

## **7.15 DARUNAVIR + COBICISTAT** **darunavir 800 mg + cobicistat 150 mg tablet, 30** **Prezcobix®, Janssen-Cilag Australia Pty Ltd**

### **1 Purpose of Application**

- 1.1 Re-submission to request Section 100 (Highly Specialised Drugs Program) Authority Required (STREAMLINED) listing for the treatment of HIV infection in combination with other antiretroviral agents in patients who are antiretroviral treatment naïve or in patients who are treatment experienced with no darunavir resistance associated mutations.

### **2 Requested listing**

- 2.1 The minor resubmission requested Section 100 Highly Specialised Drugs Program Community Access Authority Required (streamlined) listing for both treatment-naïve and treatment-experienced HIV patients, consistent with currently listed treatments. see Table 1 below.

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

### **3 Background**

- 3.1 The November 2015 submission was made under the TGA/PBAC Parallel Process. The darunavir/cobicistat FDC received TGA approval and was registered on the ARTG on 24 September 2015.
- 3.2 The TGA approved indications for the darunavir/cobicistat FDC in combination with other antiretroviral agents is for the treatment of HIV-1 infection in:
- antiretroviral treatment-naïve adult patients;
  - antiretroviral treatment-experienced adult patients with no darunavir resistance associated mutation and who have plasma HIV-1 ribonucleic acid (RNA) <100,000 copies/mL; and
  - antiretroviral treatment-experienced but HIV-1 protease inhibitor-naïve adult patients for whom HIV-1 genotype testing is unavailable.
- 3.3 This item was considered and rejected by the PBAC at its November 2015 meeting. The PBAC rejected the request to list darunavir/cobicistat fixed-dose combination (FDC) tablets for the treatment of human immunodeficiency virus (HIV) on the basis that the submission incorrectly proposed treatment in treatment-experienced patients while the evidence presented for clinical efficacy and safety also supported use in treatment naïve patients. The PBAC noted that the submission's proposed listing was also not consistent with the current Australian treatment guidelines.

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**Table 1: Summary of changes in this minor resubmission for the darunavir + cobicistat FDC**

	Previous major submission	This minor resubmission
TGA approval	Submission was lodged under the TGA/PBAC parallel process. The darunavir + cobicistat FDC was undergoing evaluation by the TGA.	The darunavir + cobicistat FDC was registered on the ARTG on 24 September 2015 for treatment naïve and treatment experienced HIV patients.
Proposed PBS restriction	Section 100 Highly Specialised Drugs Program for the treatment of HIV infection in combination with other antiretroviral agents in patients who have experienced virological failure (viral load > 400 copies/mL) or clinical failure or genotypic resistance after at least one antiretroviral regimen and have no darunavir resistance-associated mutations.	Section 100 Highly Specialised Drugs Program Community Access for the treatment of HIV infection in combination with other antiretroviral agents in patients who are antiretroviral treatment naïve or have previously received PBS-subsidised therapy for HIV infection.  The proposed PBS restriction is consistent with the TGA approved indication and the August 2015 Australian Commentary on the US HIV treatment guidelines. In the treatment-naïve listing, the Secretariat proposed the clinical criterion: 'The treatment must not be in combination with ritonavir', as proposed in the treatment-experienced listing. This change was supported by the sponsor in the pre-PBAC response.
Comparator	<u>Primary clinical and economic comparator:</u> Darunavir 800 mg co-administered with ritonavir 100 mg.  <u>Secondary comparator:</u> the FDC components, darunavir + cobicistat taken concomitantly.	<u>Primary clinical and economic comparator:</u>  <i>For treatment experienced patients:</i> Darunavir 800 mg co-administered with ritonavir 100 mg (no change).  <i>For treatment naïve patients:</i> Atazanavir 300 mg co-administered with ritonavir 100 mg.  <u>Secondary comparator:</u> the FDC components, darunavir + cobicistat taken concomitantly (no change).  At the November 2015 PBAC meeting, the PBAC considered darunavir + ritonavir the appropriate comparator in HIV treatment experienced patients (5.04 Darunavir/cobicistat Public Summary Document (PSD), November 2015, para 7.3). As such, this comparator remains unchanged in the minor resubmission. <i>The PBAC agreed with ESC that darunavir/cobicistat could be used in place of other protease inhibitors (PI) such as lopinavir/ritonavir FDC and atazanavir plus ritonavir (or cobicistat) taken concomitantly in those whom PI-based therapy is preferred (para 7.7, Nov 2015 PSD)</i>
Clinical evidence	The submission presented the best (and all) available evidence for the darunavir 800 mg + cobicistat combination, which includes: <ul style="list-style-type: none"> <li>• a randomised bioequivalence study (Study 1003) comparing the darunavir + cobicistat FDC with its components taken concomitantly,</li> <li>• a randomised relative bioavailability study (Study 1001) comparing the darunavir + cobicistat FDC with darunavir 800 mg + ritonavir taken concomitantly, and</li> <li>• a single arm efficacy and safety study of darunavir 800 mg + cobicistat taken</li> </ul>	No new data for the darunavir + cobicistat FDC is presented in this minor resubmission as no additional data, beyond what has previously been supplied, are available.

