd
CANESTEN CLOTRIMAZOLE THRUSH 6 DAY PESSARY 100 mg compressed pessary blister pack Bayer Australia Ltd
TRIMACORTE CREAM tube (S2 variant) Nova Pharmaceuticals Australasia Pty Ltd
CANESTEN CLOTRIMAZOLE THRUSH 6 DAY CREAM 1% w/w cream tube Bayer Australia Ltd
TRUST FEMZOLE DUO clotrimazole 10mg/g cream tube and fluconazole 150mg capsule Cipla Australia Pty Ltd
C-ZOLE clotrimazole 1%w/w cream tube GlaxoSmithKline Consumer Healthcare Australia Pty Ltd
CLOTRIZONE CREAM clotrimazole 10 mg/g and hydrocortisone acetate 10 mg/g cream tube Nova Pharmaceuticals Australasia Pty Ltd
PHARMACY OWN ANTI-FUNGAL CREAM clotrimazole 10mg/g tube Wockhardt Bio Pty Ltd
TRUST ANTIFUNGAL clotrimazole 10mg/g cream tube Pharmacor Pty Ltd
AFEME DUO fluconazole 150mg capsule blister pack and clotrimazole 10mg/g cream tube composite pack Alphapharm Pty Ltd
TERRYWHITE CHEMMART CLOTRIMAZOLE 6 DAY THRUSH TREATMENT 10mg/g cream tube Cipla Australia Pty Ltd
VIKADERM BROAD SPECTRUM ANTIFUNGAL 10mg/g Milpharma Pty Ltd
FEMIZOL VAGINAL CREAM clotrimazole 20mg/g tube Medis Pharma Pty Ltd
CIPLA GENPHARM CLO-ZOLE CREAM 1% clotrimazole 10mg/g tube Cipla Australia Pty Ltd
SOUL PATTINSON DUO THRUSH TREATMENT fluconazole 150 mg capsule blister pack & clotrimazole 10 mg/g cream tube composite pack Soul Pattinson Manufacturing Pty Ltd
CANESTEN CLOTRIMAZOLE THRUSH 1 DAY PESSARY 500 mg compressed

pessary blister pack Bayer Australia Ltd
APOHEALTH Thrush Treatment Duo clotrimazole 1% cream tube/fluconazole 150mg capsule blister pack Apotex Pty Ltd
CLONEA CLOTRIMAZOLE THRUSH TREATMENT 3 DAY CREAM clotrimazole 20mg/g tube Alphapharm Pty Ltd
HYDROZOLE hydrocortisone / clotrimazole cream tube GlaxoSmithKline Consumer Healthcare Australia Pty Ltd
PHARMACY ACTION FEMRELIEF DUO clotrimazole 1 % cream tube/fluconazole 150 mg capsule blister pack Cipla Australia Pty Ltd
BLOOMS THE CHEMIST ANTI-FUNGAL Cream clotrimazole 10mg/g cream tube Apotex Pty Ltd
CANDACORT MINIPAK clotrimazole 10 mg/g and hydrocortisone 10 mg/g cream tube AFT Pharmaceuticals Pty Ltd
PHARMACY ACTION FEMCREAM 3 DAY CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
APO-CLOTRIMAZOLE 3 DAY CREAM clotrimazole 20mg/g tube Apotex Pty Ltd
PHARMACY CARE FEMINA V PLUS clotrimazole 1% cream tube/fluconazole 150mg capsule blister pack Cipla Australia Pty Ltd
Adira Clotricortisone Cream AdiraMedica Pty Ltd
FEMIZOL VAGINAL CREAM clotrimazole 20mg/g tube Medis Pharma Pty Ltd
PHARMACY ACTION FEMRELIEF DUO clotrimazole 1 % cream tube/fluconazole 150 mg capsule blister pack Cipla Australia Pty Ltd
CANESTEN HC clotrimazole 1% w/w and hydrocortisone acetate 1% w/w cream tube Bayer Australia Ltd
PHARMACY OWN ANTI-FUNGAL CREAM clotrimazole 10mg/g tube Wockhardt Bio Pty Ltd
BLOOMS THE CHEMIST CLOTRIMAZOLE 3 DAY VAGINAL CREAM Clotrimazole 20mg/g tube Apotex Pty Ltd
PRICELINE PHARMACY DUO THRUSH TREATMENT fluconazole 150 mg capsule blister pack & clotrimazole 10 mg/g cream tube composite pack Soul Pattinson Manufacturing Pty Ltd
FEMAZOLE DUO fluconazole 150mg capsule blister pack and clotrimazole 10mg/g cream tube composite pack Arrow Pharma Pty Ltd
PHARMACY SELECT CLOTRIMAZOLE 1% CREAM 10 mg/g tube Cipla Australia Pty Ltd
PHARMACY ACTION FEMCREAM 3 DAY CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
OPIZOLE 6 DAY THRUSH CREAM clotrimazole 10 mg/g tube Opal Pharmaceuticals Pty Ltd
CANESTEN CLOTRIMAZOLE THRUSH 1 DAY PESSARY + CREAM 500 mg compressed pessary blister pack and 10 mg/g cream tube composite pack Bayer Australia Ltd
AMCAL ANTI FUNGAL CREAM PLUS HYDROCORTISONE clotrimazole 10 mg/g and hydrocortisone acetate 10 mg/g cream tube Nova

Pharmaceuticals Australasia Pty Ltd
TerryWhite Chemmart Clotrimazole & Hydrocortisone Cream AdiraMedica Pty Ltd
FEMAZOLE DUO fluconazole 150mg capsule blister pack and clotrimazole 10mg/g cream tube composite pack Arrow Pharma Pty Ltd
PRICELINE PHARMACY DUO THRUSH TREATMENT fluconazole 150 mg capsule blister pack & clotrimazole 10 mg/g cream tube composite pack Soul Pattinson Manufacturing Pty Ltd
CANESTEN CLOTRIMAZOLE THRUSH 1 DAY PESSARY + CREAM 500 mg compressed pessary blister pack and 10 mg/g cream tube composite pack Bayer Australia Ltd
CHEMISTS' OWN CLOZOLE VAGINAL CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
PHARMACY CHOICE CLOTRIMAZOLE THRUSH TREATMENT 6 DAY CREAM 10mg/g clotrimazole 1%w/w tube Cipla Australia Pty Ltd
CHEMISTS' OWN CLOZOLE CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
HYDROZOLE hydrocortisone / clotrimazole cream tube GlaxoSmithKline Consumer Healthcare Australia Pty Ltd
PHARMACY HEALTH CLOTRIMAZOLE 3 DAY THRUSH TREATMENT 20 mg/g cream tube Cipla Australia Pty Ltd
SOUL PATTINSON ANTIFUNGAL CLOTRIMAZOLE WOMEN'S COMBINATION TREATMENT pessary and cream Soul Pattinson Manufacturing Pty Ltd
CIPLA FEMME THRUSH AID COMBO PACK clotrimazole 1% cream tube/fluconazole 150mg capsule blister pack Cipla Australia Pty Ltd
PHARMACY CHOICE THRUSH ONE DOSE + CREAM clotrimazole 10mg/g cream tube/fluconazole 150mg capsule Cipla Australia Pty Ltd
TERRYWHITE CHEMMART DUO THRUSH TREATMENT fluconazole 150 mg capsule blister pack & clotrimazole 10 mg/g cream tube composite pack Soul Pattinson Manufacturing Pty Ltd
APOHEALTH ANTI-FUNGAL CREAM clotrimazole 10 mg/g tube Apotex Pty Ltd
CLONEA ANTIFUNGAL CREAM clotrimazole 10mg/g tube Alphapharm Pty Ltd
PHARMACY ACTION Antifungal Cream tube Cipla Australia Pty Ltd
CLONEA CLOTRIMAZOLE THRUSH TREATMENT 6 DAY CREAM Clotrimazole 10mg/g tube Alphapharm Pty Ltd
CANESTEN CLOTRIMAZOLE THRUSH 1 DAY PESSARY 500 mg compressed pessary blister pack Bayer Australia Ltd
CHEMISTS’ OWN CLOZOLE BROAD SPECTRUM ANTIFUNGAL CREAM clotrimazole 1% w/w cream tube Arrow Pharma Pty Ltd
PHARMACY ACTION FemCream clotrimazole 10mg/g cream tube Cipla Australia Pty Ltd
Priceline Pharmacy Clotrimazole & Hydrocortisone Cream AdiraMedica Pty Ltd
C-ZOLE clotrimazole 1%w/w cream tube GlaxoSmithKline Consumer Healthcare Australia Pty Ltd

