

**14.12 GOSERELIN,
3.6 mg implant,
Zoladex Implant[®], Astra Zeneca Pty Ltd.**

Application submitted by Medical Oncology Group of Australia (MOGA)

1 Purpose of Application

- 1.1 The minor resubmission was to address the issues raised by the PBAC in its previous deferral of the request to change the current PBS restriction for goserelin 3.6 mg implant to enable women with hormone receptor negative breast cancer to access this treatment to reduce premature ovarian failure (POF).

2 Requested listing

- 2.1 The submission did not provide a proposed restriction.

Suggested wording for the restriction:

- 2.2 The Secretariat proposed the following changes to the existing restriction. Changes to the existing listing are indicated in *italics* and ~~strike through~~ for deletions.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
GOSERELIN 3.6 mg, implant	1	5	Zoladex Implant	Astra Zeneca

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Breast cancer
PBS Indication:	Breast cancer
Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit
Clinical criteria:	• The condition must be hormone receptor positive

For more detail on PBAC's view, see section 5 "PBAC outcome"

3 Background

- 3.1 Goserelin 3.6 mg implant is a gonadotrophin releasing hormone (GnRH) agonist, TGA registered for prostate cancer, endometriosis, uterine fibroids, endometrial thinning, assisted reproduction, and treatment of advanced breast cancer (T3b, T4 or

any T with N2, 3 or M+) in premenopausal women suitable for hormonal manipulation (PI, p11).

- 3.2 At the December 2014 special meeting, the PBAC recommended that goserelin be listed as a restricted benefit. At the March 2015 PBAC meeting the PBAC recommended that the restriction for goserelin implant 3.6 mg be amended to allow access to hormone receptor positive breast cancer patients at all cancer stages for chemotherapy treatment.
- 3.3 At the November 2016 PBAC meeting the PBAC decided to defer the submission for goserelin implant to reduce POF on the basis that patient populations in addition to that proposed by MOGA may benefit from, and use this treatment, and therefore that the utilisation estimates may be underestimated.

For more detail on PBAC's view, see section 5 "PBAC outcome"

4 Current submission

- 4.1 The current submission to the PBAC provided additional information in relation to the proposed patient population and utilisation estimates.

Sponsor hearing

- 4.2 There was no hearing for this item.

Consumer comments

- 4.3 The PBAC noted that no consumer comments were received for this item.

Patient population

- 4.4 At the November 2016 meeting, the PBAC considered that it was likely that this treatment could reduce POF in women treated for cancers other than breast cancer. The resubmission claimed that the application was for use in breast cancer only because there is limited evidence to support the use of goserelin for all women undergoing menopause-inducing chemotherapy. The submission acknowledged that although this treatment may be effective in other cyclophosphamide-based chemotherapy regimens, trials in lymphoma have not clearly demonstrated efficacy in this setting, mostly due to the small sample size leading to under-powered studies. References for these trials were not provided in the submission.
- 4.5 The PBAC noted that the current submission referred to some additional studies in the use of goserelin to prevent POF in other cancers, specifically lymphoma (Demeestere et al., 2016). The PBAC noted that the Demeestere study had a number of limitations, including the fact that it was underpowered. However, the PBAC noted the study also showed lower rates of POF and more pregnancies in the arm exposed to GnRH agonists. The PBAC noted that stronger evidence was unlikely to be forthcoming especially in rare conditions (including rare cancers). The

PBAC also reiterated its opinion that it is biologically plausible that goserelin is also effective in preventing POF in other cancers and autoimmune diseases treated with alkylating agents such as cyclophosphamide. The PBAC recalled their previous advice that the ability of GnRH agonists to protect ovarian function relates to factors such as the nature and duration of drug exposure and the age of the woman (paragraph 7.4, goserelin November 2016 PSD).

