

**11.01 LEUPRORELIN,
Suspension for subcutaneous injection (modified
release) containing leuprorelin acetate 7.5 mg,
injection set,
Suspension for subcutaneous injection (modified
release) containing leuprorelin acetate 22.5 mg,
injection set,
Suspension for subcutaneous injection (modified
release) containing leuprorelin acetate 30 mg,
injection set,
Suspension for subcutaneous injection (modified
release) containing leuprorelin acetate 45 mg,
injection set,
Eligard[®],
Mundipharma Pty Limited**

1 Purpose of Submission

- 1.1 The Committee Secretariat submission requested Eligard with an updated injection device be included in the existing Pharmaceutical Benefits Scheme (PBS) listings for leuprorelin (Eligard[®]) in the following forms:
- Suspension for subcutaneous injection (modified release) containing leuprorelin acetate 7.5 mg, injection set
 - Suspension for subcutaneous injection (modified release) containing leuprorelin acetate 22.5 mg, injection set
 - Suspension for subcutaneous injection (modified release) containing leuprorelin acetate 30 mg, injection set
 - Suspension for subcutaneous injection (modified release) containing leuprorelin acetate 45 mg, injection set.
- 1.2 The submission stated that the intention is for the updated injection device to replace the currently listed injection device of Eligard on the PBS.

2 Background

- 2.1 Eligard 7.5 mg (1 month), 22.5 mg (3 month), 30 mg (4 month) and 45 mg (6 month) are currently listed on the PBS as General Schedule Restricted Benefit listings for locally advanced (Stage C) or metastatic (Stage D) carcinoma of the prostate (PBS item codes 8707G, 8708H, 8709J, 8859G). Eligard 45 mg is also PBS-listed as a General Schedule Restricted Benefit listing for central precocious puberty (PBS item code 13187C).
- 2.2 The submission stated that including the updated device in the current PBS listings will ensure continued access to patients as a change to the updated device will occur from May 2025 onwards. The last manufacturing cycle of the current single use kits occurred in January 2024, which is expected to provide sufficient stock to meet normal Australian demand until June 2025, and that a change to the updated device would occur from May 2025. The submission noted that Eligard with the updated device would replace Eligard with the current device, and the request was that both the current and updated devices be made available on the PBS at the same time, under the same listings, to allow use of remaining stock of the current Eligard device.

Change in device

- 2.3 The submission stated changes were made to the current injection device based on recommendations made by the European Medicines Agency (EMA) Safety Committee: In 2020 the EMA's safety committee made a number of recommendations to avoid handling errors in preparing and administering leuprorelin depot medicines, as a review had found some patients were receiving insufficient amounts of medicine. One of these recommendations was that the device used to administer the medicine for Eligard must be replaced with one that is easier to handle.¹
- 2.4 The current device is available in a single-use kit, and consists of two separate pre-filled sterile syringes that are joined by the healthcare professional prior to injecting. The contents of each syringe are mixed immediately prior to administration. The updated device is a pre-connected syringe system and is supplied pre-assembled.
- 2.5 The submission stated the updated device, as a pre-connected syringe system, reduces the number of preparation steps required prior to attaching the needle and administering the injection.
- 2.6 The submission claimed the updated syringe system is easier to mix, and subsequently inject, compared to the current device, which will reduce potential handling errors.

¹ European Medicines Agency, (2020), 'Leuprorelin-containing depot medicinal products – referral', accessed 2024 Aug 26. Available at www.ema.europa.eu/en/medicines/human/referrals/leuprorelin-containing-depot-medicinal-products

- 2.7 The submission stated that Eligard is administered subcutaneously and forms a solid drug delivery depot. It must be administered within 30 minutes of mixing, and this remains unchanged with the updated delivery device.

Registration status

- 2.8 Eligard in the 7.5 mg, 22.5 mg, 30 mg and 45 mg strengths were first Therapeutic Goods Administration (TGA) registered on 26 November 2003.
- 2.9 The TGA approved a change to the Product Information (PI) for Eligard 7.5 mg, 22.5 mg, 30 mg and 45 mg to include changes to the container closure system – addition of an alternative pre-filled syringe assembly. The PI for Eligard was revised 28 May 2024 to include this change.
- 2.10 The TGA approval letter for variation to the entry in the Australian Register of Therapeutic Goods (ARTG) and change to the approved PI stated, ‘there is no objection to concurrent supply of stock to which the former conditions apply and stock complying with the variations approved...’. Therefore, there may be concurrent supply of both the current and updated devices of Eligard for a period of time.

