

6.10 IVACAFTOR, tablet 150 mg, Kalydeco[®], Vertex

1 Purpose of Application

- 1.1 The minor submission requested changes to the current restriction, to allow flexibility in dosing of ivacaftor for patients with cystic fibrosis who are on concomitant CYP3A inhibitors.

2 Requested listing

- 2.1 The submission requested changes to the existing restrictions from November 2014 PBAC meeting.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
IVACAFTOR Tablet 150 mg	56	2	Kalydeco Vertex

Section 100 (Highly Specialised Drugs Program)

Authority required

Secretariat comments

- 2.2 The submission requested amendment to the current restriction to include the following wording:
- ~~Dosage of ivacaftor must not exceed the dose of 150 mg twice a week, if the patient is concomitantly receiving one of the following strong CYP3A4 drugs inhibitors: boceprevir, clarithromycin, conivaptan, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, mibefradil, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, voriconazole.~~
 - *Dosage of ivacaftor must commence at a dose of 150 mg twice a week but will not exceed 150 mg twice per day if the patient is concomitantly receiving one of the following strong CYP3A4 inhibitors: itraconazole, ketoconazole, posaconazole, voriconazole.*
 - ~~Where a patient is concomitantly receiving a strong CYP3A4 inhibitor, a single supply of 56 tablets of ivacaftor will last for 28 weeks.~~
 - *Where a patient is concomitantly receiving one of these strong CYP3A4 inhibitors, a single supply of 56 tablets of ivacaftor will last for a maximum of 28 weeks and a minimum of 4 weeks.*

3 Background

- 3.1 Ivacaftor was listed on the Australian Register of Therapeutic Goods (ARTG) in August 2014 "...for the treatment of cystic fibrosis (CF) in patients age 6 years and

older who have a G551D or other gating (class III) mutation in the CFTR gene.” Before this date, ivacaftor was TGA registered for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have a G551D mutation in the CFTR gene. Ivacaftor was listed on the PBS on 1 December 2014.

4 Clinical place for the proposed therapy

- 4.1 Ivacaftor is intended to be used as add on to current best supportive therapy, and has a different mechanism of action to the antibiotics and mucolytics currently available through the PBS. Under the proposed listing, CF patients aged 6 and over with a G551D or other gating (class III) mutation in the CFTR gene will be eligible for ongoing ivacaftor therapy.
- 4.2 The changes requested by the sponsor are proposed to ensure maximum therapeutic benefit by increasing the dose of ivacaftor in patients who are also on strong CYP3A4 inhibitor such as itraconazole. The sponsor stated that it was brought to their attention by cystic fibrosis treating physicians that the effect of ivacaftor diminished between doses when administered at a maximum dose of 2 tablets per week.

5 Consideration of the evidence

- 5.1 There was no sponsor hearing for this item.

Consumer comments

- 5.2 The PBAC noted and welcomed the input from individuals (2), health care professionals (1) via the Consumer Comments facility on the PBS website. The comments described a range of concerns of treatment with lower dose of ivacaftor and highlighted the importance to allow for flexibility with the dosing for patients who are on CYP3A inhibitors for the treatment of cystic fibrosis.

Clinical trials

- 5.3 As a minor submission, no new clinical trials were presented in the re-submission.
- 5.4 The submission stated that the current recommendation in the approved Product Information (PI) is based on only one study. Further there is complex interaction and AUC inter-individual variability. Therefore, the sponsor proposed to have flexibility in dosing of ivacaftor for patients on concomitant CYP3A inhibitors to ensure optimal efficacy in the interest of best outcomes for patients.

6 PBAC Outcome

- 6.1 The PBAC deferred making a recommendation. The PBAC recalled that previous amendments to the PBS restriction had been preceded by supporting changes in the

approved PI. The PBAC requested that the Secretariat seek advice from the TGA about the status of the PI for ivacaftor.

Outcome:

Deferred

7 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.

8 Sponsor's Comment

The sponsor had no comment.