

5.20 LEUPRORELIN AND BICALUTAMIDE

Pack containing 1 suspension for subcutaneous injection (modified release) containing leuprorelin acetate 7.5 mg, injection set and 28 tablets bicalutamide 50 mg

Pack containing 1 suspension for subcutaneous injection (modified release) containing leuprorelin acetate 22.5 mg, injection set and 28 tablets bicalutamide 50 mg

Pack containing 1 suspension for subcutaneous injection (modified release) containing leuprorelin acetate 22.5 mg, injection set and 84 tablets bicalutamide 50 mg

Bi ELIGARD CP® Tolmar Australia Pty Ltd

1 Purpose of Application

- 1.1 The minor submission requested an Authority Required (STREAMLINED) listing of a new combination pack containing leuprorelin acetate modified release injection and bicalutamide for the treatment of metastatic (Stage D) carcinoma of the prostate.
- 1.2 Leuprorelin (Eligard®) and bicalutamide (various brands) are currently PBS listed for the same indication, and are able to be co-prescribed.

2 Requested listing

The submission requested the following new listings of three leuprorelin and bicalutamide (LEU/BIC) combination packs.

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and and
LEUPRORELIN AND BICALUTAMIDE leuprorelin acetate 7.5 mg injection: 1 modified release [1 syringe] (& inert substance diluent [1 syringe], (& bicalutamide 50 mg tablet [28 tablets], 1 pack		5	\$ [REDACTED]	Bi ELIGARD CP®	Tolmar Australia Pty Ltd (TL)

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:	Carcinoma of the prostate
PBS Indication:	Carcinoma of the prostate
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The condition must be metastatic (stage D), AND Patient must require a combination of an antiandrogen and a GnRH (LH-RH) agonist.
Administrative Advice	Note No increase in the maximum quantity or number of units may be authorised. Note No increase in the maximum number of repeats may be authorised.

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and and
LEUPRORELIN AND BICALUTAMIDE leuprorelin acetate 22.5 mg injection: 1 modified release [1 syringe] (& inert substance diluent [1 syringe], (& bicalutamide 50 mg tablet [28 tablets], 1 pack		0	\$ [REDACTED]	Bi ELIGARD CP®	Tolmar Australia Pty Ltd (TL)

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:	Carcinoma of the prostate
PBS Indication:	Carcinoma of the prostate
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The condition must be metastatic (stage D), AND Patient must require a combination of an antiandrogen and a GnRH (LH-RH) agonist.
Administrative Advice	Note No increase in the maximum quantity or number of units may be authorised. Note No increase in the maximum number of repeats may be authorised.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
LEUPRORELIN AND BICALUTAMIDE leuprorelin acetate 22.5 mg injection: 1 modified release [1 syringe] (& inert substance diluent [1 syringe], (& bicalutamide 50 mg tablet [84 tablets], 1 pack		1	\$ [REDACTED]	Bi ELIGARD CP®	Tolmar Australia Pty Ltd (TL)

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
Episodicity:	N/A
Severity:	N/A
Condition:	Carcinoma of the prostate
PBS Indication:	Carcinoma of the prostate
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The condition must be metastatic (stage D), AND Patient must require a combination of an antiandrogen and a GnRH (LH-RH) agonist.
Administrative Advice	Note No increase in the maximum quantity or number of units may be authorised. Note No increase in the maximum number of repeats may be authorised.

For more detail on PBAC’s view, see section 7 “PBAC outcome”

3 Background

- 3.1 Combination leuprorelin and bicalutamide (Bi Eligard CP) was TGA registered on 25 May 2016. Leuprorelin was TGA registered on 21 October 1991 and is indicated for the palliative treatment of advanced prostate cancer. Bicalutamide was TGA registered on 1 July 1996 and is indicated for the treatment of advanced prostate cancer in combination with LHRH agonist therapy, and for the prevention of disease flare associated with the use of LHRH agonists.

- 3.2 The PBAC has not previously considered a LEU/BIC combination pack. Leuprorelin and bicalutamide have been individually listed on the PBS for over 10 years for their respective indications.
- 3.3 The submission stated that the PBAC has previously accepted the need for co-packaged GnRH agonists and bicalutamide and that a co-packaged product allows simpler prescribing and reduces patient co-payments.

4 Clinical place for the proposed therapy

- 4.1 The submission stated that the use of combination anti-androgen and LHRH is well established in the treatment of Stage D prostate cancer.
- 4.2 The submission claimed that due to the likelihood of unwanted side effects the risk of use outside the requested restriction is unlikely.

