Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Australian Public Assessment Report for MS-2 Step (composite pack)

Active ingredients: mifepristone & misoprostol

Sponsor: MS Health Pty Ltd

February 2024

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health and Aged Care and is responsible for regulating therapeutic goods, including medicines, medical devices, and biologicals.
- The TGA administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety, and efficacy.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to the Australian public outweigh any risks associated with the use of therapeutic goods.
- The TGA relies on the public, healthcare professionals and industry to report problems with therapeutic goods. The TGA investigates reports received to determine any necessary regulatory action.
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About AusPARs

- The Australian Public Assessment Report (AusPAR) provides information about the evaluation of a prescription medicine and the considerations that led the TGA to approve or not approve a prescription medicine submission. Further information can be found in Australian Public Assessment Report (AusPAR) guidance.
- AusPARs are prepared and published by the TGA.
- AusPARs are static documents that provide information that relates to a submission at a particular point in time. The publication of an AusPAR is an important part of the transparency of the TGA's decision-making process.
- A new AusPAR may be provided to reflect changes to indications or major variations to a prescription medicine subject to evaluation by the TGA.

Contents

List of abbreviations

Abbreviation	Meaning
ACM	Advisory Committee on Medicines
ACV	Advisory Committee on Vaccines
AHPRA	Australian Health Practitioner Regulation Agency
ARTG	Australian Register of Therapeutic Goods
ASA	Australia-specific annex
CMI	Consumer Medicines Information
hCG	Human chorionic gonadotropin
MLPs	Mid-level providers
MToP	Medical termination of pregnancy
PI	Product Information
RMP	Risk management plan
SoSC	Summary of safety concerns
TGA	Therapeutic Goods Administration

Product submission

Submission details

Type of submission:	Type J (Product Information Change Requiring Evaluation of Data)
Product name:	MS-2 Step composite pack
Active ingredients:	Mifepristone Linepharma, GyMiso misoprostol.
Decision:	Approved
Date of decision:	28 June 2023
Date of entry onto ARTG:	10 July 2023
ARTG number:	210574
Sponsor's name and address:	MS Health Pty Ltd, Suite 60, 278 Church Street, Richmond, VIC, Australia, 3121.
Dose form:	Tablet
Strength:	Each tablet of Mifepristone Linepharma contains 200 mg of mifepristone. Each tablet of GyMiso misoprostol contains 200 micrograms of misoprostol.
Container:	Carton
Pack size:	One (1) Mifepristone Linepharma tablet and four (4) GyMiso tablets per MS-2 Step pack.
Approved therapeutic use for the current submission:	MS-2 Step is indicated in females of childbearing age for the medical termination of an intrauterine pregnancy, up to 63 days of gestation. In the current submission, approval was granted to make the following changes in the Product Information (PI) and to the Risk Management Plan (RMP): PI • Amend '*medical practitioner*' in the boxed warning to '*healthcare practitioner*' • Amend '*doctors with the appropriate qualifications and certified training*' in Section 4.2 to '*healthcare practitioners with the appropriate qualifications and training*' (in accordance with individual state and territory requirements) RMP • Removal of the requirement for pharmacist registration to dispense the product • Removal of the mandatory training and certification requirement for prescribers

- Removal of the 24-hour telephone nurse aftercare service for patients.

Route(s) of administration:	Oral
Dosage:	Mifepristone: 200 mg of mifepristone (1 tablet containing 200 mg) orally, followed 36 to 48 hours later by the administration of GyMiso®. GyMiso®: 800 micrograms of misoprostol (4 tablets, each tablet containing 200 micrograms) buccally, i.e., kept between the cheek and the gum for 30 minutes before any fragments being swallowed with water. For further information regarding dosage, such as dosage modifications to manage adverse reactions, refer to the Product Information.

Clinical rationale

Mifepristone belongs to the pharmacotherapeutic group: Other sex hormone and modulator of the reproductive function/antiprogestogen, ATC code GO3XB01.

Misoprostol belongs to the pharmacotherapeutic group: Other gynaecological medicines – prostaglandins, ATC code G02AD06.

Mifepristone is a synthetic steroid with an antiprogestational action due to competition with progesterone at the progesterone receptors. In women at doses of greater than or equal to 1 mg/kg, mifepristone antagonises the endometrial and myometrial effects of progesterone. During pregnancy it sensitises the myometrium to the contraction inducing action of prostaglandins.