PHARMACY HEALTH DUO THRUSH TREATMENT fluconazole 150 mg capsule blister pack & clotrimazole 10 mg/g cream tube composite pack Soul Pattinson Manufacturing Pty Ltd
AMCAL FEM V 6 DAY CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
PRICELINE PHARMACY CLOTRIMAZOLE 6 DAY THRUSH TREATMENT 10 mg/g cream tube Cipla Australia Pty Ltd
AMCAL ANTIFUNGAL CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
CANDACORT hydrocortisone/clotrimazole cream tube AFT Pharmaceuticals Pty Ltd
CANESTEN CLOTRIMAZOLE ANTIFUNGAL TOPICAL SOLUTION clotrimazole 10 mg/mL bottle Bayer Australia Ltd
AMCAL ANTI FUNGAL CREAM PLUS HYDROCORTISONE clotrimazole 10 mg/g and hydrocortisone acetate 10 mg/g cream tube Nova Pharmaceuticals Australasia Pty Ltd
PHARMACY CARE FEMINA V 6 DAY CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
TERRYWHITE CHEMMART CLOTRIMAZOLE 6 DAY THRUSH TREATMENT 10mg/g cream tube Cipla Australia Pty Ltd
PHARMACY CARE ANTIFUNGAL CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
TerryWhite Chemmart Clotrimazole & Hydrocortisone Cream AdiraMedica Pty Ltd
DISCOUNT DRUG STORES ANTI-FUNGAL CREAM clotrimazole 10mg/g cream tube Apotex Pty Ltd
CLOTRIZONE CREAM clotrimazole 10 mg/g and hydrocortisone acetate 10 mg/g cream tube Nova Pharmaceuticals Australasia Pty Ltd
PHARMACY CARE ANTI FUNGAL CREAM PLUS HYDROCORTISONE clotrimazole 10 mg/g and hydrocortisone acetate 10 mg/g cream tube Nova Pharmaceuticals Australasia Pty Ltd
TERRYWHITE CHEMMART DUO THRUSH TREATMENT fluconazole 150 mg capsule blister pack & clotrimazole 10 mg/g cream tube composite pack Soul Pattinson Manufacturing Pty Ltd
BLOOMS THE CHEMIST CLOTRIMAZOLE 3 DAY VAGINAL CREAM Clotrimazole 20mg/g tube Apotex Pty Ltd
AMCAL FEM V 6 DAY CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
TRUST FEM V 3 DAY CREAM clotrimazole 20mg/g tube Pharmacor Pty Ltd
AMCAL FEM V3 DAY CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
DISCOUNT DRUG STORES ANTI-FUNGAL CREAM clotrimazole 10mg/g cream tube Apotex Pty Ltd
CANESTEN HC clotrimazole 1% w/w and hydrocortisone acetate 1% w/w cream tube Bayer Australia Ltd
CHEMISTS' OWN FEMAZOLE DUO clotrimazole 1% cream tube/fluconazole 150mg capsule blister pack Arrow Pharma Pty Ltd
CANESTEN PLUS ANTIFUNGAL ANTI-INFLAMMATORY cream tube Bayer Australia Ltd

TRUST ANTIFUNGAL clotrimazole 10mg/g cream tube Pharmacor Pty Ltd
TRUST FEM V 3 DAY CREAM clotrimazole 20mg/g tube Pharmacor Pty Ltd
CLONEA CLOTRIMAZOLE THRUSH TREATMENT 6 DAY CREAM Clotrimazole 10mg/g tube Alphapharm Pty Ltd
CANSOLVE PLUS clotrimazole 1% 10mg/g cream tube/fluconazole 150mg capsule First Pharma Pty Ltd
APOHEALTH ANTI-FUNGAL CREAM clotrimazole 10 mg/g tube Apotex Pty Ltd
SCHOLL CLOTRIMAZOLE ATHLETE'S FOOT CREAM 10 mg/g cream tube Soul Pattinson Manufacturing Pty Ltd
CANSOLVE PLUS clotrimazole 1% 10mg/g cream tube/fluconazole 150mg capsule First Pharma Pty Ltd
CLOTRIZONE CREAM clotrimazole 10 mg/g and hydrocortisone acetate 10 mg/g cream 15 g tube Nova Pharmaceuticals Australasia Pty Ltd
TRIMACORTE cream tube Nova Pharmaceuticals Australasia Pty Ltd
TRIMACORTE cream tube Nova Pharmaceuticals Australasia Pty Ltd
CANESTEN CLOTRIMAZOLE ATHLETE'S FOOT CREAM clotrimazole 10mg/g cream tube Bayer Australia Ltd
CANESORAL DUO fluconazole 150mg capsule blister pack and clotrimazole 10mg/g cream tube composite pack Bayer Australia Ltd
CIPLA FEMME 3 DAY THRUSH TREATMENT CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
CANESTEN EXTRA ANTIFUNGAL ANTI-INFLAMMATORY CREAM tube Bayer Australia Ltd
PHARMACY CHOICE CLOTRIMAZOLE Anti-fungal Cream 10mg/g tube Cipla Australia Pty Ltd
PHARMACY CARE ANTIFUNGAL CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
CANESTEN CLOTRIMAZOLE THRUSH 6 DAY CREAM 1% w/w cream tube Bayer Australia Ltd
CANESTEN CLOTRIMAZOLE ANTIFUNGAL CREAM 10mg/g tube Bayer Australia Ltd
APO-CLOTRIMAZOLE 3 DAY CREAM clotrimazole 20mg/g tube Apotex Pty Ltd
CANESTEN PLUS ANTIFUNGAL ANTI-INFLAMMATORY cream tube Bayer Australia Ltd
PHARMACY CARE FEMINA V PLUS clotrimazole 1% cream tube/fluconazole 150mg capsule blister pack Cipla Australia Pty Ltd
CHEMISTS' OWN CLOZOLE VAGINAL CREAM 1% clotrimazole 10mg/g tube Cipla Australia Pty Ltd
AMCAL ANTIFUNGAL CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
SCHOLL CLOTRIMAZOLE ATHLETE'S FOOT CREAM 10 mg/g cream tube Soul Pattinson Manufacturing Pty Ltd
PHARMACY CHOICE THRUSH ONE DOSE + CREAM clotrimazole 10mg/g cream tube/fluconazole 150mg capsule Cipla Australia Pty Ltd
CANESTEN CLOTRIMAZOLE THRUSH 6 DAY PESSARY 100 mg compressed

