



A Stocktake of Pharmaceutical Benefits Scheme (PBS)-Funded Medicines Available for Endometriosis and Related Conditions

Consumer Summary

Introduction

A stocktake of medicines listed on the Pharmaceutical Benefits Scheme (PBS) for the treatment of endometriosis and related conditions was considered by the Pharmaceutical Benefits Advisory Committee (PBAC) in December 2022. The purpose of the stocktake was to identify potential gaps between PBS-funded medicines and medicines available to patients privately (at full cost).

What is endometriosis?

Endometriosis is a common condition where tissue similar to the lining of the womb grows outside it in other parts of the body. Endometriosis most often affects the reproductive organs. It is also frequently found in the bowel and bladder, as well as in muscle, joints, the lungs and the brain. Some people with endometriosis experience no symptoms; others may experience pain, heavy menstrual bleeding, bleeding between periods, lethargy, and reduced fertility, among other symptoms. Conditions related to endometriosis include polycystic ovary syndrome, adenomyosis, pelvic inflammatory disease and chronic pelvic and period pain.

Endometriosis currently affects more than 11% of Australian women, girls and those who are gender diverse, with the condition often starting in the teenage years. Endometriosis has no known cure.

Patient access to PBS-listed medicines

There is an expressed need for more available PBS-funded medicines to help treat endometriosis and endometriosis-related pain. Patients and their doctors report that available medicines are often poorly tolerated, minimally effective, or are associated with risk of addiction. Stakeholders suggest the addition of several new medicines to the PBS may improve access to treatment for those with endometriosis.

Australian Government initiatives and advisory groups

The Australian Government is taking active steps to address the significant burden that endometriosis places on Australians. As part of the 2022-23 Budget, the Australian



Government invested \$58 million for the treatment of endometriosis and pelvic pain. Under the National Action Plan for Endometriosis (NAPE), focus will be on funding of a range of measures, including:

- Specific clinics in general practice
- Endometriosis-related research
- Development of treatment guidelines
- Improved access to medicines listed on the PBS and to medical services available via Medicare involved in the diagnosis and treatment of endometriosis.

The Department of Health and Aged Care has established the Endometriosis Expert Advisory Group (EAG) to provide advice and guidance to the Department on issues relating to the implementation of the NAPE. Members of the EAG suggested adding several medicines to the PBS to improve access to treatment for patients with endometriosis. These medicines included dienogest, dienogest and estradiol valerate combination, diazepam suppositories, botulinum toxin, non-steroidal anti-inflammatory drugs (NSAIDs), gonadotropin releasing hormone (GnRH) analogues, and newer combined oral contraceptive pills.

Context for the Stocktake

In May 2022, the Pharmaceutical Benefits Advisory Committee (PBAC) requested a report on the available therapies in Australia for endometriosis and related conditions and a comparison of Australian clinical guidelines, for its consideration. The PBAC recalled its previous concerns about the limited range of PBS-listed oral contraceptives and requested that a stocktake of these medicines also be included in the report.

The report aimed to identify potential gaps between PBS-listed medicines and medicines available to patients through a private (non-PBS) prescription at full cost. This list of medicines was compiled by comparing current Australian clinical guidelines for the treatment of endometriosis and related conditions, the Therapeutic Goods Administration (TGA) registered indication for those medicines, and the PBS restrictions for any PBS-listed medicines mentioned in the guidelines.

Through targeted consultation, stakeholder organisations were invited to provide feedback on the report and to comment on the current use and accessibility of medicines for treatment of endometriosis.

The PBAC considered the report and the stakeholder feedback at its December 2022 meeting. The [PBAC December 2022 outcome statement](#) was published in January 2023.

The Role of the Pharmaceutical Benefits Advisory Committee

The PBAC is made up of expert members independent of Government, comprising doctors, health professionals, health economists, and consumer representatives. Its main role is to advise the Minister for Health and Aged Care about medicines that should be PBS-funded. When the PBS evaluates medicines for PBS-funding, it must legally consider the effectiveness and cost of a medicine, compared to alternative treatments.



The PBAC's consideration process usually starts when a pharmaceutical company applies for PBS listing for a particular medicine. This is because pharmaceutical companies usually hold scientific data and other information necessary to inform the PBAC's decision-making. A pharmaceutical company is a private entity that makes its own decisions about the availability of its medicines, pricing of its medicines outside of the PBS, and whether it will apply for PBS funding. The Government cannot force companies to apply for PBS listing.

The PBS medicines listing process

Before a medicine can be listed on the PBS, it must first be approved for use in Australia by the TGA. The sponsor of the medicine, usually a pharmaceutical company, applies to the TGA to have the medicine entered in the Australian Register of Therapeutic Goods (ARTG) so that it can be sold in Australia. The sponsor must provide evidence (such as from clinical trials) that the medicine meets the required standards of quality, safety and effectiveness for the intended use.

A medicine that is listed on the ARTG can be marketed in Australia. However, the medicine will not attract an Australian Government subsidy unless the sponsor is also successful in listing the medicine on the PBS. Without the subsidy, patients pay the full cost of the medicine.