Misoprostol is a synthetic analogue of prostaglandin E1. At the recommended dosages, misoprostol induces contractions of the smooth muscle fibres in the myometrium and relaxation of the uterine cervix.

When used for early termination of pregnancy (<12 weeks gestation), the combination of misoprostol in a sequential regimen after mifepristone leads to an increased success rate and accelerates the expulsion of the conceptus.

Regulatory status

Australian regulatory status

The individual components of MS-2 Step, Mifepristone Linepharma (mifepristone 200 mg tablet) and GyMiso (misoprostol 200 microgram tablet) were both registered in Australia on 29 August 2012 for the following indications:

Mifepristone Linepharma (AUST R 175671):

> *Medical termination of a developing intra-uterine pregnancy. In sequential combination with a prostaglandin analogue up to 49 days of gestation; and preparation for the action of registered prostaglandin analogues that are indicated for the termination of pregnancy for medical reasons beyond the first trimester.*

GyMiso (AUST R 188015):

> *GyMiso is indicated in females of childbearing age for the medical termination of a developing intrauterine pregnancy in sequential combination with a mifepristone 200 mg tablet, up to 49 days of gestation.*

The MS-2 Step composite pack containing Mifepristone Linepharma (mifepristone) 200 mg tablet and GyMiso (misoprostol) 200 microgram tablets received initial registration in the Australian Register of Therapeutic Goods (ARTG) on 4 June 2014 (Submission PM-2013-01037-1-5). It was approved for the following indication:

> *MS-2 Step is indicated in females of childbearing age for the medical termination of an intrauterine pregnancy, up to 63 days of gestation.*
>
> *It is recommended that the duration of pregnancy (i.e., up to 63 days gestation) be confirmed by ultrasound. In the event that an ultrasound is not possible, extra caution should be exercised.*
>
> *Ultrasound is also useful to exclude ectopic pregnancy.*

The gestational limit was increased as part of this submission for the MS-2 Step from 49 days for the individual components, to up to 63 days gestation for the composite pack.

Following registration of the MS-2 Step composite pack, the Sponsor withdrew the GyMiso mono product from the market and removed the early termination of pregnancy indication from the Mifepristone Linepharma mono product. Mifepristone Linepharma is now only registered *in females of childbearing age for preparation for the action of registered prostaglandin analogues that are indicated for the termination of pregnancy for medical reasons beyond the first trimester*.

Foreign regulatory status

As of May 2023, the combination of active ingredients, mifepristone and misoprostol is approved for medical termination of pregnancy in over 96 countries, noting there are varying controls around access and prescribing between jurisdictions.

MS-2 Step composite pack (sponsored by MS Health) is currently only registered for use in Australia. However, the Mifegymiso composite pack (mifepristone 200 mg tablet and misoprostol 200 microgram tablets, Linepharma International Limited) is approved in Canada for a comparable indication to MS-2 Step composite pack:

> *Medical termination of a developing intra-uterine pregnancy with a gestational age up to 63 days as measured from the first day of the Last Menstrual Period (LMP) in a presumed 28-day cycle.*
>
> *Mifegymiso is not intended for routine use as a contraceptive.*

The Health Canada Product Monograph states in Section 4.1 Dosing Considerations that *Mifegymiso should be prescribed by health professionals with adequate knowledge of medical abortion and/or who have completed a Mifegymiso education program.*

Registration timeline

The following table lists the key steps and dates for this submission.

This submission was evaluated under the standard prescription medicines registration process.

Table 1: Timeline for Submission PM-2022-05475-1-5

Description	Date
Submission dossier accepted and first round evaluation commenced	31 Jan 2023
First round evaluation completed	9 Mar 2023
Second round evaluation completed	17 May 2023
Registration decision (Outcome)	28 June 2023
Number of working days from submission dossier acceptance to registration decision*	103

*Statutory timeframe for standard submissions is 255 working days

Submission overview and risk/benefit assessment

The Sponsor provided evidence from 3 studies comparing provision of early MToP by doctors and midlevel providers (MLPs; nurses and midwives and allopathic and ayuverdic physicians with appropriate training) to support the proposed changes in this submission:

- Kopp Kallner *et al.* – 1180 women receiving MTOP up to 63 days (9 weeks) gestation in a high-resource setting with ultrasound dating of pregnancy (Sweden)[1]
- Warriner *et al.* – 1077 women receiving MTOP up to 63 days (9 weeks) gestation estimated by last menstrual period and bimanual pelvic examination (Nepal)[2]
- Jejeebhoy *et al*. – 1225 women receiving MTOP up to 8 weeks gestation confirmed by urine pregnancy test and pelvic examination (India)[3].