Estimated PBS usage & financial implications

- 4.6 The November 2016 submission estimated that up to less than 10,000 patients per year would use goserelin for 3 to 6 months for POF. At the November 2016 meeting, the PBAC considered that the basis for these estimates was unclear.
- 4.7 The resubmission stated that the estimated patient numbers were based on an epidemiological approach whereby of the 15,934 women diagnosed with breast cancer in Australia in 2016¹, around █% would be pre-menopausal, █% of these would have ER negative breast cancer, with 45 having metastatic disease at diagnosis (i.e. █). Of the remaining less than 10,000 patients, the submission estimated (based on expert opinion) that at least █ of these patients would be close to natural menopause and would not seek treatment to delay onset, leaving around less than 10,000 patients potentially requiring treatment under the PBS. An expert in breast cancer and onco-fertility supported these estimates; however, the evidence base for the proportions applied is unclear.
- 4.8 The resubmission considered that the estimate of less than 10,000 patients was based on 100% uptake and was therefore the upper limit of estimated utilisation. The pre-PBAC response to the November 2016 submission also considered that approximately 30% of patients would only receive treatment for 3 months, rather than the full 6 months. The submission therefore claimed that the utilisation and cost estimate is likely to be the upper limit. The PBAC noted alternative estimates prepared by the Department supported those provided by the applicant for goserelin utilisation to prevent POF in breast cancer. This analysis also integrated assumptions from the submission that there would be low and gradual uptake and 30% of patients would only use goserelin for 3 months. This resulted in an estimated net cost to the PBS of less than \$10 million over five years, as shown below.

Year	1	2	3	4	5	6
Total number of eligible patients	█	█	█	█	█	█
Patients electing treatment (%)	20%	25%	30%	40%	40%	40%
Patients electing treatment (#)	█	█	█	█	█	█
Net cost to PBS	\$█	\$█	\$█	\$█	\$█	\$█

Source: Prepared by HTA.

Note: Based on the price of the current listing for goserelin (DPMQ \$307.67).

Up to 6 scripts per patient was assumed based on the advice from MOGA in its November 2016 minor submission.

¹ Breast Cancer statistics by Cancer Australia, (<https://canceraustralia.gov.au/affected-cancer/cancer-types/breast-cancer/breast-cancer-statistics>).

The redacted table shows that at year 5, the estimated number of patients was less than 10,000 and the net cost to the PBS would be less than \$10 million.

- 4.9 The PBAC also noted an analysis of PBS script data conducted by the Department that showed that less than 10,000 women aged 18-49 years received PBS-subsidised cyclophosphamide therapy in 2016. The PBAC considered use of cyclophosphamide to be a reasonable surrogate for drugs causing POF, but noted that this includes a much broader group than would actually elect to use goserelin to prevent POF. For this reason, the estimates represent an upper limit on utilisation if goserelin was made available for all women of childbearing age undergoing cyclophosphamide therapy.

For more detail on PBAC's view, see section 5 "PBAC outcome"

5 PBAC outcome

- 5.1 The PBAC deferred the request to change the current PBS restriction for goserelin 3.6 mg implant to enable women with hormone receptor negative breast cancer to access this treatment to prevent premature ovarian failure (POF). This will allow the Department to negotiate with the sponsor to develop an appropriate restriction that would enable access for patients at risk of POF from treatment with alkylating agents of cancers other than breast cancer, as well as autoimmune diseases treated with alkylating agents who may elect to use goserelin.
- 5.2 The PBAC noted that the clinical evidence indicated that goserelin was effective in reducing the risk of POF in women receiving cyclophosphamide for breast cancer. By extrapolation, it was biologically plausible that goserelin would also be effective in other conditions treated with alkylating agents, such as cyclophosphamide. For equity reasons, availability of goserelin should not be only restricted to use in women with breast cancer.
- 5.3 The PBAC noted that while there was unlikely to be use outside the restriction for prevention of POF due to the undesirable side effects of goserelin, an unrestricted listing may also result in increased use for other indications, such as endometriosis and uterine fibroids. Therefore, the PBAC deferred the application and requested the Department to work with the sponsor of goserelin to develop an appropriate restriction.

Outcome:
Deferred

6 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final

PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

7 Sponsor's Comment

The sponsor had no comment.