Previous PBAC consideration

- 2.11 Leuprorelin acetate injection 7.5 mg, 22.5 mg and 30 mg (Eligard) were considered, and recommended, by the PBAC at its September 2003 meeting for the treatment of locally advanced (stage C) or metastatic (stage D) carcinoma of the prostate. Leuprorelin acetate 45 mg (Eligard) was considered, and recommended, by the PBAC for the same condition at its November 2004 meeting.
- 2.12 At its July 2022 meeting the PBAC considered, and recommended, the listing of Eligard 45 mg for central precocious puberty.

3 Requested listing

- 3.1 The submission requested that both Eligard with the updated device and Eligard with the current device be covered by the existing listings for Eligard. The submission proposed no changes to the existing listings for Eligard as both devices will have the same brand name:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
LEUPRORELIN					
leuprorelin acetate 7.5 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	8707G	1	1	5	Eligard 1 month
leuprorelin acetate 22.5 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	8708H	1	1	1	Eligard 3 month

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leuprorelin acetate 30 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	8709J	1	1	1	Eligard 4 month
leuprorelin acetate 45 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	8859G	1	1	0	Eligard 6 month

Restriction Summary / Treatment of Concept: Restricted

Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type: <input checked="" type="checkbox"/> Restricted benefit
Indication: Locally advanced (stage C) or metastatic (stage D) carcinoma of the prostate

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
LEUPRORELIN					
leuprorelin acetate 45 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	13187C	1	1	0	Eligard 6 month

Restriction Summary / Treatment of Concept: Restricted

Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type: <input checked="" type="checkbox"/> Restricted benefit
Indication: Central precocious puberty
Treatment Phase: Initial treatment
Treatment criteria:
Must be treated by a paediatric endocrinologist; or
Must be treated by an endocrinologist specialising in paediatrics.
Population criteria:
Patient must be of an age that is prior to their 10 th birthday if female; or
Patient must be of an age that is prior to their 11 th birthday if male,
AND
Population criteria:
Patient must have had onset of signs/symptoms of central precocious puberty prior to their 8 th birthday if female; or
Patient must have had onset of signs/symptoms of central precocious puberty prior to their 9 th birthday if male.

Restriction Summary / Treatment of Concept: Restricted

Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type: <input checked="" type="checkbox"/> Restricted benefit
Indication: Central precocious puberty
Treatment Phase: Continuing treatment with this drug, or, switching gonadotropin releasing hormone analogue therapy
Treatment criteria:

	Must be treated by a medical practitioner identifying as one of: (i) a paediatric endocrinologist, (ii) an endocrinologist specialising in paediatrics; or
	Must be treated by a medical practitioner who has consulted at least one of the above mentioned specialist types, with agreement reached that the patient should be treated with this pharmaceutical benefit on this occasion.
	AND
	Treatment criteria:
	Patient must be undergoing continuing treatment with a gonadotropin releasing hormone analogue initiated through the PBS for this PBS indication.

4 Comparator

- 4.1 The submission proposed an updated injection device for Eligard and compared this to the current injection device for Eligard in the same strengths that is covered by the current PBS listings.

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item.

Consumer comments

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

Clinical claim

- 5.3 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of Eligard with the updated injection device compared with Eligard with the current injection device. The submission also claimed the updated device will reduce potential handling errors.
- 5.4 The clinical claim was supported by the TGA's approval to vary the PI for Eligard 7.5 mg, 22.5 mg, 30 mg and 45 mg to include the addition of the alternative pre-filled syringe assembly for the respective strengths.
- 5.5 The PBAC considered that the claim of non-inferior comparative effectiveness was reasonable.
- 5.6 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Drug cost/patient/year

- 5.7 The submission requested that Eligard with the updated injection device has the same approved ex-manufacturer price (AEMP) as Eligard that is currently PBS-listed (\$232.55 for Eligard 1 month, \$625.45 for Eligard 3 month, \$833.55 for Eligard 4 month and \$1,249.40 for Eligard 6 month).
- 5.8 The estimated drug cost/patient per year would be:

- \$3,252 Eligard 7.5 mg (1 month), based on a dispensed price for maximum quantity (DPMQ) of \$271 and 12 scripts per year
- \$2,858.24 for Eligard 22.5 mg (3 month), based on a DPMQ of \$714.56 and 4 scripts per year
- \$2,821.59 for Eligard 30 mg (4 month), based on a DPMQ of \$940.53 and 3 scripts per year
- \$2,754.36 for Eligard 45 mg (6 month), based on a DPMQ of \$1,377.18 and 2 scripts per year.

Estimated PBS usage and financial implications

5.9 The submission's request was on a cost-minimisation approach of Eligard with the updated injection device compared to Eligard with the current injection device. The submission estimated the equi-effective doses to be:

- Eligard 7.5 mg (updated injection device) = Eligard 7.5 mg (current injection device)
- Eligard 22.5 mg (updated injection device) = Eligard 22.5 mg (current injection device)
- Eligard 30 mg (updated injection device) = Eligard 30 mg (current injection device)
- Eligard 45 mg (updated injection device) = Eligard 45 mg (current injection device).