The Kopp Kallner *et.al*.[1] study is considered most relevant to use in Australia with ultrasound dating part of the protocol. The studies by Warriner *et. al*.[2] and Jejeebhoy *et. al*.[3] were conducted in low-resource settings without ultrasound assessment, and in the case of the Warriner study, without confirmation of pregnancy using human chorionic gonadotropin (hCG) testing.

The Australian MS-2 Step PI recommends confirmation of gestation by ultrasound, and lists '*pregnancy not confirmed by an ultrasound or biological test such as urine or serum hCG*' as a contraindication. The study population and dose of misoprostol used in the Jejeebhoy *et al.*[3] study also differs from approved use in Australia.

There were no safety concerns with provision of MToP by mid-level providers (MLPs) identified in any of the 3 studies, with effectiveness outcomes comparable for MLPs and doctors. The risk of failure was comparable for MToP performed by MLPs and doctors in all studies and is a known risk described in the MS-2 Step PI. There were no serious adverse events reported in any

[1] Kopp Kallner H, Gomperts R, Salomonsson E, Johansson M, Marions L, Gemzell-Danielsson K. The efficacy, safety and acceptability of medical termination of pregnancy provided by standard care by doctors or by nurse-midwives: a randomised controlled equivalence trial. BJOG. 2015;122:510-517.

[2] Warriner IK, Wang D, Huong NTM, Thapa K, Tamang A, Shah I *et al*. Can midlevel health-care providers administer early medical abortion as safely and effectively as doctors? A randomised controlled equivalence trial in Nepal. *Lancet*. 2011;377:1155-1161.

[3] Jejeebhoy SJ, Kalyanwala S, Mundle S, Tank J, Zavier AJF, Kumar R *et al*. feasibility of expanding the medication abortion provider baser in India to include ayurvedic physicians and nurses. *Int Perspect Sex Reprod Health*. 2012;38:133-142

of the 3 studies. Kopp Kallner *et al*.[1] detailed the complications observed which were noted to be consistent with the safety profile of MToP with mifepristone/misoprostol.

There was variable training background and experience of MLPs across the 3 studies. Nurse-midwives experienced in provision of MToP were recruited in the Kopp Kallner *et. al*.[1] study and provided with additional early pregnancy ultrasound training. All providers underwent MToP training in the Warriner *et al*. and Jejeebhoy *et al*. studies[2,3]. The importance of education about MToP was endorsed by the Clinical Expert (MS Health) who stated, *'MS Health proposes to continue providing the same (existing) standardised training for all potential prescribers (as detailed in the current approved Australian RMP) and doing so will ensure a minimum baseline of education regardless of training background'.* Stating further, *'The PI amendments proposed by MS Health simply enable individual jurisdictions to make decisions appropriate for their population.'.*

The TGA delegate noted that broadening the prescriber eligibility for MS-2 Step to include non-medical practitioner prescribers (in accordance with individual state and territory requirements) is consistent with established practice for MToP in comparable jurisdictions, including Canada and the USA, noting that the USA has additional requirements for all prescribers.

Overall, the evidence provided by the Sponsor supports the proposed changes to the MS-2 Step PI proposed in this submission.

The Sponsor's initial application to the TGA proposed (only) to amend '*doctors with the appropriate qualifications and certified training'* in Section 4.2 of the PI to '*healthcare practitioners with the appropriate qualifications and certified training*'. Following discussions with the TGA, MS Health submitted an amended proposal, including an updated RMP, to also remove the mandatory requirement for prescriber training, certification and recertification, the requirement for dispensing pharmacist registration and the 24-hour telephone nurse aftercare service.

The Clinical Expert (MS Health) asserted in the initial submission that a minimum baseline of education, irrespective of training background, was required for the provision of MToP. In their amended proposal, the Sponsor emphasised that the existing standardised training (the Medical Education Program) will still be available for all healthcare practitioners that prescribe MS-2 Step via the existing website (www.ms2step.com.au). They stressed that the change proposed was to remove the *mandatory* aspect of the training and certification requirement, not to change the availability of training.

