

7.14 TEZACAFTOR with IVACAFTOR, Pack containing tezacaftor 100 mg with ivacaftor 150 mg tablets and ivacaftor 150 mg tablets, Symdeko[®], Vertex Pharmaceuticals

1 Purpose of Application

- 1.1 To request extension of the March 2019 PBAC recommended Authority Required listing for tezacaftor with ivacaftor (tezacaftor/ivacaftor) for the treatment of patients aged 12 years or older with cystic fibrosis (CF) who have one copy of the F508del mutation and another residual function (RF) mutation in the CF transmembrane conductance regulator (CFTR) gene, to include all CF patients aged 12 years and older who have at least one RF mutation in the CFTR gene.

2 Requested listing

- 2.1 The Secretariat has proposed the following changes to the current draft restriction for initial treatment for patients with one F508del and one RF mutation in the CFTR gene (abbreviated form shown below) which is intended for listing on the PBS on 1 December 2019, with deletions in strikethrough and additions in italics.

| Name, Restriction, Manner of administration and form | Max. Qty | No. of Rpts | Proprietary Name and Manufacturer | |
|--|-------------|----------------|-----------------------------------|--------|
| TEZACAFTOR + IVACAFTOR (&) IVACAFTOR Tezacaftor 100 mg + ivacaftor 150 mg tablet [28] (&) ivacaftor 150 mg tablet [28], 1 pack | 1 | 5 | Symdeko® | Vertex |

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| Category / Program: | Section 100 – Highly Specialised Drugs Program |
| 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 |
| PBS Indication: | Cystic Fibrosis |
| Treatment phase: | Initial treatment |
| Restriction Level / Method: | <input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required – In Writing <input type="checkbox"/> Authority Required – Telephone/Electronic/Emergency <input type="checkbox"/> Streamlined |

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| Treatment criteria: | <p>Must be treated by a specialist respiratory physician with expertise in cystic fibrosis, OR Must be treated in consultation with a specialist respiratory physician with expertise in cystic fibrosis if attendance is not possible due to geographic isolation; AND Must be treated in a centre with expertise in cystic fibrosis, OR Must be treated in consultation with a centre with expertise in cystic fibrosis if attendance is not possible due to geographic isolation.</p> |
| Clinical criteria: | <p>Patient must have one residual function (RF) mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor with ivacaftor; AND Patient must have F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene on at least 1 allele; AND The treatment must be the sole PBS-subsidised cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapy for this condition; AND The treatment must be given concomitantly with standard therapy for this condition. AND The patient must have either chronic sinopulmonary disease or gastrointestinal and nutritional abnormalities</p> |
| Population criteria: | <p>Patient must be 12 years of age or older.</p> |
| Prescriber Instructions: | <p>The patient must be registered in the Australian Cystic Fibrosis Database Registry.</p> <p>Treatment must not be given to a patient who has an acute upper or lower respiratory infection, pulmonary exacerbation, or changes in therapy (including antibiotics) for pulmonary disease in the last 4 weeks prior to commencing this drug.</p> <p>For the purposes of this restriction, PBS subsidised 'CFTR modulator' means ivacaftor, lumacaftor/ivacaftor and tezacaftor/ivacaftor</p> <p>For the purposes of this restriction, the list of mutations considered to be responsive to tezacaftor with ivacaftor is defined in the TGA approved product information.</p> <p>Dosage of tezacaftor with ivacaftor is tezacaftor 100 mg/ivacaftor 150 mg and ivacaftor 150 mg tablets on alternate days if the patient is concomitantly receiving one of the following moderate CYP3A4 drugs inhibitors: amprenavir, aprepitant, atazanavir, darunavir/ritonavir, diltiazem, erythromycin, fluconazole, fosamprenavir, imatinib, verapamil.</p> <p>Dosage of tezacaftor with ivacaftor is tezacaftor 100 mg/ivacaftor 150 mg twice weekly (approximately 3 or 4 days apart) if the patient is concomitantly receiving one of the following strong CYP3A4 inhibitors: boceprevir, clarithromycin, conivaptan, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, mibefradil, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, voriconazole</p> <p>Tezacaftor with ivacaftor is not PBS-subsidised for this condition in a patient who is currently receiving one of the following CYP3A4 inducers:</p> <p>Strong CYP3A4 inducers: avasimibe, carbamazepine, phenobarbital, phenytoin, rifabutin, rifampicin, St. John's wort</p> <p>Moderate CYP3A4 inducers: bosentan, efavirenz, etravirine, modafinil, nafcillin</p> |