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	Previous major submission	This minor resubmission
	concomitantly (Study 0130). An unadjusted non-randomised comparison of darunavir 800 mg + cobicistat with the darunavir 800 mg + ritonavir treatment arms of four randomised controlled trials was presented.	

Source: Table 1.9 from Page 3 of the March 2016 minor submission

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

### 4 Clinical place for the proposed therapy

- 4.1 Darunavir is a protease inhibitor (PI), while cobicistat is a pharmacokinetic enhancer of protease inhibitors, with no detectable antiretroviral activity. It is used in the treatment of HIV infection.
- 4.2 The current Australian Commentary to the US Department of Health and Human Services Guidelines for the use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents (August 2015), which lists darunavir/ritonavir (with tenofovir disoproxil fumarate/emtricitabine) as a recommended regimen and darunavir/cobicistat (with tenofovir disoproxil fumarate/emtricitabine or abacavir/lamivudine) as an alternative option in first line therapy for treatment naïve patients.
- 4.3 Darunavir and ritonavir taken concomitantly is a second-line treatment for patients with HIV infection who have experienced virological or clinical failure (treatment experienced). The place in therapy for darunavir/cobicistat FDC was also proposed to be the same as, darunavir and ritonavir taken concomitantly.

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

### 5 Comparator

- 5.1 The two main comparators for treatment-experienced patients have remained unchanged in the minor resubmission:
  - Darunavir 800 mg co-administered with ritonavir 100 mg
  - Darunavir and cobicistat taken concomitantly. Cobicistat is not listed on the PBS. The PBAC accepted these as the appropriate comparators.
- 5.2 The minor resubmission nominated atazanavir 300 mg co-administered with ritonavir 100 mg as the comparator for treatment-naïve patients. The minor resubmission states this is the most commonly prescribed protease inhibitor and is the therapy most likely to be replaced by the darunavir + cobicistat FDC as a first line therapy in treatment naïve patients.

*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 No new clinical trials were presented in the resubmission. The resubmission claimed that there is no additional data available for the FDC including no direct head-to-head studies or studies that can be used in an indirect comparison with other HIV medicines (such as providing a comparison between darunavir/cobicistat FDC and alternative FDCs in the first line setting).
- 6.4 The November 2015 submission presented evidence from two pharmacokinetic studies in healthy volunteers, where darunavir/cobicistat FDC was compared to darunavir and ritonavir (Study 1001), and to its components taken concomitantly (Study 1003).
- 6.5 The submission also presented a naïve indirect comparison of one non-randomised study with darunavir and cobicistat (Study 0130), to single arms of four randomised trials with darunavir and ritonavir (ARTEMIS; ODIN; FLAMINGO and 2LADY).
- 6.6 The submission used the pharmacokinetics evidence for darunavir/cobicistat FDC as a link to the clinical evidence provided on efficacy and safety on darunavir and cobicistat versus darunavir and ritonavir, the main comparator. Table 2 summarises the evidence provided in the November 2015 submission.

**Table 2: Evidence provided in the November 2015 submission**

Studies	Proposed drug	Common reference <sup>a</sup>	Main comparator	Other arms	Population
<b>Pharmacokinetics evidence</b>					
Study 1001	DRV/c FDC	—	DRV + r	—	Healthy volunteers
Study 1003	DRV/c FDC	DRV + c	—	—	
<b>Efficacy and Safety evidence</b>					
Study 0130	—	DRV + c <sup>b</sup>	—	—	Naïve/experienced
ARTEMIS	—	—	DRV + r + TDF + FTC	LPV/r FDC + TDF + FTC	Tx-naïve
ODIN	—	—	DRV + r + ≥ 2 NRTIs <sup>c</sup>	DRV (600 mg) + r + NRTIs	Tx-experienced
FLAMINGO	—	—	DRV + r + 2 NRTIs <sup>d</sup>	DTG + 2 NRTIs	Tx-naïve
2LADY	—	—	DRV + r + TDF + FTC	LPV/r FDC + TDF + FTC	Tx-experienced

Source: compiled during the November 2015 evaluation

FDC = fixed-dose combination; HIV = human immunodeficiency virus; NRTI = nucleoside/nucleotide reverse transcriptase inhibitors; ABC = abacavir; c = cobicistat; DRV = darunavir; DTG = dolutegravir; FTC = emtricitabine; LPV = lopinavir; r = ritonavir; TDF = tenofovir disoproxil fumarate; Tx = treatment; 3TC = lamivudine