As summarised in paragraph 5.4, Eligard with both the updated and current injection devices are included in the same PI for the doses outlined above.

5.10 The submission estimated that there would be no net financial implications to the PBS if Eligard with the updated device is recommended for PBS listing, as it will only replace the current Eligard products that are PBS-listed.

Quality use of medicines

5.11 The sponsor was asked to provide details of any education initiatives planned for patients and health professionals on the updated device, such as education on using the updated device, to ensure it is administered appropriately and to support quality use of medicines, however no details of planned education initiatives were provided.

6 PBAC Outcome

6.1 The PBAC recommended Eligard with an updated injection device be included in the existing PBS listings for leuprorelin (Eligard), alongside Eligard with the current injection device, in the following forms:

- Suspension for subcutaneous injection (modified release) containing leuprorelin acetate 7.5 mg, injection set

- Suspension for subcutaneous injection (modified release) containing leuprorelin acetate 22.5 mg, injection set
 - Suspension for subcutaneous injection (modified release) containing leuprorelin acetate 30 mg, injection set
 - Suspension for subcutaneous injection (modified release) containing leuprorelin acetate 45 mg, injection set.
- 6.2 The PBAC noted the intention was for the updated injection device to replace the currently PBS-listed injection device of Eligard.
- 6.3 The PBAC accepted Eligard with the current injection device as the comparator. The PBAC noted the TGA approved a variation to the PI for Eligard 7.5 mg, 22.5 mg, 30 mg and 45 mg to include the addition of the alternative pre-filled syringe assembly for the respective strengths. The PBAC advised the equi-effective doses were:
- Eligard 7.5 mg (updated injection device) = Eligard 7.5 mg (current injection device)
 - Eligard 22.5 mg (updated injection device) = Eligard 22.5 mg (current injection device)
 - Eligard 30 mg (updated injection device) = Eligard 30 mg (current injection device)
 - Eligard 45 mg (updated injection device) = Eligard 45 mg (current injection device).
- 6.4 The PBAC noted the listing of Eligard with the updated injection device is expected to have no net cost to the PBS.
- 6.5 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Eligard with the updated injection device is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over Eligard with the current injection device currently PBS-listed, or not expected to address a high and urgent unmet clinical need, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.
- 6.6 The PBAC noted that this submission is not eligible for an Independent Review because it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 No change to the existing listings:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands

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LEUPRORELIN						
leuprorelin acetate 7.5 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	8707G	1	1	5	Eligard 1 month	
leuprorelin acetate 22.5 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	8708H	1	1	1	Eligard 3 month	
leuprorelin acetate 30 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	8709J	1	1	1	Eligard 4 month	
leuprorelin acetate 45 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	8859G	1	1	0	Eligard 6 month	
Restriction Summary / Treatment of Concept: Restricted						
	Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)					
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
	Restriction type: <input checked="" type="checkbox"/> Restricted benefit					
	Indication: Locally advanced (stage C) or metastatic (stage D) carcinoma of the prostate					

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
LEUPRORELIN					
leuprorelin acetate 45 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	13187C	1	1	0	Eligard 6 month
Restriction Summary / Treatment of Concept: Restricted					
	Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Restricted benefit				
	Indication: Central precocious puberty				
	Treatment Phase: Initial treatment				
	Treatment criteria:				
	Must be treated by a paediatric endocrinologist; or				
	Must be treated by an endocrinologist specialising in paediatrics.				
	Population criteria:				
	Patient must be of an age that is prior to their 10 th birthday if female; or				
	Patient must be of an age that is prior to their 11 th birthday if male,				
	AND				
	Population criteria:				
	Patient must have had onset of signs/symptoms of central precocious puberty prior to their 8 th birthday if female; or				
	Patient must have had onset of signs/symptoms of central precocious puberty prior to their 9 th birthday if male.				
Restriction Summary / Treatment of Concept: Restricted					
	Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)				

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	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Restricted benefit
	Indication: Central precocious puberty
	Treatment Phase: Continuing treatment with this drug, or, switching gonadotropin releasing hormone analogue therapy
	Treatment criteria:
	Must be treated by a medical practitioner identifying as one of: (i) a paediatric endocrinologist, (ii) an endocrinologist specialising in paediatrics; or
	Must be treated by a medical practitioner who has consulted at least one of the above mentioned specialist types, with agreement reached that the patient should be treated with this pharmaceutical benefit on this occasion.
	AND
	Treatment criteria:
	Patient must be undergoing continuing treatment with a gonadotropin releasing hormone analogue initiated through the PBS for this PBS indication.

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.