5 Comparator

- 5.1 The minor submission nominated co-prescribed leuprorelin and bicalutamide as the primary comparator, and goserelin and bicalutamide combination pack (ZolaCos CP) as a secondary comparator.

For more detail on PBAC's view, see section 7 "PBAC outcome"

6 Consideration of the evidence

Sponsor hearing

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

Consumer comments

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

Clinical trials

- 6.3 As a minor submission, no clinical trials were presented in the submission.

Economic analysis

- 6.4 The sponsor requested listing on the basis of the sum of the prices of the individual components at the ex-manufacturer level. A summary of the comparative prices from the submission is shown below.

Table 1: Summary of Comparative Costs

	AEMP	AEMP vs Bi ELIGARD	DPMQ	DPMQ vs Bi ELIGARD
1 month of LHRH therapy and 28 tablets of bicalutamide				
Bi ELIGARD 1 month	\$ [REDACTED]		\$ [REDACTED]	
Individual components	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
ZolaCos 3.6(28)	\$406.82	\$ [REDACTED]	\$456.84	\$14.69
3 months of LHRH therapy and 28 tablets of bicalutamide				
Bi ELIGARD 3 month	\$ [REDACTED]		\$ [REDACTED]	
Individual components	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
ZolaCos 10.8 (28)	\$1,074.67	\$ [REDACTED]	\$1,188.79	\$ [REDACTED]
3 months of LHRH therapy and 84 tablets of bicalutamide				
Bi ELIGARD 3 month	\$ [REDACTED]		\$ [REDACTED]	
Individual components	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
ZolaCos 10.8 (84)	\$1,340.01	\$ [REDACTED]	\$1,463.42	\$ [REDACTED]

Source: Bi ELIGARD submission, pg. 18.

Drug cost/patient/prescription:

- Bi ELIGARD CP 1 month (leuprorelin acetate 7.5 mg and 28 bicalutamide 50 mg tablets) \$ [REDACTED]
- Bi ELIGARD CP 3 month (leuprorelin acetate 22.5 mg and 28 bicalutamide 50 mg tablets) \$ [REDACTED]
- Bi ELIGARD CP 3 month (leuprorelin acetate 22.5 mg and 84 bicalutamide 50 mg tablets) \$ [REDACTED]

6.5 Patients may receive a 1-month injection of leuprorelin with four weeks supply of bicalutamide, or a 3-month leuprorelin injection with either four or twelve weeks supply of bicalutamide.

Estimated PBS usage & financial implications

6.6 The submission used a market share approach to estimate utilisation. The market was defined as treatment regimens containing an LHRH agonist with bicalutamide. To estimate concomitant use it was assumed that:

- 5.46% of LHRH agonists prescribed as monthly injections are co-prescribed with 28 days of bicalutamide;
- 1.49% of LHRH agonists prescribed as 3-monthly injections are co-prescribed with 28 days of bicalutamide; and
- 6.65% of LHRH agonists prescribed as 3-monthly injections are co-prescribed with 84 days of bicalutamide.

6.7 The submission assumed that listing the LEU/BIC combination pack will not increase the number of patients treated with a LHRH agonist and bicalutamide.

6.8 The submission assumed market growth of 5.26% per annum for co-prescribed regimens including a 3-monthly LHRH agonist and 84 days of bicalutamide, and 9.63% per annum for the GOS/BIC combination pack containing 3-monthly goserelin with 84 days of bicalutamide. No growth was assumed for the remaining combinations (i.e. those with either a 1-monthly LHRH agonist or a 3-monthly LHRH agonist with 28 days of bicalutamide).

6.9 This submission assumed the LEU/BIC pack would substitute co-prescribed leuprorelin and bicalutamide, combination GOS/BIC packs, and co-prescribed triptorelin and bicalutamide. The following substitution rates were assumed:

- 10-17.5% from combination GOS/BIC packs
- 70-90% from leuprorelin (Eligard brand) co-prescribed with bicalutamide
- 10-20% from leuprorelin (Lucrin brand) co-prescribed with bicalutamide
- 1-6% from triptorelin co-prescribed with bicalutamide

6.10 The submission estimated a cost saving per prescription over the combination GOS/BIC product. .

6.11 The submission estimated less than 10,000 prescriptions of the LEU/BIC combination pack in year 1, and less than 10,000 prescriptions per year in year 5. Utilisation estimates are provided in the table below.