pessary blister pack Bayer Australia Ltd
CANESTEN CLOTRIMAZOLE ANTIFUNGAL CREAM 10mg/g tube Bayer Australia Ltd
CLONEA ANTIFUNGAL CREAM clotrimazole 10mg/g tube Alphapharm Pty Ltd
AFEME DUO fluconazole 150mg capsule blister pack and clotrimazole 10mg/g cream tube composite pack Alphapharm Pty Ltd
PHARMACY CHOICE CLOTRIMAZOLE 3 DAY THRUSH TREATMENT CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
PHARMACY ACTION Antifungal Cream tube Cipla Australia Pty Ltd
PHARMACY CARE FEMINA V 3 DAY CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
CLONEA clotrimazole 10mg/g cream tube Alphapharm Pty Ltd
CANDACORT hydrocortisone/clotrimazole cream tube AFT Pharmaceuticals Pty Ltd
CANESTEN CLOTRIMAZOLE THRUSH 3 DAY CREAM 2% w/w cream tube Bayer Australia Ltd
CLONEA CLOTRIMAZOLE THRUSH TREATMENT 3 DAY CREAM clotrimazole 20mg/g tube Alphapharm Pty Ltd
CANESTEN CLOTRIMAZOLE THRUSH 1 DAY CREAM 500 mg/5 g single dose cream tube Bayer Australia Ltd
CLOTRIZONE CREAM clotrimazole 10 mg/g and hydrocortisone acetate 10 mg/g cream 15 g tube Nova Pharmaceuticals Australasia Pty Ltd
CANESTEN EXTRA ANTIFUNGAL ANTI-INFLAMMATORY CREAM tube Bayer Australia Ltd
Pharmacy Health Clotrimazole & Hydrocortisone Cream AdiraMedica Pty Ltd
SOUL PATTINSON ANTIFUNGAL CLOTRIMAZOLE WOMEN'S TREATMENT 2% w/w vaginal cream tube Soul Pattinson Manufacturing Pty Ltd
BLOOMS THE CHEMIST ANTI-FUNGAL Cream clotrimazole 10mg/g cream tube Apotex Pty Ltd
CA CLOTRIMAZOLE 3 DAY THRUSH TREATMENT clotrimazole 20 mg/g cream tube Opal Pharmaceuticals Pty Ltd
OPIZOLE 6 DAY THRUSH CREAM clotrimazole 10 mg/g tube Opal Pharmaceuticals Pty Ltd
CHEMISTS' OWN CLOZOLE VAGINAL CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
Priceline Pharmacy Clotrimazole & Hydrocortisone Cream AdiraMedica Pty Ltd
SOUL PATTINSON ANTIFUNGAL CLOTRIMAZOLE WOMEN'S COMBINATION TREATMENT pessary and cream Soul Pattinson Manufacturing Pty Ltd
CANESTEN CLOTRIMAZOLE ATHLETE'S FOOT CREAM clotrimazole 10mg/g cream tube Bayer Australia Ltd
TRUST FEMZOLE DUO clotrimazole 10mg/g cream tube and fluconazole 150mg capsule Cipla Australia Pty Ltd
AMCAL FEM-V PLUS fluconazole 150mg capsule and clotrimazole 10mg/g cream Cipla Australia Pty Ltd
PHARMACY CHOICE CLOTRIMAZOLE Anti-fungal Cream 10mg/g tube Cipla Australia Pty Ltd

VIKADERM BROAD SPECTRUM ANTIFUNGAL 10mg/g Milpharma Pty Ltd
CLONEA clotrimazole 10mg/g cream tube Alphapharm Pty Ltd
SOUL PATTINSON ANTIFUNGAL CLOTRIMAZOLE WOMEN'S TREATMENT 2% w/w vaginal cream tube Soul Pattinson Manufacturing Pty Ltd
TRIMACORTE CREAM tube (S2 variant) Nova Pharmaceuticals Australasia Pty Ltd
CIPLA FEMME 3 DAY THRUSH TREATMENT CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
APO-CLOTRIMAZOLE 6 DAY CREAM clotrimazole 10mg/g tube Apotex Pty Ltd
PHARMACY CARE ANTI FUNGAL CREAM PLUS HYDROCORTISONE clotrimazole 10 mg/g and hydrocortisone acetate 10 mg/g cream tube Nova Pharmaceuticals Australasia Pty Ltd
PHARMACY CHOICE CLOTRIMAZOLE 3 DAY THRUSH TREATMENT CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
CIPLA FEMME THRUSH AID COMBO PACK clotrimazole 1% cream tube/fluconazole 150mg capsule blister pack Cipla Australia Pty Ltd
CHEMISTS' OWN FEMAZOLE DUO clotrimazole 1% cream tube/fluconazole 150mg capsule blister pack Arrow Pharma Pty Ltd
PRICELINE PHARMACY CLOTRIMAZOLE 3 DAY THRUSH TREATMENT clotrimazole 20 mg/g cream tube Cipla Australia Pty Ltd
APO-CLOTRIMAZOLE 6 DAY CREAM clotrimazole 10mg/g tube Apotex Pty Ltd
PHARMACY CHOICE CLOTRIMAZOLE THRUSH TREATMENT 6 DAY CREAM 10mg/g clotrimazole 1%w/w tube Cipla Australia Pty Ltd
Pharmacy Health Clotrimazole 6 Day Thrush Treatment 10 mg/g cream tube Cipla Australia Pty Ltd
CIPLA FEMME 6 DAY THRUSH TREATMENT CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
PHARMACY CARE FEMINA V 3 DAY CREAM clotrimazole 20mg/g tube Cipla Australia Pty Ltd
TRUST FEM V 6 DAY CREAM clotrimazole 10 mg/g tube Cipla Australia Pty Ltd
CIPLA FEMME 6 DAY THRUSH TREATMENT CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
PHARMACY HEALTH DUO THRUSH TREATMENT fluconazole 150 mg capsule blister pack & clotrimazole 10 mg/g cream tube composite pack Soul Pattinson Manufacturing Pty Ltd
CANESORAL DUO fluconazole 150mg capsule blister pack and clotrimazole 10mg/g cream tube composite pack Bayer Australia Ltd
CHEMISTS’ OWN CLOZOLE BROAD SPECTRUM ANTIFUNGAL CREAM clotrimazole 1% w/w cream tube Arrow Pharma Pty Ltd
CHEMISTS' OWN CLOZOLE CREAM clotrimazole 10mg/g tube Cipla Australia Pty Ltd
TRUST FEM V 6 DAY CREAM clotrimazole 10 mg/g tube Cipla Australia Pty Ltd
TOPIZOL ANTIFUNGAL CREAM clotrimazole 10mg/g tube Medis Pharma Pty Ltd

APOHEALTH Thrush Treatment Duo clotrimazole 1% cream tube/fluconazole 150mg capsule blister pack Apotex Pty Ltd
PHARMACY ACTION FemCream clotrimazole 10mg/g cream tube Cipla Australia Pty Ltd
CHEMISTS' OWN CLOZOLE VAGINAL CREAM 1% clotrimazole 10mg/g tube Cipla Australia Pty Ltd
Pharmacy Health Clotrimazole 6 Day Thrush Treatment 10 mg/g cream tube Cipla Australia Pty Ltd
Pharmacy Health Clotrimazole & Hydrocortisone Cream AdiraMedica Pty Ltd
PHARMACY HEALTH CLOTRIMAZOLE 3 DAY THRUSH TREATMENT 20 mg/g cream tube Cipla Australia Pty Ltd
CIPLA GENPHARM CLO-ZOLE CREAM 1% clotrimazole 10mg/g tube Cipla Australia Pty Ltd
CA CLOTRIMAZOLE 3 DAY THRUSH TREATMENT clotrimazole 20 mg/g cream tube Opal Pharmaceuticals Pty Ltd
CANESTEN CLOTRIMAZOLE THRUSH 3 DAY CREAM 2% w/w cream tube Bayer Australia Ltd
PRICELINE PHARMACY CLOTRIMAZOLE 6 DAY THRUSH TREATMENT 10 mg/g cream tube Cipla Australia Pty Ltd
Adira Clotricortisone Cream AdiraMedica Pty Ltd

Australian Government
Department of Health
Therapeutic Goods Administration

Database of Adverse Event Notifications - medicines

Medicine summary

You searched for the following **14 medicines** between **01/01/1971 – 31/12/2019**:

- Afeme Duo composite pack [Clotrimazole] (Clotrimazole)
- AMCAL Fem V 6 Day Cream (Clotrimazole)
- APO-Clotrimazole 6 day Cream (Clotrimazole)
- Canesten (Clotrimazole)
- Canesten 6 Day Pessary (Clotrimazole)
- Canesten Clotrimazole Thrush Treatment 6 Day Cream 1% (Clotrimazole)
- Clonea (Clotrimazole)
- Gyne-lotremin Vaginal (Clotrimazole)
- Hydrozole (Clotrimazole; Hydrocortisone)
- Lotremin (Clotrimazole)
- Pharmacy Choice Clotimazole Thrush Treatment 6 Day Cream (Clotrimazole)
- Pharmacy Choice Clotrimazole Antifungal Cream (Clotrimazole)
- Tradename not specified (Clotrimazole)
- Trust Femzole Duo composite pack [Clotrimazole] (Clotrimazole)

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FOI 27-3697 - Document 6

Important information

The TGA uses adverse event reports to identify when a safety issue may be present. An adverse event report does not mean that the medicine is the cause of the adverse event. If you are experiencing an adverse event, or think you may be experiencing one, please seek advice from a health professional as soon as possible. The TGA strongly advises people taking prescription medicines not to change their medication regime without prior consultation with a health professional.

