5.22 INSULIN LISPRO
injections (human analogue), cartridges, 200 units per mL, 3 mL, 5
Humalog® U200 Kwikpen®, Eli Lilly Australia Pty Ltd.

1 Purpose of Application

1.1 The minor submission requested a new listing of a new strength of insulin lispro, 200 units per mL, 5 × 3 mL for the treatment of type I and II diabetes mellitus (DM).

2 Requested listing

2.1 The submission sought the same listing (restriction and price per unit) as the current insulin lispro 100 units per mL, 5 × 3 mL cartridges.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
INSULIN LISPRO 200 units/mL, 3 mL, 5	5	5	[redacted]*	Humalog® Kwikpen® Eli Lilly Australia Pty Ltd

* as calculated by the sponsor assuming a 16% statutory price reduction. Without the 16% the reduction the DPMQ would be $[redacted].

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☒Nurse practitioners ☐Optometrists ☐Midwives
Restriction Level / Method:	Unrestricted

3 Background

3.1 Humalog 200 U/mL has been TGA registered since 9 November 2015 for the treatment of patients with Type 1 (IDDM) and Type 2 (NIDDM) diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis.

3.2 Humalog 200 U/mL was not considered previously by the PBAC.

4 Population and disease

4.1 Diabetes mellitus is a chronic condition characterised by abnormal sugar glucose levels in the blood.

4.2 Submission's proposed place in therapy is for patients who require higher daily insulin dose of >20 U.

5 Comparator

5.1 The minor submission nominated Humalog 100 U/mL Kwikpen as a main comparator based on the TGA approval and acceptance of bioequivalence.

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 The submission presented a PK study which was designed to determine bioequivalence between Humalog U100 and Humalog U200. The study was single-centre, open label, two-sequence, four period, randomised, cross-over euglycemic clamp study. The study was referenced in the TGA Clinical evaluator report. The report stated that the two formulations are closely bioequivalent when administered in the same amount and can be considered identical for clinical use on a unit for unit basis.

6.4 The TGA stated that bioequivalence between the U200 and U100 formulations of insulin was clearly demonstrated by the single supporting study.

Economic analysis

6.5 As a minor submission, there was no economic comparison presented/ an economic comparison was not relevant.

6.6 While not stated in the explicitly in the submission the price requested for Humalog 200 U/mL equated to a cost minimisation at a cost per unit insulin basis with an incorrect adjustment for a statutory 16% price reduction.

6.7 The submission stated that 16% statutory price reduction may apply to insulin lispro once the new form is listed on the PBS. While not a matter for the PBAC this is not correct as the proposed new brand of pharmaceutical item is not bioequivalent or biosimilar to an existing brand of a pharmaceutical item (ie subsection 99ACB(c)(ii) is not satisfied). For the purposes of the *National Health Act 1953* (Act), the bioequivalence test is applied at the pharmaceutical item level. Two pharmaceutical items containing the same drug but in different quantities can only be bioequivalent if the bioavailability of the drug from those two pharmaceutical items is different. In other words the Act test for bioequivalence does not allow the quantity of drug administered to be varied to achieve bioequivalence – rather it assumes the quantity of drug contained in the pharmaceutical item is the quantity that is administered. The total insulin units in the pharmaceutical item for the currently listed forms of insulin lispro are 1000 U for the 100 U/mL 10 mL vial and 1500 U for the 100 U/mL 5 × 3 ml cartridges, the requested listing of Humalog 200 U/mL 5 × 3 mL would result

in a pharmaceutical item containing 3000 U of insulin. Insulin lispro will also not move into the F2 formulary as a result of this listing.

6.8 Based off the current AEMP for Humalog 100 U/mL per pack of $42.38 the AEMP for Humalog 200 U/mL per pack would be $[redacted], which would equate to a DPMQ as proposed of $[redacted].

6.9 The sponsor in its pre-PBAC response (p 1,2) argued that the Department's statement that bioequivalence can only be determined by the same effective quantity of the drug delivered to a patients if the entire quantity of the drug in each pharmaceutical item is administered was an error of interpretation of the Act. The sponsor claimed that as per subsection 99ACB(1), the Humalog U100 and U200 on the day of listing would become existing brands of existing items; both Humalog's have the same manner of administration and are of the same form (cartridges) therefore both items were bioequivalent. Moreover, the sponsor argued that the bioequivalence should not be determined at the pharmaceutical item level. The PBAC noted the advice from the Department and the sponsor pre-PBAC response however, it considered that this was a matter for the Minister (delegate) to determine.