Table 2: Estimated net cost to the PBS/RPBS

	Year 1	Year 2	Year 3	Year 4	Year 5
Bi ELIGARD CP services provided					
Bi ELIGARD CP 1 month + 28					
Bi ELIGARD CP 3 month + 28					
Bi ELIGARD CP 3 month + 84					
Total services					
Cost of services					
Cost of Bi ELIGARD to PBS/RPBS					
Bi ELIGARD CP 1 month + 28					
Bi ELIGARD CP 3 month + 28					
Bi ELIGARD CP 3 month + 84					
Total					
PBS Co-payments offset					
Bi ELIGARD CP 1 month + 28					
Bi ELIGARD CP 3 month + 28					
Bi ELIGARD CP 3 month + 84					
Total					
Net cost of services					
Bi ELIGARD CP 1 month + 28					
Bi ELIGARD CP 3 month + 28					
Bi ELIGARD CP 3 month + 84					
Total					

Source: Bi ELIGARD CP submission, pg. 26.

6.12 At the requested DPMQ and accounting for estimated substitution of other services, the submission estimated a net PBS saving of less than \$10 million in year 5 and less than \$10 million over 5 years. This is summarised in the table below.

Table 3: Estimated change in cost and use of other drugs

Net cost of Drug to PBS and RPBS	Year 1	Year 2	Year 3	Year 4	Year 5
Bi ELIGARD CP					
Total Services provided					
Net Cost to PBS	\$	\$	\$	\$	\$
Net Cost to RPBS	\$	\$	\$	\$	\$
Total Net Cost	\$	\$	\$	\$	\$
Changes in use and cost of other medicines					
Total Services provided					
Net Cost to PBS	\$	\$	\$	\$	\$
Net Cost to RPBS	\$	\$	\$	\$	\$
Total Net Cost	\$	\$	\$	\$	\$
Net cost to PBS/RPBS					
Net Services provided					
Net Cost to PBS	-\$	-\$	-\$	-\$	-\$
Net Cost to RPBS	-\$	-\$	-\$	-\$	-\$
Total Net Cost	-\$	-\$	-\$	-\$	-\$

Source: Bi ELIGARD CP submission, pg. 25.

6.13 Sensitivity analyses in the submission included changes to the proportion of goserelin use for prostate cancer, changes to the number of co-prescribed regimens, and varied market growth and uptake estimates. Goserelin is also used in the treatment of breast cancer and endometriosis, but not in combination with bicalutamide. These analyses are included in the table below.

Table 4: Summary of sensitivity analyses

Sensitivity Analysis	Year 1	Year 2	Year 3	Year 4	Year 5
Base case	-\$	-\$	-\$	-\$	\$
Market sizing estimates					
Proportion of Goserelin specific to prostate cancer, base case, 36%					
Lower estimate, 20%	-\$	-\$	-\$	-\$	\$
Upper estimate, 70%	-\$	-\$	-\$	-\$	\$
Proportion of co-prescribed regimen of LHRH utilisation, base case, 5.46% (1m28), 1.49% (3m28), 6.65% (3m84)					
Lower estimate, 3%, 1%, 5%	-\$	-\$	-\$	-\$	\$
Upper estimate, 10%, 5%, 10%	-\$	-\$	-\$	-\$	\$
Market growth estimates					
Growth of ZolaCos, base case, 9.63%					
Lower estimate, 7.13%	-\$	-\$	-\$	-\$	\$
Upper estimate, 12.13%	-\$	-\$	-\$	-\$	\$
Growth of 3m84 co-prescribed market, base case, 5.26%					
Lower estimate, 2.76%	-\$	-\$	-\$	-\$	\$
Upper estimate, 7.76%	-\$	-\$	-\$	-\$	\$
Uptake estimates					
Lower estimate, -5%	-\$	-\$	-\$	-\$	\$
Upper estimate, +10%	-\$	-\$	-\$	-\$	\$

Legend: 1m28 – Bi ELIGARD 1 month; 3m28 – Bi ELIGARD 3 month (28 BIC tablets); 3m84 – Bi ELIGARD 3 month (84 BIC tablets), Source: Bi ELIGARD CP submission, pp. 26-27.

The redacted table shows that, at year 5, the net saving to the PBS would be less than \$10 million under each set of assumptions.