About the Database of Adverse Event Notifications (DAEN) - medicines

- The DAEN - medicines contains information from reports of adverse events that the TGA has received in relation to medicines including vaccines used in Australia.
- The DAEN - medicines does not contain all known safety information about a particular medicine. Please do not make an assessment about the safety of a medicine based on the information in the DAEN - medicines.

The TGA medicine safety monitoring program

More information about the DAEN - medicines and the TGA medicines safety monitoring program is available at:

- About the DAEN - medicines <http://www.tga.gov.au/safety/daen-about.htm>
- Medicines safety <http://www.tga.gov.au/safety/information-medicines.htm>

You are encouraged to report an adverse event suspected of being related to a medicine used in Australia. Reports of adverse events in relation to medicines and vaccines can be reported using the 'blue card' reporting form, by phone and online <http://www.tga.gov.au/safety/problem.htm>.

Other useful sources of information on Australian medicines

More information about a medicine is available from the Product Information (PI) <http://www.tga.gov.au/hp/information-medicines-pi.htm> and Consumer Medicine Information (CMI) <http://www.tga.gov.au/consumers/information-medicines-cmi.htm> leaflet or the labelling of the medicine. Australian Public Assessment Report for Prescription Medicines (AusPARs) <http://www.tga.gov.au/industry/pm-auspar.htm> for some prescription medicines, are also available from the TGA website. <http://www.tga.gov.au>
Your health professional can also provide help and assistance on how to use medicines.
Information on medicines used in Australia is available from NPS MedicineWise <http://www.nps.org.au/>.

About the release of this information

While reasonable care is taken to ensure that the information is an accurate record of the adverse events reported to the TGA, the TGA does not guarantee or warrant the accuracy, reliability, completeness or currency of the information or its usefulness in achieving any purpose.
To the fullest extent permitted by law, including but not limited to section 61A of the Therapeutic Goods Act 1989, the TGA will not be liable for any loss, damage, cost or expense incurred in or arising by reason of any person relying on this information.
Copyright restrictions apply to the DAEN - medicines <http://www.tga.gov.au/about/website-copyright.htm>.

FOI 27-3697 - Document 6

Results

Number of reports (cases): 176

(Multiple adverse events have been reported for some patients)

Number of cases with a single suspected medicine: 128

(The TGA thinks there is a possibility that the medicine caused the adverse event)

Number of cases where death was a reported outcome: 1

(These reports of death may or may not have been a result of taking a medicine)

MedDRA system organ class[i]	MedDRA reaction term[ii]	Number of cases[iii]	Number of cases with a single suspected medicine[iv]	Number of cases where death was a reported outcome[v]
General disorders and administration site conditions	Application site reaction	32	29	0
Skin and subcutaneous tissue disorders	Pruritus	22	15	0
Reproductive system and breast disorders	Vaginal haemorrhage	21	17	0
Skin and subcutaneous tissue disorders	Rash	13	7	0
Skin and subcutaneous tissue disorders	Rash erythematous	10	7	0
Skin and subcutaneous tissue disorders	Urticaria	9	5	0
Skin and subcutaneous tissue disorders	Rash maculo-papular	9	2	0
Skin and subcutaneous tissue disorders	Dermatitis bullous	8	8	0
General disorders and administration site conditions	Drug ineffective	7	6	0
Nervous system disorders	Burning sensation	7	6	0
General disorders and administration site conditions	Pain	7	6	0
Nervous system disorders	Dizziness	6	4	0
Gastrointestinal disorders	Abdominal pain	6	4	0
General disorders and administration site conditions	Inflammation	5	5	0
Skin and subcutaneous tissue disorders	Erythema	5	5	0
Vascular disorders	Haemorrhage	5	5	0
Skin and subcutaneous tissue disorders	Skin exfoliation	5	3	0
Gastrointestinal disorders	Nausea	5	3	0
Injury, poisoning and procedural complications	Vulvovaginal injury	5	5	0

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FOI 27-3697 - Document 6

MedDRA system organ class[i]	MedDRA reaction term[ii]	Number of cases[iii]	Number of cases with a single suspected medicine[iv]	Number of cases where death was a reported outcome[v]
Reproductive system and breast disorders	Vulvovaginal burning sensation	5	4	0
General disorders and administration site conditions	Malaise	4	3	0
Respiratory, thoracic and mediastinal disorders	Dyspnoea	4	4	0
General disorders and administration site conditions	Injury associated with device	4	4	0
Injury, poisoning and procedural complications	Exposure during pregnancy	4	4	0
Infections and infestations	Candida infection	4	1	0
Nervous system disorders	Paraesthesia	4	3	0
Gastrointestinal disorders	Vomiting	3	1	0
Injury, poisoning and procedural complications	Maternal exposure during pregnancy	3	1	0
Nervous system disorders	Headache	3	2	0
Pregnancy, puerperium and perinatal conditions	Abortion spontaneous	3	2	1
General disorders and administration site conditions	Fatigue	3	1	0
Gastrointestinal disorders	Abdominal discomfort	3	0	0
Skin and subcutaneous tissue disorders	Rash pruritic	3	2	0
General disorders and administration site conditions	Medical device discomfort	3	3	0
Nervous system disorders	Syncope	3	3	0
Reproductive system and breast disorders	Vulvovaginal pain	3	3	0
General disorders and administration site conditions	Oedema	3	3	0
General disorders and administration site conditions	Pyrexia	3	0	0
Eye disorders	Periorbital oedema	2	1	0
Musculoskeletal and connective tissue disorders	Pain in extremity	2	1	0
Injury, poisoning and procedural complications	Product use in unapproved indication	2	2	0
General disorders and administration site conditions	Chest pain	2	1	0
Reproductive system and breast disorders	Vaginal discharge	2	2	0
Respiratory, thoracic and mediastinal disorders	Asthma	2	2	0

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FOI 27-3697 - Document 6

MedDRA system organ class[i]	MedDRA reaction term[ii]	Number of cases[iii]	Number of cases with a single suspected medicine[iv]	Number of cases where death was a reported outcome[v]
Blood and lymphatic system disorders	Thrombocytopenia	2	1	0
Nervous system disorders	Somnolence	2	0	0
Renal and urinary disorders	Dysuria	2	2	0
Nervous system disorders	Lethargy	2	1	0
Product issues	Product quality issue	2	2	0
Skin and subcutaneous tissue disorders	Skin ulcer	2	2	0
Eye disorders	Lacrimation increased	2	2	0
Reproductive system and breast disorders	Genital haemorrhage	2	1	0
Reproductive system and breast disorders	Vulval disorder	2	2	0
Respiratory, thoracic and mediastinal disorders	Wheezing	2	1	0
General disorders and administration site conditions	Condition aggravated	2	0	0
Renal and urinary disorders	Pollakiuria	2	2	0
Reproductive system and breast disorders	Metrorrhagia	2	1	0
Reproductive system and breast disorders	Vaginal disorder	2	0	0
Skin and subcutaneous tissue disorders	Angioedema	2	2	0
Infections and infestations	Vaginal infection	2	1	0
Metabolism and nutrition disorders	Decreased appetite	2	1	0
Reproductive system and breast disorders	Ovarian cyst	2	0	0
Blood and lymphatic system disorders	Lymphadenopathy	2	2	0
Reproductive system and breast disorders	Testicular swelling	2	2	0
Product issues	Product shape issue	1	1	0
Psychiatric disorders	Depressed mood	1	0	0
Skin and subcutaneous tissue disorders	Rash morbilliform	1	0	0
Skin and subcutaneous tissue disorders	Red man syndrome	1	0	0
Skin and subcutaneous tissue disorders	Skin haemorrhage	1	1	0
Vascular disorders	Hot flush	1	0	0
Infections and infestations	Conjunctivitis	1	1	0

