6.11 LEUPRORELIN injection, 30 mg, Lucrin® Depot Paediatric, Abbvie Pty Ltd

1 Purpose of Application

1.1 The minor submission requested amending the restriction wording of Lucrin® Depot Paediatric 30 mg PDS (leuprorelin) for the treatment of central precocious puberty (CPP), to specify that the patient must have had onset of signs or symptoms of central precocious puberty prior to the age of 8 years (girls) or 9 years (boys).

2 Requested listing

2.1 The submission sought the following changes to the existing 'initial' treatment phase restriction. There were no requested changes to the 'continuing' treatment phase restriction:

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
LEUPRORELIN Leuprorelin acetate 30 mg injection: modified release [1 syringe] (&) inert substance diluent [1 syringe], 1 pack	1	1	$1,451.67	Lucrin® Depot Paediatric 30 mg PDS Abbvie Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Episodicity:	-
Severity:	-
Condition:	Central precocious puberty
PBS Indication:	Central precocious puberty
Treatment phase:	Initial
Restriction Level / Method:	☐Restricted benefit ☒Authority Required - In Writing ☒Authority Required - Telephone ☒Authority Required – Emergency ☒Authority Required - Electronic ☐Streamlined
Treatment criteria:	Must be treated by a paediatric endocrinologist; OR Must be treated by an endocrinologist specialising in paediatrics.

Population criteria:	~~Patient must be under 8 years of age (girls) or 9 years of age (boys)~~ *Patient must have onset of signs or symptoms of central precocious puberty prior to the age of 8 years (girls) or 9 years (boys)*; OR Patient must have received treatment with a gonadotropin releasing hormone analogue (GnRHa) for this condition prior to 1 May 2015.

For more detail on PBAC's view, see section 6 "PBAC outcome"

3 Background

3.1 At the November 2014 meeting, the PBAC recommended listing leuprorelin as an Authority Required benefit for the treatment of CPP.

3.2 The PBAC recommended that "initiation criteria should specify that treatment be initiated in patients with CPP onset before the age of 8 years in girls and 9 years in boys" (paragraph 7.2 of leuprorelin November 2014 PBAC minutes).

4 Current situation

4.1 Leuprorelin for the treatment of CPP was listed on the PBS on 1 May 2015.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

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

Clinical trials

5.3 As a minor submission, no new clinical trials were presented in the submission.

5.4 The basis of the minor submission's request to amend the wording of the restriction was for better alignment with clinical practice. The submission claimed that the current wording "has come about from a misinterpretation of the evidence".

Economic analysis

5.5 As a minor submission, an economic comparison was not relevant.

Estimated PBS usage & financial implications

5.6 The minor submission estimated there to be no changes to the financial implications to the PBS. The submission stated that the patient population used in the financial

forecast in the major submission that was recommended by the PBAC in November 2014, is the same as the patient population in the proposed amendment to the restriction.

For more detail on PBAC's view, see section 6 "PBAC outcome"

6 PBAC Outcome

6.1 The PBAC recommended that the criterion pertaining to patient age in the initial treatment restriction for leuprorelin for the treatment of CPP, be amended as follows: "Patient must be aged 10 years or younger (girls) or 11 years or younger (boys) AND Patient must have had onset of signs or symptoms of central precocious puberty prior to the age of 8 years (girls) or 9 years (boys)".

6.2 The PBAC recalled its previous consideration of leuprorelin for the treatment of CPP in November 2014, when it was recommended for listing on the PBS. In the pivotal trial (L-CP07-167) provided in that submission, the inclusion criteria limited the age of subjects who were naïve to GnRHa treatment to 2 to 8 years inclusive (female subjects) and 2 to 9 years inclusive (male subjects) at Day 1 of the trial. This inclusion criterion from the trial informed the age criterion of the existing PBS initial treatment restriction.

6.3 The PBAC noted, however, that there may be a very small number of patients who may not have initiated treatment (or may have initiated an alternate treatment) before 8 years (girls) or 9 years (boys) despite onset of symptoms before 8 years (girls) or 9 years (boys), and therefore considered it may be reasonable to extend the PBS age limit for initiating leuprorelin therapy. The PBAC recalled that the course of treatment of leuprorelin was from confirmation of diagnosis until an appropriate pubertal age, and that the expert opinion survey presented in the previous submission indicated that the average age of stopping treatment for CPP was around 10 years for girls and 11 years for boys. There was no data presented in the original submission for children commencing therapy at over 10 years in girls or over 11 years in boys. Therefore, the PBAC considered that the restriction should maintain an age criteria of 10 years (girls) or 11 years (boys) as an upper limit for initiating leuprorelin for CPP, given that the treatment is not effective when given too late in puberty. In making its recommendation, the PBAC considered it would be prudent to seek advice from the Australasia Paediatric Endocrine Group on the recommended restriction wording before it was finalised.

6.4 The PBAC considered that the number of additional patients who would become eligible due to this change in the restriction would be very small, and the resulting financial impact would not be significant. In addition, the PBAC noted that the sponsor claimed that these patients were included in the financial estimates in the November 2014 major submission.

Outcome:
Recommended

7 Recommended listing

7.1 Amend existing listing as follows:

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
LEUPRORELIN				
Leuprorelin acetate 30 mg injection: modified release [1 syringe] (&) inert substance diluent [1 syringe], 1 pack	1	1	Lucrin® Depot Paediatric 30 mg PDS	Abbvie Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Episodicity:	-
Severity:	-
Condition:	Central precocious puberty
PBS Indication:	Central precocious puberty
Treatment phase:	Initial 1 – New patients
Restriction Level / Method:	☐Restricted benefit ☒Authority Required - In Writing ☒Authority Required - Telephone ☒Authority Required – Emergency ☒Authority Required - Electronic ☐Streamlined
Treatment criteria:	Must be treated by a paediatric endocrinologist; OR Must be treated by an endocrinologist specialising in paediatrics.
Population criteria:	Patient must be aged 10 years or younger (girls) or 11 years or younger (boys) AND Patient must have had onset of signs or symptoms of central precocious puberty prior to the age of 8 years (girls) or 9 years (boys)

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Episodicity:	-
Severity:	-
Condition:	Central precocious puberty
PBS Indication:	Central precocious puberty
Treatment phase:	Initial 2 – Grandfather patients

Restriction Level / Method:	☐Restricted benefit ☒Authority Required - In Writing ☒Authority Required - Telephone ☒Authority Required – Emergency ☒Authority Required - Electronic ☐Streamlined
Treatment criteria:	Must be treated by a paediatric endocrinologist; OR Must be treated by an endocrinologist specialising in paediatrics.
Population criteria:	Patient must have received treatment with a gonadotropin releasing hormone analogue (GnRHa) for this condition prior to 1 May 2015.

8 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.

9 Sponsor's Comment

The sponsor had no comment.