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| | <p>Weak CYP3A4 inducers: armodafinil, echinacea, pioglitazone, rufinamide.</p> <p>The authority application must be in writing and must include:</p> <p>(1) a completed authority prescription form; and</p> <p>(2) a completed Cystic Fibrosis Tezacaftor with Ivacaftor Authority Application Supporting Information Form; and</p> <p>(3) a copy of the pathology report detailing the molecular testing for the patient having at least one RF mutation on the CFTR gene; and</p> <p>(4) a copy of the pathology report detailing the molecular testing for the patient having at least one F508del mutation on the CFTR gene;</p> <p>(5) the result of a FEV₁ measurement performed within a month prior to the date of application. Note: FEV₁ must be measured in an accredited pulmonary function laboratory, with documented no acute infective exacerbation at the time FEV₁ is measured; and</p> <p>(6) (5) a copy of a current medication history, including any current CYP3A4 inhibitors, or CYP3A4 inducers and IV antibiotics; and</p> <p>(7) (6) height and weight measurements at the time of application; and</p> <p>(8) (7) a baseline measurement of the number of days of CF-related hospitalisation (including hospital-in-the home) in the previous 12 months.</p> <p>For patients who've initiated non-PBS subsidised treatment prior to 1 December 2019, date of initiating treatment, baseline FEV₁ and hospitalisation dates prior to initiating treatment (where available) should be provided.</p> |
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- 2.1 The pre-PBAC response stated that the sponsor has received reports from CF clinics that mandating the use of an accredited pulmonary function laboratory to collect FEV₁ (percent predicted forced expiratory volume in one second) measurements places an additional burden on some CF centres and patients. The pre-PBAC response considered that FEV₁ measurements from CF centres would be sufficient for medical records. The pre-PBAC response also stated that a telephone authority should be considered for continuing PBS authority applications.

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

3 Background

Registration status

- 3.1 Tezacaftor/ivacaftor is TGA registered for the treatment of patients with CF aged 12 years and older who are homozygous for the F508del mutation or who have at least one mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence, as defined in Table 1 of the TGA approved Product Information. The TGA approved Product Information currently specifies a total of 25 CFTR gene mutations (not including the F508del mutation) that produce CFTR protein responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence.

Previous PBAC considerations

3.1 The PBAC previously considered a major submission for tezacaftor/ivacaftor for the treatment of two CF patient groups: those who are homozygous for (i.e. have two copies of) the F508del mutation (tezacaftor with ivacaftor (F508del deletion) Public Summary Document (PSD), March 2019 PBAC meeting) and those who have at least one RF mutation (tezacaftor with ivacaftor (RF mutation) PSD, March 2019 PBAC meeting) in the CFTR gene at the March 2019 PBAC meeting. The PBAC recommended tezacaftor/ivacaftor for the treatment of patients with CF aged 12 years and older who:

- are homozygous for the F508del mutation in the CFTR gene, on a cost-minimisation basis to lumacaftor with ivacaftor (paragraph 7.1, tezacaftor with ivacaftor (F508del deletion), Public Summary Document (PSD), March 2019 PBAC meeting); and
- have one copy of the F508del mutation and another RF mutation in the CFTR gene, in line with the patient population in the key clinical trial, Study 108 on the basis of cost effectiveness compared with best supportive care (BSC) (paragraphs 7.1-2, tezacaftor with ivacaftor (RF mutation), PSD, March 2019 PBAC meeting).

On 21 October 2019, the Minister for Health announced that tezacaftor/ivacaftor will be listed for these patients on 1 December 2019.