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FOI 27-3697 - Document 6

MedDRA system organ class[i]	MedDRA reaction term[ii]	Number of cases[iii]	Number of cases with a single suspected medicine[iv]	Number of cases where death was a reported outcome[v]
Nervous system disorders	Extrapyramidal disorder	1	0	0
Nervous system disorders	Loss of consciousness	1	1	0
Pregnancy, puerperium and perinatal conditions	Foetal hypokinesia	1	1	0
Reproductive system and breast disorders	Vulval oedema	1	1	0
Skin and subcutaneous tissue disorders	Pigmentation disorder	1	1	0
Blood and lymphatic system disorders	Thrombocytosis	1	0	0
General disorders and administration site conditions	Crying	1	0	0
Hepatobiliary disorders	Hepatic function abnormal	1	0	0
Musculoskeletal and connective tissue disorders	Back pain	1	0	0
Nervous system disorders	Dementia	1	0	0
Psychiatric disorders	Delirium	1	0	0
Psychiatric disorders	Hallucinations, mixed	1	0	0
Skin and subcutaneous tissue disorders	Hyperhidrosis	1	0	0
Skin and subcutaneous tissue disorders	Skin atrophy	1	0	0
Eye disorders	Glaucoma	1	1	0
Gastrointestinal disorders	Anal incontinence	1	0	0
Gastrointestinal disorders	Dysphagia	1	0	0
Gastrointestinal disorders	Stomatitis	1	0	0
Nervous system disorders	Hypoaesthesia	1	1	0
Nervous system disorders	Peripheral sensory neuropathy	1	0	0
Gastrointestinal disorders	Dyschezia	1	1	0
Gastrointestinal disorders	Hypoaesthesia oral	1	0	0
General disorders and administration site conditions	Swelling	1	1	0
Hepatobiliary disorders	Hepatitis	1	0	0
Injury, poisoning and procedural complications	Off label use	1	1	0
Investigations	Weight decreased	1	0	0
Musculoskeletal and connective tissue disorders	Osteoporosis	1	1	0
Reproductive system and breast disorders	Breast tenderness	1	1	0

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FOI 27-3697 - Document 6

MedDRA system organ class[i]	MedDRA reaction term[ii]	Number of cases[iii]	Number of cases with a single suspected medicine[iv]	Number of cases where death was a reported outcome[v]
Reproductive system and breast disorders	Pelvic pain	1	1	0
Reproductive system and breast disorders	Vulvovaginal inflammation	1	1	0
Skin and subcutaneous tissue disorders	Alopecia	1	0	0
Skin and subcutaneous tissue disorders	Rash macular	1	1	0
Gastrointestinal disorders	Paraesthesia oral	1	1	0
Immune system disorders	Hypersensitivity	1	1	0
Investigations	Prothrombin level decreased	1	0	0
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	1	1	0
Congenital, familial and genetic disorders	Cleft lip	1	0	0
Eye disorders	Eye swelling	1	1	0
Gastrointestinal disorders	Abdominal distension	1	0	0
Gastrointestinal disorders	Flatulence	1	0	0
Gastrointestinal disorders	Lip oedema	1	0	0
Gastrointestinal disorders	Oral discomfort	1	0	0
Hepatobiliary disorders	Hyperbilirubinaemia	1	0	0
Injury, poisoning and procedural complications	Device difficult to use	1	1	0
Injury, poisoning and procedural complications	Traumatic haemorrhage	1	1	0
Nervous system disorders	Disturbance in attention	1	0	0
Nervous system disorders	Neuropathy peripheral	1	1	0
Vascular disorders	Pallor	1	0	0
Gastrointestinal disorders	Abdominal pain lower	1	1	0
General disorders and administration site conditions	Application site discomfort	1	1	0
General disorders and administration site conditions	Asthenia	1	1	0
Injury, poisoning and procedural complications	Wrong technique in product usage process	1	0	0
Psychiatric disorders	Confusional state	1	0	0
Gastrointestinal disorders	Lip swelling	1	1	0
Immune system disorders	Anaphylactic reaction	1	1	0
Infections and infestations	Herpes zoster	1	0	0
Nervous system disorders	Dysarthria	1	0	0

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FOI 27-3697 - Document 6

MedDRA system organ class[i]	MedDRA reaction term[ii]	Number of cases[iii]	Number of cases with a single suspected medicine[iv]	Number of cases where death was a reported outcome[v]
Psychiatric disorders	Insomnia	1	0	0
Renal and urinary disorders	Renal impairment	1	0	0
Respiratory, thoracic and mediastinal disorders	Cough	1	1	0
Blood and lymphatic system disorders	Leukopenia	1	0	0
Ear and labyrinth disorders	Deafness	1	1	0
Eye disorders	Ocular hyperaemia	1	1	0
Infections and infestations	Urinary tract infection	1	0	0
Musculoskeletal and connective tissue disorders	Arthralgia	1	0	0
Reproductive system and breast disorders	Vulvovaginal erythema	1	0	0
General disorders and administration site conditions	Chills	1	0	0
General disorders and administration site conditions	Swelling face	1	1	0
Infections and infestations	Vulvovaginal candidiasis	1	0	0
Product issues	Product quality control issue	1	1	0
Psychiatric disorders	Anxiety	1	0	0
Psychiatric disorders	Suicide attempt	1	0	0
Reproductive system and breast disorders	Vulvovaginal rash	1	0	0
Skin and subcutaneous tissue disorders	Dermatitis	1	0	0
Skin and subcutaneous tissue disorders	Dermatitis exfoliative	1	1	0
Skin and subcutaneous tissue disorders	Photosensitivity reaction	1	1	0
Skin and subcutaneous tissue disorders	Skin discolouration	1	1	0
Gastrointestinal disorders	Diarrhoea	1	1	0
General disorders and administration site conditions	Complication of device insertion	1	1	0
General disorders and administration site conditions	Feeling hot	1	0	0
Injury, poisoning and procedural complications	Head injury	1	1	0
Investigations	Body temperature decreased	1	1	0
Product issues	Device defective	1	1	0
Product issues	Device physical property issue	1	1	0

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MedDRA system organ class[i]	MedDRA reaction term[ii]	Number of cases[iii]	Number of cases with a single suspected medicine[iv]	Number of cases where death was a reported outcome[v]
Reproductive system and breast disorders	Pruritus genital	1	1	0
Skin and subcutaneous tissue disorders	Swelling face	1	1	0

Footnotes

[i] A description of what, in general terms, was affected by the adverse event, as described by the Medical Dictionary for Regulatory Activities MedDRA (for example 'cardiac disorders')

[ii] A description of the adverse event as defined by MedDRA; these adverse events are grouped by system organ class. You can use the MedlinePlus medical dictionary <http://www.nlm.nih.gov/medlineplus/mplusdictionary.html> to look up terms.

[iii] The number of cases for which each type of adverse event was reported

[iv] Results show where a medicine is the only medicine suspected to be related to the adverse event

[v] These reports of death may or may not have been the result of taking a medicine

The TGA uses adverse event reports to identify when a safety issue may be present. An adverse event report does not mean that the medicine is the cause of the adverse event. If you are experiencing an adverse event, or think you may be experiencing one, please seek advice from a health professional as soon as possible. The TGA strongly advises people taking prescription medicines not to change their medication regime without prior consultation with a health professional. Please read all the important information at the beginning of this report.

Comments from OTC Medicines Evaluation on items for June 2020 ACMS #31

Item 1.6 Clotrimazole

Scheduling proposal

Current scheduling	Proposal for ACMS consideration
Schedule 6 - CLOTRIMAZOLE for the external treatment of animals. **Schedule 4 -** CLOTRIMAZOLE except: a) when included in Schedule 2, 3 or 6; or b) in preparations for dermal use for the treatment of tinea pedis. **Schedule 3 -** CLOTRIMAZOLE in preparations for vaginal use. **Schedule 2 -** CLOTRIMAZOLE for human use in dermal preparations and for application to the nails **except** in preparations for the treatment of tinea pedis. **Appendix F, Part 3** **Appendix H#**	A proposal has been made to amend the Schedule 2, Schedule 3 and Appendix F, Part 3 entries for clotrimazole as follows: • **Amend** the Schedule 3 entry to: CLOTRIMAZOLE in preparations for vaginal use **except** when included in Schedule 2. • **Amend** the Schedule 2 entry to: CLOTRIMAZOLE for human use: a) in preparations for vaginal use containing 1 per cent or less of clotrimazole; or b) in dermal preparations; and c) for application to the nails. **except** in preparations for the treatment of tinea pedis. • **Amend** the Appendix F, Part 3 entry to: CLOTRIMAZOLE in vaginal preparations when included in Schedule 2 or Schedule 3.