The justification provided by the Clinical Expert in the Clinical Overview Addendum to expand prescriber eligibility to include non-medical practitioner prescribers (in accordance with individual state and territory requirements) included assurance that the existing standardised training for all potential prescribers as per current approved Australian RMP (i.e. mandatory practitioner training and certification) would be maintained and was supported by data provided in the dossier.

As noted in the clinical evaluation report, all the MLPs underwent MToP training in the Warriner *et al*. and Jejeebhoy *et al*. studies (including certification in the Warriner *et al*. study)[2,3] and the Kopp Kallner study[1] recruited nurse-midwives experienced in provision of MToP who then received additional ultrasound training. The proposed removal of '*certified training*' from the PI provided with the Section 31 response did not completely align with the data included in the submission in support of the original proposed expansion of prescriber eligibility and the Clinical Expert's assertion that '*a minimum baseline of education regardless of training background will continue to be provided*'.

Recommendation following the clinical evaluation

The evidence provided in the submission supports the proposed changes to the boxed warning to amend '*medical practitioner*' to '*healthcare practitioner*' and to amend Section 4.2 '*doctors with the appropriate qualifications and certified training*' to '*healthcare practitioners with the appropriate qualifications and training*' (in accordance with individual state and territory requirements) on the basis that the existing standardised training for all potential prescribers is maintained. However, the Sponsor's proposal to remove the certified training requirement from the PI and RMP created uncertainty regarding the risk of expanding prescriber eligibility which required ACM advice and further consideration by the clinical delegate.

Risk management plan (RMP)

An updated RMP was submitted with changes to the summary of safety concerns (SoSC) and the risk minimisation plan which addressed the proposed amendments in the current submission.

Key changes proposed for risk minimisation activities:

- To remove the requirement for pharmacists to be registered to be able to dispense the product.
- To remove the need for prescribers to complete mandatory training and receive certification to be able to prescribe the product.
- To remove the requirement for prescriber recertification.
- To remove the requirement for a sponsor provided 24-hour telephone nurse aftercare service for patients.

The Sponsor proposed to remove the phrase '*Potential for loss to follow-up*' from the RMP and this is acceptable from an RMP perspective. However, the sponsor has also proposed to remove '*Potential safety risks in vulnerable groups including women in regional and remote areas of Australia, who may be particularly at risk of being lost to follow-up*', which is not supported as there are additional considerations to this risk with regards to access to further advice or treatment if follow-up does not occur.

Routine pharmacovigilance is proposed for all safety concerns. There is one additional pharmacovigilance activity – an ongoing Canadian post-market surveillance study on the effectiveness and safety of combination mifepristone/misoprostol for medical abortion under 63 days gestation.

Risk minimisation activities outlined in the current RMP and maintained in the updated RMP include a black box warning, inclusion of CMI and instruction insert in the pack, and a Patient Information and Consent Agreement form. The sponsor will continue to make educational materials available to support prescribers and dispensers.

The proposed risk minimisation plan aligns with that in Canada and the UK. The RMP evaluator has noted the post-market experience with MS-2 Step, its well-established safety profile, and existing safety frameworks in place. The RMP evaluator has also noted the importance of timely access of this medicine in terms of patient-safety and the need to remove requirements that hinder patient access to reproductive services.

The proposed changes to the risk minimisation plan were acceptable from an RMP perspective. The sponsor was requested to include a copy of the Educational Program materials and Patient Information and Consent Agreement form in the appendix of the RMP.

The summary of safety concerns and their associated risk monitoring and mitigation strategies are summarised in Table 2. The TGA may request an updated RMP at any stage of a product's life-cycle, during both the pre-approval and post-approval phases.