4 Population and disease

4.1 Patients with RF mutations constitute a small group of CF patients with various rare mutations. RF mutations may cause reduced synthesis or stability of the CFTR protein that may result in retention of residual activity and therefore less severe disease. Patients with RF mutations tend to have a later onset of disease compared with patients homozygous for the F508del mutation however, still develop significant and progressive disease with a reduced life expectancy characteristic of CF.

5 Comparator

5.1 The PBAC previously accepted BSC as the appropriate main comparator for the requested population (paragraph 7.4, tezacaftor with ivacaftor (RF mutation), PSD, March 2019 PBAC meeting).

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 and welcomed the input from individuals (175), health care professionals (2) and organisations (1) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with tezacaftor/ivacaftor including improvement in lung function, reduction of infections, reduced need for other medications, reduction of hospital visits and improvement in quality of life. The comments emphasised that patients with rarer CF mutations also experience debilitating effects of the disease and strongly expressed that tezacaftor/ivacaftor should also be subsidised for these patients.
- 6.3 Cystic Fibrosis Australia (CFA) also indicated its support for tezacaftor/ivacaftor to be made available to patients with rarer CF mutations.

Clinical trials

- 6.4 The minor resubmission acknowledged there is no randomised clinical trial data to quantify the magnitude of FEV₁ improvement in CF patients with an RF mutation without an F508del mutation.
- 6.5 The March 2019 submission was based on Study 108, which compared tezacaftor/ivacaftor plus BSC and placebo plus BSC in patients who have one copy of the F508del mutation who also have an RF mutation.
- 6.6 Study 108 included 12 RF mutations with each of the RF mutations being associated with ≤ 21 patients. However given the rarity of the RF mutations, the PBAC previously acknowledged that more reliable clinical data from studies with adequate power to assess the impact of treatment across all RF mutations would not be forthcoming (paragraph 7.6, tezacaftor with ivacaftor (RF mutation) PSD, March 2019 PBAC meeting).

Comparative effectiveness

- 6.7 The minor resubmission presented in vitro data of the effect of tezacaftor/ivacaftor on CFTR processing, trafficking and function on cells each expressing a single RF mutation of the CFTR gene as supporting evidence.
- 6.8 The minor resubmission noted that treatment with tezacaftor/ivacaftor increased the efficiency of CFTR processing and trafficking and increased chloride transport over baseline for all RF CFTR forms tested. The minor submission noted that this increase was greater than that observed with either agent alone (with the exception of R347H which is not included in the TGA registered indication for tezacaftor with ivacaftor).
- 6.9 In the context of its March 2019 recommendation for patients who have one copy of the F508del mutation and another RF mutation in the CFTR gene, the PBAC was satisfied that tezacaftor/ivacaftor provides, for some patients, a significant

improvement in efficacy over BSC (paragraph 7.1, tezacaftor with ivacaftor (RF mutation) PSD, March 2019 PBAC meeting). However, the PBAC was uncertain that the magnitude of treatment effect was representative of the likely clinical benefit across the group of requested RF mutations given the potential variability of treatment outcomes between patients with different RF mutations (paragraph 7.6, tezacaftor with ivacaftor (RF mutation) PSD, March 2019 PBAC meeting).

Economic analysis

- 6.10 The minor resubmission did not present an economic analysis.
- 6.11 The March 2019 submission presented a cost-utility analysis with the same structure as that for previous CFTR modulator submissions and included the application of a decrease in the rate of decline in ppFEV₁ (per cent predicted forced expiratory volume in one second) of 42% based on longer-term data from the lumacaftor with ivacaftor PROGRESS study for patients homozygous for the F508del mutation, compared with a matched historical control cohort.
- 6.12 The PBAC noted that this may not reflect the RF mutation population and that it previously considered the rate of decline to be overly optimistic noting that lumacaftor with ivacaftor was recommended using this estimate on the basis that (among other factors) a managed access program (MAP) would apply to ensure that the price paid was consistent with the evidence (paragraph 7.9, tezacaftor with ivacaftor (RF mutation) PSD, March 2019 PBAC meeting). The PBAC acknowledged that more reliable data regarding the decrease in the rate of decline in ppFEV₁ associated with treatment with tezacaftor/ivacaftor (as well as other clinical benefits) for this patient population are unlikely to become available. Accordingly, the PBAC pragmatically considered that the ICER for tezacaftor/ivacaftor for the RF mutation patient population [i.e. patients with one F508del and one RF mutation in the CFTR gene] would likely be no higher than that for lumacaftor with ivacaftor for the F508del homozygous patient population if the price for tezacaftor/ivacaftor was no higher than the price previously recommended for lumacaftor with ivacaftor (of \$ [REDACTED] per patient per year) (paragraph 7.10, tezacaftor with ivacaftor (RF mutation) PBAC minutes, March 2019 PBAC meeting).