Background

- Clotrimazole for vaginal use is indicated for the treatment of vulvovaginal candidiasis (fungal infections).
- Clotrimazole creams for the treatment of vaginal thrush are currently available over the counter (Schedule 3) in the following strengths:
  - Clotrimazole 100 mg/g (10%) – one day cream
  - Clotrimazole 20 mg/g (2%) – 3 day cream
  - Clotrimazole 10 mg/g (1%) – 6 day cream

OTC Medicines Evaluation Section comments

- The proposal to down-schedule vaginal preparations of 1% or less of clotrimazole to Schedule 2 would result in such preparations being available for self-selection in pharmacies. The advantage of self-selection is that consultation with a pharmacist is no longer required.
- The disadvantages of availability of vaginal preparations of clotrimazole for self-selection in a pharmacy are concerns in relation to a reduction of safety/efficacy, summarised as follows:

- Frequency of infection is an important decision making metric for the pharmacist, and infections more frequent than 3 times in a 12 month period are referrable to a medical practitioner.
- The list of differential diagnoses is extensive and can include serious conditions such as bacterial vaginosis, trichomoniasis, lichen sclerosis, dermatitis, eczema, STIs, which benefit from the early intervention of a pharmacist who can differentiate the symptoms, where treatment with clotrimazole could exacerbate the condition or be ineffective.
- Vaginal fungal infection can be an indicator of a severe underlying condition, or sub-optimal management of serious co-morbidities, such as undiagnosed or mismanaged T2DM or immunosuppression.
- Clotrimazole creams may damage latex contraceptive devices.
- While listed in Pregnancy Category A, use of vaginal creams internally can irritate the cervix resulting in premature contractions.
- Vaginal clotrimazole creams are currently listed in Appendix H.
- The seriousness of the condition during pregnancy or in children < age of first menarche.
- The rationale behind making the 1% preparation Schedule 2, while two other strengths of the same medicine remain in the Schedule 3 seems illogical.

OTC Medicines Evaluation's recommendation

Recommend rejection of the application (i.e. no change to current scheduling) on the basis of safety and efficacy concerns with use of vaginal clotrimazole products without appropriate pharmacist intervention.

OTC Medicines Evaluation Section
Complementary & OTC Medicines Branch
May 2020

Australian Government
Department of Health
Therapeutic Goods Administration

Seeking advice on proposed scheduling amendments

According to subsection 52E(4) of the Act, in exercising a power under subsection 52D(2), the Secretary may seek advice from any person or any committee that the Secretary considers appropriate (whether or not the committee is established under the Act or the *Therapeutic Goods Regulations 1990* (the Regulations)). This includes an evaluator, the Advisory Committee on Medicines Scheduling (ACMS) and/or the Advisory Committee on Chemicals Scheduling (ACCS). Subsection 52E(3) of the Act also sets out that, where the Secretary decides to seek the advice of the ACMS and/or the ACCS, the Secretary must have regard to that advice.

Delegations

As an EL2 in the Scientific Evaluation Branch, or a Medical Officer Class 5 in the Pharmacovigilance and Special Access Branch, you have powers delegated by the Secretary of the Department of Health under subsections 52D(2) and 52E(4) of the *Therapeutic Goods Act 1989* (the Act) to amend or replace the Poisons Standard [52D(2)] and in doing so, seek advice from any person or committee that the Secretary considers appropriate [52E(4)].

Contents

1. Clotrimazole Error! Bookmark not defined.

Timeframes

Evaluations

If you decide an evaluation is required for an application, the evaluator will require at least 6 weeks to complete an evaluation (see table below). The secretariat would appreciate your decision to evaluate an application by **1 April 2020.**

Timeframes for an evaluation

Application to evaluator	17 April 2020
Evaluation report due to Secretariat and to applicant	15 May 2020
Comments due to Secretariat and to evaluator	29 May 2020
Rejoinder due to Secretariat	12 May 2020

ACMS or Joint ACMS-ACCS

If you decide these matters require ACMS or Joint ACCS-ACMS advice, then the public notice of proposed amendments must be published on the TGA website on 17 April 2020. Your decision regarding referral to ACMS or Joint ACMS-ACCS for advice and your confirmation of the details to be included in the public notices is required by **1 April 2020.**

Delegate-only decision

1. If you decide that an application *does not require ACMS or Joint ACMS-ACCS advice* and that a delegate-only decision is appropriate and that it is *the same as the applicant's proposal*, then the final decision and reasons for the decision will be published on the TGA website with the March 2020 cycle final decisions, on 24 August 2020. Your final decision is therefore required by **3 August 2020**; or

2. If you decide that an application *does not require ACMS or Joint ACCS-ACMS advice* and that a delegate-only decision is appropriate but that it is *different from the applicant's proposal*, then the decision will be an interim decision and will be published on the TGA website with the March 2018 cycle interim decisions on 10 June 2020. The secretariat will also notify the applicant in writing of your interim decision and provide the applicant at least 20 working days to make a written submission in response to your decision. Delegate-only decisions that are different from the applicant's proposal are therefore required by **18 May 2020**.

R1. Having considered the attachments listed below, that you decide to consider this matter as a delegate-only decision.[1]

AGREE ☐
DISAGREE ☒

Reasons:* AS this is a down scheduling application and has previously been discussed at ACMS it 9is appropriate for it to go to ACMS.

R2. That you decide to refer this matter to the ACMS.

AGREE ☒
DISAGREE ☐

Reasons:* As above.

If you refer this matter to ACMS, please provide specific issues/questions you wish the committee/s to consider:

- Noting this was previously been seen in ACMS in 2017 are there reasons to change the provious advice?
- If so, noting the strength re quested to down schedule is this appropriate or should it also cover stronger preparations?

R3. That you decide that the application requires an external evaluation.

AGREE ☐
DISAGREE ☒

Reasons:* Enough is known.

Authorised by

_____

s.47E(d)
Scheduling Delegate

6 April 2020

Attachments for clotrimazole

Attachment A: Agenda Paper (Draft document) D20-311143

Attachment B: Application D20-306156

[1] Please note that by accepting this recommendation the delegate is not making an interim decision or final decision

Australian Government
Department of Health
Therapeutic Goods Administration

CHAIRS' NOTES

Advisory Committee on Medicines Scheduling (ACMS) #31

DATE	Tuesday 23 June 2020 & Wednesday 24 June 2020
TIME	9:30 am – 1:00 pm (AEST) Tuesday 23 June 2020 2:00 pm – 5:00 pm (AEST) Wednesday 24 June 2020
VENUE	Teleconference Message stick number: 1800 047 396 Participant code: 46297710

Introduction

Chair to welcome everyone and open the meeting with the *Acknowledgement to Country*:

'I would like to acknowledge the traditional custodians of the lands on which we are meeting on today and pay my respects to their Elders both past and present. I would like to extend that acknowledgement to any Aboriginal and Torres Strait Islander peoples joining us today.'

Notes for the Chair

Housekeeping matters for teleconference:

- Members and observers must ensure that no one who is located nearby can hear the committee discussion, in part (you speaking) or in full. Participants must declare if they are unable to maintain confidentiality.
- Members must inform the full meeting when they leave (excludes restroom breaks) and also on their return.
- Members are asked to avoid undertaking non-meeting related tasks during the meeting e.g. checking emails.
- Members and observers must not record the Committee discussion.
- Mute your device if you are not speaking. Do not use the hold function.
- State your full name when prompted by the message stick facility so your registration can be recorded.