Table 2: Summary of safety concerns

Summary of safety concerns		Pharmacovigilance		Risk Minimisation	
		Routine	Additional	Routine	Additional
Important identified risks	Infection, toxic shock syndrome	✓	–	✓	✓
	Method failure	✓	–	✓	✓
	Cardiac disorders	✓	–	✓	✓
Important potential risks	Inadvertent pregnancy exposure and risk of incomplete abortion with severe bleeding	✓	–	✓	✓
	Inadvertent pregnancy exposure (risk of malformations)	✓	–	✓	✓
	Potential interaction with CYP3A4 inhibitors or inducers	✓	–	✓	–
	Potential interaction with products interacting with the glucocorticoid receptor	✓	–	✓	–
	Induced bronchial asthma	✓	–	✓	–
	Effects in lactating women	✓	–	✓	–
	Effects in women with impaired liver function	✓	–	✓	–
	Effects in women with impaired renal function	✓	–	✓	–
	Effects in women with malnutrition	✓	–	✓	–
	Incorrect determination of gestational age	✓	–	✓	–
	Potential for missed ectopic pregnancy	✓	–	✓	✓
	Potential for postnatal developmental delay	✓	–	✓	–
	Potential for off-label use beyond the first trimester	✓	–	✓	–
Missing information	Inherited porphyria	✓	–	–	–
	Theoretical interaction with NSAIDs	✓	–	–	–
	Potential interaction with products interacting with the progesterone receptor	✓	–	–	–
	Use in adolescents	✓	–	–	–
Pharmacological class effect	Risks related to the use of prostaglandin	✓	–	✓	✓

Further information regarding the TGA's risk management approach can be found in risk management plans for medicines and biologicals and the TGA's risk management approach. Information on the Australia-specific annex (ASA) can be found on the TGA website.

Advisory Committee considerations

The Advisory Committee on Medicines (ACM) having considered the evaluations and the Delegate's overview, as well as the Sponsor's response to these documents, provided the following advice.

Specific advice to the Delegate

The ACM acknowledged that the healthcare and evidentiary landscape related to medical MToP has changed since MS-2 Step was originally registered in Australia (2012). The ACM noted the widespread promulgation of comprehensive guidelines and educational resources for the use of MS-2 Step in Australia. The ACM also noted international changes to the regulation of MToP with the use of a broader range of health professional prescribers including nurse led models. The ACM also acknowledged the importance of improving access to pregnancy termination services and reducing stigma.

The ACM considered the impacts of broadening the prescribing group to healthcare practitioners within the Australian context. The ACM commented that there were instances where the PI outlines which medical specialist should prescribe, manage and/or supervise treatment. However, the ACM noted that currently for the majority of products, the prescribing requirements are defined by scope of practice and jurisdictional regulatory arrangements, with no recommendations about the prescriber included in the PI.

The ACM discussed the three key studies (Kopp Kallner et al. (2014), Warriner et al. (2011), and Jejeebhoy et al. (2012)) provided by the sponsor in support of this application.

The ACM noted that the Kopp Kallner et al. (2014) study appeared the most relevant to the Australia context. Within this study the WHO protocol was followed and all women received an ultrasound prior to treatment. Within the doctor prescribed arm, 34 doctors prescribed treatment to 583 women. While in the nurse-midwife arm, 2 nurses prescribed treatment to 597 patients. Outcomes were comparable within both arms.

The ACM also considered the Canadian experience (Schummers et al. 2022) using Mifegymiso and noted that Canadian Regulations were amended in May 2017 and November 2017, together removing the requirements for:

- Pharmacist registration
- Healthcare profession registration
- Mandatory training
- Removing the limitation on an eligible prescriber from ‘physician’ to be ‘authorised health professional’ leaving the authority for authorising health professional with the provincial licensing bodies.

The ACM discussed the term healthcare practitioner and noted the AHPRA list of health practitioners. The ACM did not consider it appropriate for all health practitioners as per the AHPRA list to be able to prescribe MS-2 Step (or other prescription medicines). The ACM acknowledged that there are additional checks and balances beyond the wording of the PI that control prescribing, for example medicine scheduling. However, the ACM noted that changing the boxed warning (and associated parts of the PI) to state healthcare practitioners may inadvertently assume the PI is supportive of all healthcare practitioners prescribing MS-2 Step. The ACM suggested that some additional wording such as ‘healthcare practitioners with an appropriate scope of practice’ or ‘authorised healthcare practitioners’ (as per Canada) may be appropriate.

Prior to coming to a final position, the ACM requested additional clarification regarding the wider eligibility criteria for healthcare practitioners prescribing and/or authorisation, including further information on scope of practice and jurisdictional arrangements and consideration of PIs where prescribing information is included.

The ACM was supportive of the removal of the requirement for prescriber certification from the PI and as part of the updated RMP. The ACM noted that good guidance and training material is now widely available.

The ACM advised that the phrase '*with the appropriate qualifications and training*' should remain within the Dose and Method of Administration section of the PI. The ACM noted the obligation on the prescriber to ensure they have the relevant skill and capability and undertake the appropriate due diligence and clinical assessment prior to prescribing the medication.