Drug cost/patient/year

- 6.13 Based on the requested published price of \$21,000 per 28-day pack proposed in the March 2019 submission, the drug cost per patient per year would be \$273,938 (\$21,000/56 tablets per pack*2 tablets per day*365.25 days per year). The March 2019 submission proposed an intended annual price of \$ [REDACTED] per patient for tezacaftor/ivacaftor to be implemented through subsidisations caps through a Risk Sharing Arrangement (RSA).

Estimated PBS usage & financial implications

- 6.14 The minor resubmission did not provide patient estimates and financial implications specific to the sub-group of CF patients who have an RF mutation without an F508del mutation. The estimated use and financial implications for all CF patients with at least one RF mutation were presented in the March 2019 submission, and therefore this listing will not result in additional patients beyond those presented at that time.
- 6.15 The minor resubmission claimed that the number of CF patients aged 12 years and older who have an RF mutation without an F508del mutation is likely to be small given approximately 90% of patients carry an F508del mutation. The minor resubmission estimated there are approximately 10-15 patients who have an RF mutation without an F508del mutation, based on consultations with Australian CF directors.

Financial Management – Risk Sharing Arrangements

- 6.16 The March 2019 submission proposed a reduction in the gross cost of tezacaftor/ivacaftor to the PBS via a subsidisation cap based on an intended annual price of \$ [REDACTED] per patient, to be implemented through an RSA, in line with lumacaftor with ivacaftor for patients who are homozygous for the F508del mutation.
- 6.17 In its March 2019 recommendation for tezacaftor/ivacaftor, the PBAC was of the view that the RF mutation patient population should be included in the existing lumacaftor with ivacaftor Deed of Agreement and any change to the lumacaftor with ivacaftor price per patient per year as a result of the MAP should also be applicable to the price of tezacaftor/ivacaftor, in order to manage the uncertain cost-effectiveness of tezacaftor/ivacaftor in this treatment setting (paragraph 7.11, tezacaftor with ivacaftor (RF mutation) PSD, March 2019 PBAC meeting).
- 6.18 The PBAC noted the advice from the Department regarding [then] current utilisation of lumacaftor/ivacaftor and that Government expenditure per patient in Year 1 of listing is likely to be significantly higher than what was considered acceptably cost-effective (i.e. \$ [REDACTED] per patient per year) in its July 2018 recommendation. In this regard, the PBAC advised that any increase to the existing financial caps for lumacaftor/ivacaftor to include patients with an RF mutation would need to account for the difference between the expected and actual utilisation of lumacaftor/ivacaftor in the homozygous F508del population. Given that uptake of lumacaftor/ivacaftor appears significantly lower than estimated utilisation in July 2018, it may be appropriate to include tezacaftor/ivacaftor for the treatment of the RF patient population to the existing financial caps for lumacaftor/ivacaftor without any increase. The PBAC considered that it may be appropriate for the Department to implement other measures to ensure tezacaftor/ivacaftor does not exceed the price of \$ [REDACTED] per patient per year; this could be achieved through a Special Pricing Arrangement, as per the July 2018 recommendation for lumacaftor/ivacaftor. (paragraph 7.12, tezacaftor with ivacaftor (RF mutation) PBAC minutes, March 2019 PBAC meeting)

- 6.19 The minor resubmission indicated that the sponsor is willing to discuss a financial arrangement that is specific to the additional patient population within the broader financial negotiations currently underway for the recommended listing of tezacaftor/ivacaftor for CF patients with an RF mutation and one copy of the F508del mutation.
- 6.20 On 21 October 2019, the Minister for Health announced that tezacaftor/ivacaftor will be listed on 1 December 2019 for the populations recommended in July 2019. The Deed of Agreement for lumacaftor with ivacaftor has been updated to include tezacaftor/ivacaftor with increases in the subsidisation caps for years 3, 4, and 5 of the Deed, with no increase for year 2 (current year). The Deed also includes a mechanism for reconciliation of the subsidisation cap in any current or future year if Government expenditure per FTE patient is higher than \$ [REDACTED] per patient per year.