For more detail on PBAC's view, see section 7 "PBAC outcome"

7 PBAC Outcome

- 7.1 The PBAC recommended the listing of the combination drug leuprorelin and bicalutamide on a cost minimisation basis compared with the individual components.
- 7.2 The PBAC accepted the nominated comparators of co-prescribed leuprorelin and bicalutamide (primary comparator) and goserelin and bicalutamide combination pack (secondary comparator). The PBAC noted that the components of the proposed product and comparator combination pack are TGA registered and PBS listed for metastatic prostate cancer.
- 7.3 The PBAC considered that the clinical outcomes with the leuprorelin and bicalutamide combination drug would be equivalent to those with co-prescribing of the individual components.
- 7.4 The PBAC recommended that the wording of the restriction be the same as for the currently listed goserelin and bicalutamide combination drug.
- 7.5 The PBAC recommended that the leuprorelin and bicalutamide combination drug be made available as a Restricted Benefit to align with the listings for the components (a Restricted Benefit listing was recommended for leuprorelin at the March 2016 PBAC meeting) and the goserelin and bicalutamide combination pack.
- 7.6 The PBAC noted that the submission proposed a lower price for the leuprorelin and bicalutamide combination packs than the currently listed prices for an equivalent supply of the goserelin and bicalutamide combination pack, and that there may be a modest cost saving associated with the flow-on of this price reduction to other combination LHRH agonist/bicalutamide products.
- 7.7 The PBAC considered the utilisation estimates appear reasonable and noted the financial impact for the proposed listing is minimal. The PBAC agreed that the listing of the leuprorelin and bicalutamide combination pack was unlikely to grow the overall market for LHRH agonists in combination with bicalutamide for metastatic prostate cancer. The PBAC considered there was a small risk of leakage to Stage C prostate cancer but this risk would not change with the listing of the proposed combination pack.
- 7.8 The PBAC advised, under Section 101(3BA) of the *National Health Act 1953*, that combination drug leuprorelin and bicalutamide should be treated as interchangeable on an individual patient basis with combination drug goserelin and bicalutamide.
- 7.9 The PBAC advised that the leuprorelin and bicalutamide combination drug is not suitable for prescribing by nurse practitioners.
- 7.10 The PBAC recommended that the Early Supply Rule should apply.
- 7.11 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

8 Recommended listing

8.1 Add new item:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
LEUPRORELIN AND BICALUTAMIDE leuprorelin acetate 7.5 mg injection: 1 modified release [1 syringe] (& inert substance diluent [1 syringe], (& bicalutamide 50 mg tablet [28 tablets], 1 pack	1	5	Bi ELIGARD CP® Tolmar Australia Pty Ltd (TL)

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:	Carcinoma of the prostate
PBS Indication:	Carcinoma of the prostate
Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Clinical criteria:	The condition must be metastatic (stage D), AND Patient must require a combination of an antiandrogen and a GnRH (LH-RH) agonist.
Administrative Advice	Note No increase in the maximum quantity or number of units may be authorised. Note No increase in the maximum number of repeats may be authorised.

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
LEUPRORELIN AND BICALUTAMIDE leuprorelin acetate 22.5 mg injection: 1 modified release [1 syringe] (& inert substance diluent [1 syringe], (& bicalutamide 50 mg tablet [28 tablets], 1 pack		0	Bi ELIGARD Tolmar Australia Pty Ltd (TL) CP®

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
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Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Clinical criteria:	The condition must be metastatic (stage D), AND Patient must require a combination of an antiandrogen and a GnRH (LH-RH) agonist.
Administrative Advice	Note No increase in the maximum quantity or number of units may be authorised. Note No increase in the maximum number of repeats may be authorised.

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
LEUPRORELIN AND BICALUTAMIDE leuprorelin acetate 22.5 mg injection: 1 modified release [1 syringe] (& inert substance diluent [1 syringe], (& bicalutamide 50 mg tablet [84 tablets], 1 pack	1	1	Bi ELIGARD Tolmar Australia Pty Ltd (TL) CP®

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:	Carcinoma of the prostate
PBS Indication:	Carcinoma of the prostate
Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Clinical criteria:	The condition must be metastatic (stage D), AND Patient must require a combination of an antiandrogen and a GnRH (LH-RH) agonist.
Administrative Advice	Note No increase in the maximum quantity or number of units may be authorised. Note No increase in the maximum number of repeats may be authorised.

9 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.

10 Sponsor's Comment

TOLMAR Australia welcomes the PBAC decision and is pleased that Bi ELIGARD cp® will now be available for patients with metastatic (Stage D) carcinoma of the prostate.