- Introduce yourself before speaking.
- Members are asked not to interrupt others when they are speaking (or attempt to speak over them). The Chair is responsible for moderating the Committee discussion if needed.
- Please join the meeting early. If you are late, you must introduce yourself so other members know you are present and so your attendance can be recorded. The Chair will prompt members if not response is provided.
- The chair will re-confirm attendees after all breaks.
- Messages sent using the instant messaging (IM) function on GovTeams can be viewed by all members and the messages cannot be deleted. The use of the IM function is not encouraged at the present time.

Locking the teleconference:

- Once everyone has joined the conference, the secretariat will lock the conference.
- This feature stops anyone else from being able to dial into the meeting.
- If a member arrives late or they need to leave and redial in, they may need to wait a moment on the call while the secretariat unlocks the conference to let them in.

Participant count or roll call:

- The secretariat will periodically check how many people are connected to the call and advise if you if the numbers connected do not match the roll call.
- When entering the meeting, it is important for participants to state their full name when prompted by the message stick facility. This will allow the secretariat to confirm the details of everyone on the call.

Preliminary Matters:

- Welcome to new members:

  s.47F(1) [redacted]

  These members will be joining today as specialist advisors.

- Confirm members who are present at the meeting:

Minister Appointments	**Jurisdictional Members**
Suzanne NIELSEN (Chair)	Jane CARPENTER
Diana ROBINSON	Peter GILFEDDER
John STUBBS	Danica IVKOVIC

- FOR OFFICE USE ONLY -

Lubna TABASSUM	Angela FITZHENRY
Julie VIATOS	Julie STOKES
Michael WARD	Helgi STONE
Jane COOK (Commonwealth representative)	Wendy YANG
	Natalie JOHNS

- Welcome to observers:

  Secretariat to provide confirmation to the Chair on the meeting day if the observers listed below are in attendance

Standing and invited observers:

s.47E(d)	Delegate, Commonwealth Dept. of Health (TGA)
Adj. Prof John Skerritt	Deputy Secretary, Commonwealth Dept. of Health (TGA)
Mr Avi Rebera	Assistant Secretary, Regulatory Engagement & Planning Branch, Commonwealth Dept. of Health (TGA)
s.47E(d)	Commonwealth Dept. of Health (TGA)
	Commonwealth Dept. of Health (TGA)
	Commonwealth Dept. of Health (TGA)
	Commonwealth Dept. of Health (TGA)
	Commonwealth Dept. of Health (TGA)

Apologies

- s.47E(d) (ACMS nominated member for ACT). s.47E(d) is attending in s.47E place.

Additional Points

- Chair to remind members and observers that the discussions and recommendations of the committee are considered confidential until the interim decisions are published.
- Staff will be taking notes during the meeting – the chair is requested to summarise discussions for them at the end of each item.

Meeting work plan

- Tuesday's meeting starts at 9:30 am and is expected to finish at 1 pm. There will be a break at 11:30 am (15 minutes).
- Wednesday's meeting starts at 2 pm and is expected to finish at 5pm. There will be a break at 3:30 pm (15 min).

- The agenda indicates the timing of particular agenda items and the names of those nominated to present the items.
- I wish to remind speakers to keep their presentation/talking points to 5-10 minutes each to ensure timely running of the meeting as per the agenda.

Conflict of interest and confidentiality obligations

The *Declaration and Managing Conflict of Interests and Confidentiality Obligations Form* has been distributed to all the committee members before the meetings and they have been requested to fill in the form and submit that to the Committee Support Unit (CSU) before the meeting. However, the CSU will provide the forms in the beginning of the meeting as usual for those who may have not completed it earlier.

All members and observers **must** complete this form and return it to the Chair prior to commencement of committee business. This form is required to be completed at each meeting and relates only to those items on the agenda for discussion at this meeting. Where a potential conflict of interest exists (real or perceived), members must also raise the issue at the commencement of discussion of the relevant agenda item(s). The nature of the potential conflict, as well as the Committee's decision in each case, will be recorded in the minutes.

Declared conflicts of interests:

Member	Declared conflict of interest	Comments	Assigned substance(s)
s.47E(d)			

Public submissions received after the published closing date

The Committee will decide whether to accept the public submissions received after the first closing date of 18 May 2020. The Secretariat will record the Committee's decision.

According to the *Therapeutic Goods Regulations 1990* (Section 42ZCZL) the Committee must consider all public submissions received by the first closing date that address a matter mentioned in section 52E of the Act and are relevant to the proposed amendment.

The Committee is not required to consider a public submission received after the first closing date.

Australian Government

Department of Health
Therapeutic Goods Administration

ACMS MEETING #31

23-24 June 2020

MEETING RECORD OF RESOLUTIONS AND 52E TABLES

s.22



D20-323519

s.22

[redacted]

2.4 Clotrimazole

Scheduling Proposal

Schedule 3 – Amend Entry

CLOTRIMAZOLE in preparations for vaginal use **except** when included in Schedule 2.

Schedule 2 – Amend Entry

CLOTRIMAZOLE for human use:

a. in preparations for vaginal use containing 1 per cent or less of clotrimazole; or

b. in dermal preparations; and

c. for application to the nails.

except in preparations for the treatment of tinea pedis.

Appendix F, Part 3 – Amend Entry

Poison	**Warning statements**	**Safety directions**
CLOTRIMAZOLE in vaginal preparations when included in Schedule 2 or Schedule 3.	54,63,64,66	

OPTIONS

OPTION 1

The Committee recommends that the current scheduling of clotrimazole remains appropriate.

OPTION 2

The Committee recommends that the current Schedule 2 and Schedule 3 entries for clotrimazole be amended as follows:

Schedule 3 – Amend Entry

CLOTRIMAZOLE in preparations for vaginal use **except** when included in Schedule 2.

Schedule 2 – Amend Entry

CLOTRIMAZOLE for human use:

a. in preparations for vaginal use containing 1 per cent or less of clotrimazole; or

b. in dermal preparations; and

c. for application to the nails.

except in preparations for the treatment of tinea pedis.

OPTION 3

The Committee also recommends the Appendix F entry be amended as follows:

Poison	**Warning statements**	**Safety directions**
CLOTRIMAZOLE in vaginal preparations when included in Schedule 2 or Schedule 3.	54,63,64,66	

IMPLEMENTATION DATE

The Committee is asked to discuss and consider the resolutions with an implementation date of 1 February 2021/1 June 2021/1 October 2021.

RECOMMENDATION FOR OTHER ACTION BY THE DELEGATE

REASONS FOR RECOMMENDATIONS (BOTH SPEAKERS)

52E(1) Considerations	***Reasons***
a – the risks and benefits of the use of a substance	Clotrimazole vaginal preparations are effective treatments for vulvovaginal candidiasis. The risks associated with their use are related to misdiagnosis and delayed treatment for the actual cause, as well as the financial impact of purchasing an ineffective product. Risks - Self-misdiagnosis & self-mistreatment - Potential of masking more serious underlying conditions including bacterial vaginosis, UTI, STI and undiagnosed or uncontrolled diabetes and delaying appropriate treatment Benefits More ready access a safe and effective treatment of vulvovaginal candidiasis caused by Candida albicans without pharmacist intervention/consultation (removes embarrassment seeking treatment)
b – the purposes for which a substance is to be used and the extent of use of a substance	Clotrimazole vaginal preparations are used for vuvovaginal candidiasis. The estimated probability of VVC by age 50 varied widely by country (from 23% to 49%, mean 39%) in research drawn from 7 countries. For the treatment of vulvovaginal candidiasis caused by Candida albicans (clotrimazole 1% for vaginal use)
c – the toxicity of a substance	Clotrimazole is an imidazole derivative that has low levels of systemic absorption from vaginal administration. It is extensively metabolised in the liver to inactive compounds. No carcinogenicity or mutagenicity was observed in animal studies. Vaginal clotrimazole is considered safe to use in pregnancy (a 1-week course) and in breastfeeding.