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

7 PBAC Outcome

- 7.1 The PBAC recommended extending its March 2019 recommendation for Section 100 (Highly Specialised Drugs Program) Authority Required listing of tezacaftor with ivacaftor (tezacaftor/ivacaftor) to include CF patients aged 12 years and older who have at least one RF mutation in the CFTR gene. Given the limited supporting evidence, the PBAC considered the magnitude of incremental benefit and therefore cost-effectiveness of tezacaftor/ivacaftor compared with BSC across the group of requested RF mutations was uncertain. The PBAC advised that tezacaftor/ivacaftor for the treatment of patients with at least one RF mutation, should be included under the Risk Sharing Arrangement (RSA) for lumacaftor with ivacaftor and tezacaftor/ivacaftor without any increase to the subsidisation caps, such that the extension of the recommended listing will not result in any additional cost to Government.
- 7.2 The PBAC acknowledged the many consumer comments and correspondence from Cystic Fibrosis Australia, which support subsidised access to tezacaftor/ivacaftor for CF patients with RF mutations. The PBAC acknowledged that the burden of disease could also be significantly debilitating for patients who have an RF mutation without an F508del mutation in the CFTR gene.
- 7.3 The PBAC noted that no clinical data for patients with an RF mutation without an F508del mutation in the CFTR gene was available. However, the PBAC acknowledged that obtaining efficacy data through a clinical trial would be difficult given the individual rarity of these CFTR genotypes. Although the PBAC noted the in vitro data indicated the panel of known RF mutations is responsive to tezacaftor/ivacaftor, it was uncertain how these results would translate to the likely magnitude of benefit for these patients in clinical practice. The PBAC noted that there is considerable variation in chloride transport at baseline and change in chloride transport from baseline across the RF mutations based on the in vitro data presented. The PBAC noted that data from

the Italian Cystic Fibrosis Registry showed that of the patients with an RF mutation, patients who also had an F508del mutation have worse lung function than those without. The PBAC further noted there was considerable heterogeneity in lung function across patients with at least one RF mutation in the registry. Overall, the PBAC considered the incremental benefit of treatment with tezacaftor/ivacaftor compared with BSC across all known RF mutations in this patient population is uncertain.

- 7.4 The PBAC recalled that in its March 2019 consideration of the previous submission for tezacaftor/ivacaftor for patients with at least one RF mutation, it pragmatically considered that the ICER for tezacaftor/ivacaftor would likely be no higher than that for lumacaftor with ivacaftor for the F508del homozygous patient population if the price for tezacaftor/ivacaftor was no higher than the price previously recommended for lumacaftor with ivacaftor (\$██████ per patient per year). The PBAC noted that this advice was in the context of the recommended population of patients who have one RF mutation and one F508del mutation in the CFTR gene, in line with the population in Study 108. The PBAC considered that the cost-effectiveness of tezacaftor/ivacaftor compared with BSC in patients with one RF mutation without an F508del mutation is uncertain given the incremental benefit of treatment is uncertain.
- 7.5 The PBAC noted that the resubmission claimed there are currently around 10-15 CF patients who have an RF mutation without an F508del mutation, based on consultations with Australian CF directors. The PBAC recalled that the estimated use and financial implications for all CF patients with at least one RF mutation were presented in the March 2019 submission.
- 7.6 The PBAC advised that the additional patients with an RF mutation without an F508del mutation to be treated with tezacaftor/ivacaftor should be included under the current RSA for lumacaftor with ivacaftor and tezacaftor/ivacaftor without any increase to the subsidisation caps, such that the listing will not result in any additional cost to Government.
- 7.7 The PBAC considered that the restriction should restrict the collection of FEV₁ measurements to accredited pulmonary functional laboratories as the reliability of FEV₁ measurements outside accredited laboratories may vary.
- 7.8 The PBAC noted the request in the pre-PBAC response for the restriction level for continuing treatment to be made a telephone authority. However, the PBAC considered that the restriction levels for tezacaftor/ivacaftor should be consistent with those for the current lumacaftor/ivacaftor listings. As such, the PBAC considered it would be appropriate that the restriction level for continuing treatment of tezacaftor/ivacaftor be written authority.
- 7.9 The PBAC previously advised that tezacaftor/ivacaftor is not suitable for prescribing by nurse practitioners.