Applications for PBS listing are considered by the PBAC. A new medicine cannot be listed on the PBS unless the PBAC makes a positive recommendation for its listing. Under section 101 of the *National Health Act 1953*, the PBAC must take into account both the cost and clinical effectiveness of the medicine when compared with other treatments for the same condition.

The PBAC uses a Health Technology Assessment (HTA) process to evaluate applications. This allows the PBAC to assess new medicines against existing treatments to ensure the medicines subsidised on the PBS achieve the greatest health improvement at the lowest cost. The PBAC can consider other factors in addition to cost-effectiveness, for example, whether the new medicine is less toxic than existing treatments, or fills a treatment gap for a particular medical condition.

If the PBAC recommends that the new medicine be listed on the PBS, there are steps that need to be completed before the medicine can be listed on the PBS. These include negotiations regarding PBS costs, PBS listing details and consideration by Government.

Types of PBS listings

Medicines can be listed on the PBS as an unrestricted, Restricted or Authority Required item:

- *Unrestricted medicines* under the PBS Schedule may be prescribed by a prescriber within their scope of practice at their discretion.
- *Restricted medicines* listed in the schedule on the PBS, are only prescribed if the condition meets the stated restrictions.
- *Authority Required (STREAMLINED)* medicines are prescribed for specific conditions and do not need prior approval from Services Australia or the Department of



Veterans' Affairs. Instead, the process is streamlined by providing a four or five digit streamlined authority code.

- *Authority Required* medicines are medicines that can only be prescribed by a prescriber if prior approval is obtained from Services Australia or the Department of Veterans' Affairs as appropriate.

Summary of Stocktake Findings

Australian Clinical Guidelines

The Report presented a summary of recommendations from three Australian clinical guidelines on managing endometriosis with medication. These were the electronic Therapeutic Guidelines (eTG), the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) Endometriosis Guideline (released May 2021) and the Australian Medicines Handbook (AMH).

The guidelines review identified five classes of medicines used to manage endometriosis and related conditions:

- combined hormonal contraceptives (oral tablets, intra vaginal ring)
- progestogens (oral tablets, under the skin implants, intrauterine devices, long-acting injection),
- gonadotrophin-releasing hormone (GnRH) agonists (under the skin implant, nasal spray),
- androgenic (male) hormones (oral tablets),
- pain relief medicines

PBS- listings

The stocktake found three medicines were TGA registered for endometriosis **and** currently listed on the PBS for specific use in endometriosis (known as a 'restricted listing'):

- Goserelin (implant under the skin)
- Nafarelin (nasal spray)
- Medroxyprogesterone acetate (oral tablet)

Other medicines that are TGA registered specifically for endometriosis **and** are not restricted to use for endometriosis for PBS subsidy (known as an 'unrestricted listing') include:

- Norethisterone (oral tablet)
- Medroxyprogesterone (injection)



Table 1: Medicines TGA-registered and PBS subsidised for endometriosis

Medicine	Brands	TGA registered	TGA registered specifically for endometriosis	PBS listing
progestogens				
medroxyprogesterone acetate (oral tablet)	Ralovera® Provera®	√	√	endometriosis
medroxyprogesterone (injection)	Depo-Ralovera® Depo-Provera®	√	√	unrestricted
norethisterone (oral tablet)	Primolut N®	√	√	unrestricted
gonadotrophin-releasing hormone (GnRH) agonists				
goserelin (implant under the skin)	Zoladex®	√	√	endometriosis
nafarelin (nasal spray)	Synarel®	√	√	endometriosis

The treatment of endometriosis is not specifically included in the TGA-registered indications for combined oral contraceptives (COCs), intravaginal contraception (Nuvaring®) and intrauterine contraceptive devices, also known as IUDs (Kyleena®, Mirena®). Intravaginal contraception is not PBS-listed. IUDs are listed on the PBS with a 'restricted' listing for contraception and heavy menstrual bleeding. Some COCs are available for PBS-funding as unrestricted benefit listings. However, many of the newer generation COCs (which are preferentially prescribed in endometriosis) are not available on the PBS. A long-acting progestogen (etonogestrel implant) is TGA registered for contraception and has an unrestricted PBS listing,

Table 2: PBS subsidised combined oral contraceptives

Medicine	Brands include	TGA registered	TGA registered specifically for endometriosis	PBS listing
combined oral contraceptive pill (COCP)				
levonorgestrel+ethinylestradiol in fixed combinations	Eleanor 150/30 ED Evelyn 150/30 ED Femme-Tab ED 30/150 Lenest 30 ED Micronelle 30 ED Levlen ED Femme-Tab ED 20/100 Microgynon 50 ED	√	x	unrestricted



Medicine	Brands include	TGA registered	TGA registered specifically for endometriosis	PBS listing
levonorgestrel+ethinylestradiol in sequential combinations	Logynon ED Trifeme 28 Triphasil 28 Triquilar ED	√	x	unrestricted
norethisterone+ethinylestradiol in fixed combinations	Norimin 28 Day Norimin-1 28 Day	√	x	unrestricted

Clinical guidelines recommend use of non-steroidal anti-inflammatory drugs (NSAIDs) as first line treatment for the management of endometriosis-related pain. Paracetamol may be used with, or as an alternative to, NSAIDs. NSAIDs are not TGA registered specifically for endometriosis pain, but three NSAIDs have TGA registration for period pain and are PBS listed. Two of these, diclofenac and ibuprofen, have unrestricted PBS listings. PBS subsidised use of mefenamic acid is restricted to period pain and heavy menstrual bleeding.