	Vaginal clotrimazole is generally well tolerated with the main reported adverse reactions being local irritation (e.g. burning, erythema). Hypersensitivity/allergic reactions are rare. Low toxicity
d – the dosage, formulation, labelling, packaging and presentation of a substance	Warning statements are already required for clotrimazole vaginal preparations. The effectiveness of the proposed packaging warning statement 'For women who have previously been diagnosed with vaginal thrush' is unclear given there is evidence that women do not read the package information and that reading the label does not improve the accuracy of self-diagnosis. Labelling on its own does not mitigate risk of self-misdiagnosis or delay seeking treatment of more serious underlying condition. Evidence of women who do not read the label and that reading the label does not improve accuracy of self-diagnosis.
e – the potential for abuse of a substance	There is no evidence of dependence or abuse of clotrimazole vaginal preparations, however misuse due to misdiagnosis is probable. Low potential for abuse
f – any other matters that the Secretary considers necessary to protect public health	Consideration should be given to strengthening the required warning statements if a Schedule 2 entry for clotrimazole is made

s.22

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Department of Health
Therapeutic Goods Administration

PRE-MEETING BRIEFING

Advisory Committee on Medicines Scheduling (ACMS) #31

23 June 2020

Item	Substance	Sensitivities
s.22		

[1] Therapeutic Goods (Medicines Advisory Statements) Specification 2019
https://www.legislation.gov.au/Details/F2019L00213

Item	Substance	Sensitivities
s.22		
2.3	**Clotrimazole**	• An application was submitted by Bayer Australia requesting the Schedule 2 entry for clotrimazole be amended to include preparations for vaginal use containing 1 per cent or less of clotrimazole.

Item	Substance	Sensitivities
		• The Therapeutic Goods (Medicines Advisory Statements) Specification 2019[2] requires the following warning statements pertaining to clotrimazole for vaginal use to be included on the labelling: – Seek medical advice before first course of treatment. – See a doctor if you are pregnant or diabetic. – See a doctor if no better after [Insert number of days as per approved Product Information] days. – See a doctor if problem returns. • Four public submissions were received in response to the proposal. Two in support, one in support with caveats and one in opposition (see D20-845073). Internal consultation • OTC medicines recommended that the scheduling of clotrimazole remain unchanged on the basis of safety concerns with the use of clotrimazole products without appropriate pharmacists intervention. The following were identified by OTC as impediments to down-scheduling: – Frequency of infection is an important decision making metric for the pharmacist, and infections more frequent than 3 times in a 12-month period are referrable to a medical practitioner. – The list of differential diagnoses is extensive and can include serious conditions such as bacterial vaginosis, trichomoniasis, lichen sclerosis, dermatitis, eczema, STIs, which benefit from the early intervention of a pharmacist who can differentiate the symptoms, where treatment with clotrimazole could exacerbate the condition or be ineffective. – Vaginal fungal infection can be an indicator of a severe underlying condition, or suboptimal management of serious co-morbidities, such as undiagnosed or mismanaged T2DM or immunosuppression. – Clotrimazole creams may damage latex contraceptive devices. – While listed in Pregnancy Category A, use of vaginal creams internally can irritate the cervix resulting in premature contractions. – Vaginal clotrimazole creams are currently listed in Appendix H. – The seriousness of the condition during pregnancy or in children < age of first menarche. – The rationale behind making the 1% preparation Schedule 2, while two other strengths of the same medicine remain in the Schedule 3 seems illogical. The full OTC submission is available at D20-720778.
s.22		

[2] Therapeutic Goods (Medicines Advisory Statements) Specification 2019
https://www.legislation.gov.au/Details/F2019L00213

DECISION MINUTE

The medicines scheduling delegate's final decisions on proposed amendments to the current Poisons Standard and the public notice of those decisions

To: s.47E(d)
Medicines Scheduling Delegate
Principal Medical Advisor
Director
Medical Devices Surveillance Branch
Medical Devices & Product Quality Division
Health Products Regulation Group

From: s.47E(d)
Director
Scheduling and Committee Support
Regulatory Engagement Education and Planning Branch
Regulatory Practice and Support Division
Health Products Regulation Group

Purpose

Final Decisions

For you to approve the scheduling final decisions in the *Notice of the final decisions to amend (or not amend) the current Poisons Standard* **(Attachment A)**, and confirm that Attachment A correctly reflects your final decisions for those decisions, in relation to the below substances:

- Substances referred to the June 2020 meetings of the:
  - Advisory Committee on Medicines Scheduling (ACMS #31)

s.22

    - clotrimazole;

s.22

Scheduling final decisions public notice

For you to note that, as per regulations 42ZCZS of the *Therapeutic Goods Regulations 1990* (the Regulations), the *Notice of the final decisions to amend (or not amend) the current Poisons Standard* (**Attachment A**) will inform the public of the final scheduling decisions, the reasons for those decisions and the proposed dates of effect.

Background

The Secretary of the Department of Health is granted powers concerning the making of final decisions to amend the current Poisons Standard under regulations 42ZCZR of the *Therapeutic Goods Regulations 1990* (Cth) (**Regulations**).

Where the Secretary exercises the powers granted under regulations 42ZCZR, regulation 42ZCZS of the Regulations (respectively) requires that the Secretary publish, in a manner that the Secretary considers appropriate, the decision, the reasons for the decision, and the date of effect of the decision.

The powers of the Secretary under regulations 42ZCZR, 42ZCZS, 42ZCZU and 42ZCZX are delegated to, among others, an MO5 in the Medical Devices & Product Quality Division (**Attachment B**).

Timing

The *Notice of the final decisions to amend (or not amend) the current Poisons Standard* must be finalised and provided to the TGA webs team by 20 November 2020 for publication on the TGA website on 25 November 2020. Therefore, this request must be actioned before 20 November 2020.

Scheduling amendments referred to expert advisory committee

In exercising a power under subsection 52D(2) of the *Therapeutic Goods Act 1989* (Act), you must have regard to any recommendations or advice of the Advisory Committee on Medicines Scheduling:

- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS#31) is available at D20-926060;

Consultation

Consultations occurred in accordance with regulations 42ZCZK and 42ZCZP of the Regulations. Notices inviting public submissions on proposed amendments to the Poisons Standard referred to the June 2020 meetings of the ACMS #31 were made available on the TGA website on 17 April 2020 (closed on 15 May 2020) and 9 September 2020 (closed on 13 October 2020).

- The public submissions received in response to an invitation (first closing date) under regulation 42ZCZK of the Regulations are available at D20-569059.
- The public submissions received in response to the call for further submissions (second closing date) under regulation 42ZCZP of the Regulations are available at D20-3525018.

In reconsidering an interim decision under regulations 42ZCZQ you must:

- consider all public submissions (the relevant submissions) made by the second closing date that:
  - address a matter mentioned in section 52E of the Act; and
  - are relevant to the Secretary's interim decision.

Medicines Scheduling Delegate's Decision

I am a delegate of the Secretary for the purpose of regulation 42ZCZR of the *Therapeutic Goods Regulations 1990* (**Regulations**). After considering all relevant submissions and advice received from the Advisory Committee on Medicines Scheduling (ACMS#31), I have made final decisions under regulation 42ZCZR with respect to the following substances:

s.22

- clotrimazole;

s.22

I **approve** the scheduling final decisions in the *Notice of the final decisions to amend (or not amend) the current Poisons Standard* **(Attachment A)**, and I confirm it correctly reflects my final decisions for the above named substances.

I **approve** the publication of *Notice of the final decisions to amend (or not amend) the current Poisons Standard* **(Attachment A)** on the TGA website

I note that the publication of the *Notice of the final decisions to amend (or not amend) the current Poisons Standard* **(Attachment A)** is in compliance with regulations 42ZCZS and 42ZCZX of the Regulations.

Electronically signed

_____

s.47E(d)

Medicines Scheduling Delegate
20/11/ 2020

Attachments:

Attachment A	*Notice of the final decisions to amend (or not amend) the current Poisons Standard* for publication on the TGA website (D20-3554032)
Attachment B	Commonwealth of Australia Department of Health *Therapeutic Good Act 1989* and Therapeutic Goods Regulations 1990 Therapeutic Goods (Secretarial) Delegation Instrument 2020 - dated 11 August 2020

Contact officer:	s.47E(d)
Phone:	s.47E(d)