- 7.10 The PBAC previously recommended that the Early Supply Rule should apply
- 7.11 The PBAC noted the submission is not eligible for an Independent Review, because the PBAC has made a positive recommendation.

Outcome:

Recommended

8 Recommended listing

8.1 Amend recommended listing as follows:

| Name, Restriction, Manner of administration and form | Max. Qty | No. of Rpts | Proprietary Name and Manufacturer | |
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| Category / Program: | Section 100 – Highly Specialised Drugs Program |
| 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 |
| PBS Indication: | Cystic Fibrosis |
| Treatment phase: | Initial treatment |
| Restriction Level / Method: | <input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required – In Writing <input type="checkbox"/> Authority Required – Telephone/Electronic/Emergency <input type="checkbox"/> Streamlined |
| Treatment criteria: | Must be treated by a specialist respiratory physician with expertise in cystic fibrosis, OR Must be treated in consultation with a specialist respiratory physician with expertise in cystic fibrosis if attendance is not possible due to geographic isolation; AND Must be treated in a centre with expertise in cystic fibrosis, OR Must be treated in consultation with a centre with expertise in cystic fibrosis if attendance is not possible due to geographic isolation. |
| Clinical criteria: | Patient must have one residual function (RF) mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor with ivacaftor; AND Patient must have F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene on at least 1 allele; AND The treatment must be the sole PBS-subsidised cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapy for this condition; AND The treatment must be given concomitantly with standard therapy for this condition. AND The patient must have either chronic sinopulmonary disease or gastrointestinal and nutritional abnormalities |
| Population criteria: | Patient must be 12 years of age or older. |
| Prescriber Instructions: | The patient must be registered in the Australian Cystic Fibrosis Database Registry. |