The ACM noted that limited information on the use of the 24-hour telephone nurse aftercare service for patients was provided in the dossier and advised that this information would be helpful to determine whether it is appropriate to remove this service. The ACM recommended that prior to a decision on removal of the 24-hour phone service, the sponsor be requested to provide information on utility of the service.

The ACM advised that consideration of inconsistencies noted in Sections 4.2, 4.4, 4.6 and 4.8 of the MS-2 Step composite pack PI would be discussed following a recommendation on the proposed expansion of prescriber eligibility.

Initial conclusion of the ACM

The ACM was generally supportive of amending 'medical practitioner' to a broader category noting that there are other controls in place (i.e. scheduling) to ensure appropriate prescribing. However, the ACM did express some hesitation with the wider scope of healthcare practitioners and wanted to consider this wording further and potentially add a statement such as 'with appropriate scope of practice' (an example full statement might be 'should be prescribed by health practitioners with appropriate scope of practice').

The ACM was supportive of the removal of prescriber certification from the PI noting that education material is widely available and prescribing will be by those with an appropriate scope of practice.

The ACM advised that additional information was required to allow the ACM to appropriately consider the application and provide an overall benefit risk outcome.

The ACM requested the following information be gathered:

- Clarification on the eligibility criteria for prescribing should MS-2-Step prescribing be broadened to healthcare practitioners
- Sponsor to provide information on the utility of the 24-hour phone service.

Risk/benefit assessment (post ACM Meeting)

In response to the ACM advice, the Sponsor provided 24 hour aftercare phone service data to the Delegate and confirmation that Health Canada removed the requirement for a 24hr aftercare service in 2016.

Over a 12 month period, the majority of calls to the Australian aftercare service occurred between 8am-8pm, with less than 25% of calls being received between 8pm-8am. The majority of calls received (>85%) were to provide patient support either through general advice and reassurance (56%), advising a patient to monitor and reassess (19%), or to contact their prescribing GP for a follow-up appointment (10%).

The telephone aftercare service does not have access to the caller's clinical history, does not hold prescriber contact details, is unable to contact the caller's prescribing GP or hospital ED on their behalf, and can only direct the caller to contact their prescriber or attend an emergency department (if advised/as needed). As a result, most callers were directed to attend an emergency department or contact their prescriber.

The Clinical Delegate decided to amend '*medical practitioner*' to '*healthcare practitioner*' and amend '*doctors with the appropriate qualifications and certified training*' to '*healthcare practitioners with the appropriate qualifications and training*' on the basis that the existing standardised training for all potential prescribers is maintained (in accordance with individual state and territory requirements).

Given similar aftercare can be managed by the existing national Healthdirect helpline, the decision was made to remove the sponsor provided 24 hour aftercare phone service. Subsequently, Healthdirect confirmed they have sufficient resources to support women undergoing medical abortion from their existing service and has been provided with training materials by MS Health.

The Deputy Secretary, Health Products Regulation Group wrote to all jurisdictions on 26 July 2023 regarding these changes, noting that it is the responsibility of each state and territory government to determine specific healthcare practitioner requirements for prescribing MS-2 Step under relevant jurisdictional legislation.

Legislative amendments to enable nurse practitioners and midwives to prescribe MS-2 Step are a matter for the states and territories.

Outcome

In the current submission, approval was granted to make the following changes in the PI and RMP:

- Amend '*medical practitioner*' in the boxed warning to '*healthcare practitioner*'
- Amend '*doctors with the appropriate qualifications and certified training*' in Section 4.2 to '*healthcare practitioners with the appropriate qualifications and training*' (in accordance with individual state and territory requirements) on the basis that the existing standardised training for all potential prescribers is maintained.
- Removal of the requirement for prescribers to complete mandatory training and receive certification to be able to prescribe the product (including recertification), to align with the approved changes and as per the proposed changes on page 10 (above).
- Removal of the requirement for pharmacists to be registered to be able to dispense
- Removal of the 24-hour phone service for patients.

Attachment 1. Product Information

The Product Information (PI) approved with the submission for MS-2 Step which is described in this AusPAR can be found as Attachment 1. It may have been superseded. For the most recent PI and Consumer Medicines Information (CMI), please refer to the TGA PI/CMI search facility.

Therapeutic Goods Administration

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Reference/Publication #