Table 3: PBS subsidised pain relief medicines- non-steroidal anti-inflammatory drugs (NSAIDs)

Medicine	TGA registered	TGA registered specifically for endometriosis	PBS listing
pain relief medicines- non-steroidal anti-inflammatory drugs (NSAIDs),			
diclofenac	√	x Includes period pain,	unrestricted
ibuprofen.	√	x Includes period pain	unrestricted
mefenamic acid	√	x Includes period pain, heavy menstrual bleeding	primary dysmenorrhoea (period pain) menorrhagia (heavy menstrual bleeding)

There is limited evidence for the use of neuropathic (nerve) pain medicines for the management of endometriosis pain. Pregabalin is the only medicine used to treat neuropathic pain that is TGA-registered and PBS listed specifically for neuropathic pain. Gabapentin is TGA-registered for neuropathic pain but not PBS listed for this purpose. Amitriptyline is not TGA-registered for neuropathic pain and has an unrestricted benefit PBS listing.



Table 4 PBS subsidised nerve pain medicines

Medicine	TGA registered	TGA registered specifically for neuropathic (nerve) pain	PBS listed
pregabalin	√	√	Authority Required (STREAMLINED) for neuropathic pain
gabapentin	√	√	Authority Required (STREAMLINED) for the treatment of partial epileptic seizures
amitriptyline	√	×	unrestricted

Other medicine treatment options

Dienogest, a progestogen, is TGA registered for endometriosis. Qlaira® (dienogest + estradiol) is a newer CoC that is TGA registered for contraception and the treatment of heavy menstrual bleeding. The PBAC has not considered an application to list either of these medicines on the PBS. Companies make their own commercial decisions and cannot be forced by the government to apply for PBS funding.

Another medicine, danazol (androgenic hormone) has some side effects that limit its use. It is available only through the TGA's Special Access Scheme, a program that allows health practitioners to prescribe medicines not included in the ARTG in certain circumstances.

Other treatment options, including botulinum toxin and diazepam suppositories, are not recommended in any current clinical guidelines for the treatment of endometriosis. These treatments are not approved in Australia for this indication.

Table 5: Other medicine treatment options

Medicine	TGA registered	TGA registered specifically for endometriosis	PBS listing
progestogen			
dienogest	√	√	X
combined oral contraceptive			
dienogest + estradiol (Qlaira®)	√	X contraception and heavy menstrual bleeding	X
androgenic hormone			
danazol	X Special Access Scheme	X	X
other			
botulinum toxin injection	√	X	Authority Required (STREAMLINED) Multiple indications excluding endometriosis
diazepam suppositories	X	X	X



Barriers to accessing medicines to treat endometriosis

The stocktake identified several barriers to accessing medicines used to treat endometriosis. These include:

- Lack of health professional training in the insertion of hormonal devices
- Lack of access to health care professionals
- Lack of willingness and/or incentive for pharmaceutical companies to pursue TGA registration and PBS listing for endometriosis when patients can already access medicines privately.

Consideration by the PBAC

The PBAC considered the stocktake of PBS funded medicines available for the treatment of endometriosis and related conditions and invited external stakeholders to provide feedback on the report. Stakeholders suggested the need for PBS funding of the following medicines for endometriosis treatment:

- Dienogest
- Dienogest and estradiol valerate (Qlaira®)
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Newer generation COC pills
- Medicines used for neuropathic pain

The PBAC noted the findings of the report and stakeholder feedback and provided the following considerations:

- The oral progestogen dienogest (2000 mcg) is specifically TGA registered for endometriosis and its use is supported by clinical guidelines, however the sponsor has not made a submission for PBS listing.
- The two unrestricted PBS listed NSAIDs (ibuprofen, diclofenac) were considered appropriate to treat endometriosis/pelvic pain without the need to expand the PBS listings of other NSAIDs.
- There is not sufficient evidence to support the expansion of PBS listings for botulinum toxin, diazepam suppositories, and neuropathic pain medicines to include treatment of endometriosis.
 - The PBAC proposed referring investigation of the effectiveness of these medicines in endometriosis/related conditions to the Medical Research Future Fund for consideration as a research initiative to evaluate the benefits.

The PBAC expressed its intention to continue to work with the Department to address the identified issues within its scope to improve access for patients with endometriosis and related conditions to effective PBS subsidised medicines.