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| | <p>Treatment must not be given to a patient who has an acute upper or lower respiratory infection, pulmonary exacerbation, or changes in therapy (including antibiotics) for pulmonary disease in the last 4 weeks prior to commencing this drug.</p> <p>For the purposes of this restriction, PBS subsidised 'CFTR modulator' means ivacaftor, lumacaftor/ivacaftor and tezacaftor/ivacaftor</p> <p>For the purposes of this restriction, the list of mutations considered to be responsive to tezacaftor with ivacaftor is defined in the TGA approved product information.</p> <p>Dosage of tezacaftor with ivacaftor is tezacaftor 100 mg/ivacaftor 150 mg and ivacaftor 150 mg tablets on alternate days if the patient is concomitantly receiving one of the following moderate CYP3A4 drugs inhibitors: amprenavir, aprepitant, atazanavir, darunavir/ritonavir, diltiazem, erythromycin, fluconazole, fosamprenavir, imatinib, verapamil.</p> <p>Dosage of tezacaftor with ivacaftor is tezacaftor 100 mg/ivacaftor 150 mg twice weekly (approximately 3 or 4 days apart) if the patient is concomitantly receiving one of the following strong CYP3A4 inhibitors: boceprevir, clarithromycin, conivaptan, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, mibefradil, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, voriconazole</p> <p>Tezacaftor with ivacaftor is not PBS-subsidised for this condition in a patient who is currently receiving one of the following CYP3A4 inducers:</p> <p>Strong CYP3A4 inducers: avasimibe, carbamazepine, phenobarbital, phenytoin, rifabutin, rifampicin, St. John's wort</p> <p>Moderate CYP3A4 inducers: bosentan, efavirenz, etravirine, modafinil, nafcillin</p> <p>Weak CYP3A4 inducers: armodafinil, echinacea, pioglitazone, rufinamide.</p> <p>The authority application must be in writing and must include:</p> <ol style="list-style-type: none">(1) a completed authority prescription form; and(2) a completed Cystic Fibrosis Tezacaftor with Ivacaftor Authority Application Supporting Information Form; and(3) a copy of the pathology report detailing the molecular testing for the patient having at least one RF mutation on the CFTR gene; and(4) a copy of the pathology report detailing the molecular testing for the patient having at least one F508del mutation on the CFTR gene;(5) the result of a FEV₁ measurement performed within a month prior to the date of application. Note: FEV₁, must be measured in an accredited pulmonary function laboratory, with documented no acute infective exacerbation at the time FEV₁ is measured; and(6)(5) a copy of a current medication history, including any current CYP3A4 inhibitors, or CYP3A4 inducers and IV antibiotics; and(7)(6) height and weight measurements at the time of application; and(8)(7) a baseline measurement of the number of days of CF-related hospitalisation (including hospital-in-the home) in the previous 12 months. <p>For patients who've initiated non-PBS subsidised treatment prior to 1 December 2019, date of initiating treatment, baseline FEV1 and hospitalisation dates prior to initiating treatment (where available) should be provided.</p> |
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| Clinical criteria: | Patient must have previously received PBS-subsidised treatment with this drug for this condition AND The treatment must be given concomitantly with standard therapy for this condition. |
| Population criteria: | Patient must be 12 years of age or older. |
| Prescriber Instructions: | The patient must be registered in the Australian Cystic Fibrosis Database Registry. Treatment must not be given to a patient who has an acute upper or lower respiratory infection, pulmonary exacerbation, or changes in therapy (including antibiotics) for pulmonary disease in the last 4 weeks prior to commencing this drug. For the purposes of this restriction, PBS subsidised 'CFTR modulator' means ivacaftor, lumacaftor/ivacaftor and tezacaftor/ivacaftor For the purposes of this restriction, the list of mutations considered to be responsive to tezacaftor with ivacaftor is defined in the TGA approved product information. Dosage of tezacaftor with ivacaftor is tezacaftor 100 mg/ivacaftor 150 mg and ivacaftor 150 mg tablets on alternate days if the patient is concomitantly receiving one of the following moderate CYP3A4 drugs inhibitors: amprenavir, aprepitant, atazanavir, darunavir/ritonavir, diltiazem, erythromycin, fluconazole, fosamprenavir, imatinib, verapamil. Dosage of tezacaftor with ivacaftor is tezacaftor 100 mg/ivacaftor 150 mg twice weekly (approximately 3 or 4 days apart) if the patient is concomitantly receiving one of the following strong CYP3A4 inhibitors: boceprevir, clarithromycin, conivaptan, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, mibefradil, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, voriconazole |

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| | <p>Tezacaftor with ivacaftor is not PBS-subsidised for this condition in a patient who is currently receiving one of the following CYP3A4 inducers:</p> <p>Strong CYP3A4 inducers: avasimibe, carbamazepine, phenobarbital, phenytoin, rifabutin, rifampicin, St. John's wort</p> <p>Moderate CYP3A4 inducers: bosentan, efavirenz, etravirine, modafinil, nafcillin</p> <p>Weak CYP3A4 inducers: armodafinil, echinacea, pioglitazone, rufinamide.</p> <p>The authority application must be in writing and must include:</p> <p>(1) a completed authority prescription form; and</p> <p>(2) a completed Cystic Fibrosis Tezacaftor with Ivacaftor Authority Continuing Application Supporting Information Form; and</p> <p>(3) the result of a FEV₁ measurement performed within a month prior to the date of application. Note: FEV₁ must be measured in an accredited pulmonary function laboratory, with documented no acute infective exacerbation at the time FEV₁ is measured; and</p> <p>(4) a copy of a current medication history, including any current CYP3A4 inhibitors, or CYP3A4 inducers and IV antibiotics; and</p> <p>(5) height and weight measurements at the time of application; and</p> <p>(6) the number of days of CF-related hospitalisation (including hospital-in-the home) in the previous 12 months.</p> |
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This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

The sponsor had no comment.