

## **6.14 RANIBIZUMAB**

**2.3 mg/0.23 mL, 1 x 0.23 mL vial,**

**1.65 mg/0.165 mL, pre-filled syringe;**

**Lucentis®; Novartis Pharmaceuticals Australia Pty Ltd.**

### **1 Purpose of Application**

- 1.1 The minor submission requested PBAC advise the Minister that ranibizumab pre-filled syringe and vial presentations could be 'a' flagged for the current treatment of neovascular age-related macular degeneration (AMD) and for the listings in the treatment of visual impairment due to diabetic macular oedema (DME) and in the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (RVO), recommended at July 2014 PBAC meeting.

### **2 Requested listing**

- 2.1 The submission proposed to retain the current existing Section 85 listings of ranibizumab injection for both the vial and pre-filled syringe presentations with an added 'a' flag between the two formulations to enable pharmacists to substitute presentations.

### **3 Background**

- 3.1 At the March 2014 PBAC meeting, the committee recommended the listing of the pre-filled syringe presentation of ranibizumab for the treatment of subfoveal choroidal neovascularisation (CNV) due to age-related macular degeneration (AMD) with the same restriction as the currently listed vial presentation. Listing was recommended on a cost minimisation basis with the vial presentation, with the equi-effective doses of one pre-filled syringe containing 1.65 mg of ranibizumab in 0.165 mL equivalent to one vial containing 2.3 mg ranibizumab in 0.23 mL.
- 3.2 Although PBAC noted that both the pre-filled syringe and the vial presentation deliver a single dose of 0.5 mg ranibizumab for intravitreal injection, "...", the potential for "a" flagging was not implemented because of the concern that the pre-filled syringe could only deliver a 0.5 mg dose whereas the vial could be used for a 0.5 mg and a 0.3 mg dose.
- 3.3 At the July 2014 PBAC meeting, the committee recommended two further indications be added for ranibizumab for the treatment of visual impairment due to diabetic macular oedema (DME) and for the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (RVO).

### **4 Current situation**

- 4.1 Vial

The dosing preparation from the vial requires the withdrawal of all the liquid from the vial into a syringe. Clinicians are then instructed to expel the air from the syringe and adjust the dose to 0.05 mL or 0.03 mL mark on the syringe to sufficiently prepare both doses.

Pre-filled syringe (PFS)

The total volume of the PFS is 0.165 mL, the dosing preparation for PFS is to expel the air and the excess solution and set the dose to 0.5 mg (0.05 mL) using the fixed dose mark on the PFS. The submission stated that in practice it is possible to expel an additional 0.02 mL, as occurs currently in preparing a 0.3 mg dose with a standard intravitreal syringe from the vial. Thus it is possible in practice to administer 0.03 mL from the PFS should this dose be required. The submission indicated that a permanent marker could be used to make a mark equivalent to 0.03 mL on the PFS, below the 0.05 mL mark on the PFS, to assist with preparing the 0.03 mL dose.

- 4.2 The submission claimed that due to the nature of the distribution chain for this product, the majority of injection clinics or injecting clinicians have a refrigerator to store ranibizumab and it would be unlikely that pharmacists would make a switch decision (vial for PFS) without consulting the prescriber and a switch would only be necessary in the event of a one or other presentations being temporarily unavailable.
- 4.3 It was proposed by the submission that ranibizumab be substitutable to each formulation for each recommended listing (current and anticipated).

## **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. The submission provided excerpts of the clinical evidence from the ranibizumab Product Information relating to 0.3 mg and 0.5 mg doses for each of the indications registered.

### **Clinical claim**

- 5.4 The submission claimed that an 'a' flag would alleviate the administrative burden on clinicians and patients to have authority codes for the script of one presentation (e.g. PFS) switched to a new script of the other presentation (e.g. vial) by Medicare in Tasmania should one or other presentations be unavailable at the time of dispensing.

### **Estimated PBS usage & financial implications**

- 5.5 The minor submission estimated no incremental cost to the PBS or the government if an 'a' flag was to be applied.
- 5.6 The submission indicated there was no change in price and the current risk-sharing arrangements for ranibizumab will remain in place.

## **6 PBAC Outcome**

- 6.1 The PBAC advised the Minister that ranibizumab 2.3 mg/0.23 mL solution for injection and ranibizumab 1.65 mg/0.165 mL pre-filled syringe for injection could be considered equivalent for the purposes of substitution at the point of dispensing ('a' flagged in the Schedule).
- 6.2 The PBAC noted that in practice a health care professional, rather than the patient, would be required to determine the volume of 0.03 ml in the PFS. The PBAC considered that mark on the syringe during the manufacturing process would be more accurate for the delivery of 0.3 mg, than the method suggested in the submission.
- 6.3 In providing this advice, the PBAC also recalled its previous advice in November 2012 that the multi-use pump (Aldrara) and single use sachet presentations of imiquimod (including Aldrara) be marked as equivalent for the purposes of substitution at the point of dispensing. The Product information for Aldrara states that four actuations of the pump is equivalent to one 250 mg sachet of Aldrara cream.

### **Outcome:**

Recommended

## **7 Recommended listing**

- 7.1 Add NOTE to PBS Item 10138N and 1382R as follows:

### Note

Pharmaceutical benefits that have the form ranibizumab 0.165 ml injection vial and pharmaceutical benefits that have the form ranibizumab 0.23 ml injection syringe are equivalent for the purposes of substitution.

## **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.