6.10 The PBAC also noted that the sponsor provided a similar argument as above in their pre-PBAC response (p 2) as to why the listing of Humalog U200 would trigger a move to the F2 formulary. However, it also considered that this was a matter for the Minister (delegate) to determine.

Estimated PBS usage & financial implications

6.11 The submission presented the budget impact modelling with a market share approach.

6.12 The minor submission estimated a net save to the PBS of less than $10 million per year over the first 6 years of listing, The additional cost of listing Humalog 200 U/mL is summarised in the table below (with no cost offsets) as well as the expected patient/prescription numbers. The PBAC noted that the following estimates included the effect of a 16% price reduction. The PBAC considered that if the price reduction does not proceed, it was likely that the listing of the 200 U/mL presentation will result in a cost to the PBS from reduced co-payments and from increased wastage (as patients will receive up to 3000 rather than up to 1500 units of insulin at each dispensing).

Table 1. Estimated number of Humalog 200 U/mL scripts per year.

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Number of insulin lispro scripts dispensed	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Humalog U200 share of market	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Number of Humalog U200 scripts dispensed	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scripts dispensed through PBS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scripts dispensed through RPBS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Source: Submission p13

The redacted table shows that at year 5, the estimated number of scripts dispensed was less than 10,000 per year.

Table 2. Estimated cost of listing Humalog 200 U/mL to the PBS and RPBS over six years (no offsets)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
PBS						
Estimated cost of Humalog U200 to PBS*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Estimated PBS patient co-payment	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost to the PBS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
RPBS						
Estimated cost of Humalog U200 to RPBS*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Estimated RPBS patient co-payment	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost to the PBS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Combined PBS and RPBS						
Estimated cost of Humalog U200 to PBS/RPBS*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Estimated PBS/RPBS patient co-payment	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost to the PBS/RPBS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Source: Submission p14

* including a 16% price reduction.

Table 3. Estimated overall net cost of listing Humalog 200 on the PBS

RPBS	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Overall net cost to the PBS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Overall net cost to the RPBS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Overall net cost to the PBS/RPBS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Combined overall net cost to the PBS/RPBS over six years*	[redacted]					

Source: Submission p16

* including a 16% price reduction.

The redacted table shows that at year 5, the estimated net savings to the PBS would be less than $10 million per year.

Quality Use of Medicines

6.13 The submission did not identify any QUM issues however, the Department was concerned that the listing of a new higher strength form of insulin lispro in the same injection device as the 100 U/mL form may lead to patient confusion and possibly result in over - and/or under - dosing and increased hypoglycaemic events. The sponsor was requested to indicate how it proposed to mitigate this QUM issue.

6.14 In its Pre-PBAC response (p 2), the sponsor proposed the following to address the above QUM issue:

a) Both Humalog packaging will be visually distinctive in colouring and style;

b) Both injectors will deliver the same dose by altering the volume;

c) It will continue to conduct a "know your insulin" program to educate patients on the insulin products, dosing and device;

d) It will continue to run a patient support program (LDSS) to make sure patients commence their therapy correctly.

6.15 The PBAC noted this response and advised that it was important that the sponsor continue to provide support and education for diabetic patients.

7 PBAC Outcome

7.1 The PBAC recommended the listing of the new strength of insulin lispro Humalog U200 for the treatment of type 1 and 2 diabetes mellitus. Listing was recommended on a cost minimisation basis per unit of insulin with insulin lispro Humalog U100, noting that a price reduction may be appropriate to achieve a listing that is cost-neutral to Government in the context of an increased potential for wastage resulting from the higher amount of drug provided with each dispensing.

7.2 The PBAC considered that the listing of Humalog U200 may meet a small clinical need for patients who require high daily doses of insulin lispro.

7.3 The PBAC recommended the listing of insulin lispro Humalog U200 under the same listing conditions as the currently listed insulin Humalog U100.

7.4 The PBAC advised that Humalog U200 should be included in items for prescribing by nurse practitioners similar to the U100 strength.

7.5 The PBAC recommended that the Early Supply Rule should apply.

7.6 The PBAC noted that this submission was 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	№.of Rpts	Proprietary Name	Manufacturer
INSULIN LISPRO 200 units/mL, 3 mL, 5	5	5	Humalog® Kwikpen®	Eli Lilly Australia Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☒Nurse practitioners ☐Optometrists ☐Midwives
Restriction Level / Method:	Unrestricted

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

The sponsor had no comment.