<sup>a</sup> The common reference was also the supportive comparator

<sup>b</sup> Plus 2 NRTIs

<sup>c</sup> Emtricitabine and tenofovir disoproxil fumarate took up nearly all NRTI usage

<sup>d</sup> 66.9% was TDF + FTC and 33.1% was ABC/3TC

- 6.7 No new data was presented in the submission on the comparison of darunavir with cobicistat versus atazanavir with ritonavir.
- 6.8 The PBAC noted the outcomes of the ACTG 5257 study (ClinicalTrials.gov Identifier: NCT00811954). The Phase 3, randomized, open label trial of treatment naïve patients included treatment arms of 300 mg of atazanavir with 100 mg of ritonavir both once daily (ritonavir-boosted atazanavir) and 800 mg of darunavir with 100 mg of ritonavir both once daily (ritonavir-boosted darunavir) each with a fixed-dose combination of 300 mg of tenofovir plus 200 mg of emtricitabine (Lennox et al, Ann Intern Med. 2014 Oct 7;161(7):461-71) . The cumulative probability difference of first virologic failure by week 96 between ritonavir-boosted atazanavir and ritonavir-boosted darunavir was reported to be -2.2% (97.5% CI -6.7 to 2.3%).

***Clinical claim***

- 6.9 Based from the pharmacokinetic evidence presented in November 2015, the PBAC considered that the claim of non-inferior comparative effectiveness and safety against darunavir and cobicistat taken concomitantly was reasonable.
- 6.10 Based from the pharmacokinetic evidence presented above in November 2015, the PBAC considered that the claim of non-inferior comparative effectiveness and safety against darunavir and ritonavir taken concomitantly was reasonable.
- 6.11 The PBAC noted the results of the ACTG 5257 study and that at the November 2015; the PBAC agreed there appears to be no difference in benefits and harms between darunavir/cobicistat FDC and darunavir plus cobicistat or ritonavir. The PBAC, despite the limitations of the comparison, considered it was reasonable to conclude that darunavir/cobicistat FDC would provide the same clinical benefits as ritonavir-boosted atazanavir.

***Economic analysis***

- 6.12 The submission presented a cost-minimisation analysis (CMA). Prices used in the cost minimisation have been updated to reflect the S100 HSD Community Access prices for HIV medicines.
- 6.13 The equi-effective doses were estimated as:  
For treatment experienced patients:
- darunavir 800 mg (with cobicistat 150 mg in the FDC) once daily is equivalent to darunavir 800 mg (with ritonavir 100 mg taken concomitantly) once daily; and
  - cobicistat 150 mg (in the FDC) once daily is equivalent to ritonavir 100 mg (with darunavir 800 mg) once daily.
- For treatment naïve patients:
- darunavir 800 mg + cobicistat 150 mg FDC to atazanavir 300 mg co-administered with ritonavir 100 mg
- 6.14 A weighted cost minimisation analysis has been conducted, based upon these equi-effective doses:

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- 6.15 For the purpose of calculating a weighted price for the darunavir + cobicistat FDC, the cost-minimisation assumes that █% of patients treated with the darunavir + cobicistat FDC are treatment naïve and █% are treatment experienced.
- 6.16 The resubmission presented the outcomes of an analysis of a 10% sample of PBS data that was used to determine the proportion of atazanavir patients who are treatment naïve (i.e receiving atazanavir as their first HIV therapy) and treatment experienced (i.e have previously received a different HIV therapy). This analysis showed 41.2% of atazanavir patients are treatment naïve upon initiation and 58.8% are treatment experienced. The resubmission proposed that the likely uptake of the darunavir + cobicistat FDC in treatment naïve patients will be lower than atazanavir, and considered that █% is a reasonable estimate of treatment naïve patients.
- 6.17 The CMA was calculated at the Commonwealth Expenditure level (DPMQ less average co-pay), while Department’s usual method is at the ex-manufacturer level.

**Table 3: Cost minimisation results**

Drug	Max Quantity (tablets)	Tablets /day	Days of supply per DPMQ	Commonwealth expenditure (DPMQ less avg co-payment) / 2 months
<b>Darunavir 800 mg + cobicistat 150 mg FDC cost minimised to darunavir 800 mg co-administered with ritonavir</b>				
Darunavir 800 mg	60	1	60	\$ █
Ritonavir 100 mg	720	1	720	\$ █
Total Commonwealth Expenditure				\$ █
Darunavir 800 mg + cobicistat 150 mg FDC	60	1	60	\$ █
<b>Darunavir 800 mg + cobicistat 150 mg FDC cost minimised to atazanavir 300 mg co-administered with ritonavir</b>				
Atazanavir 150 mg (0.94% of services)	120	2	60	\$ █
Atazanavir 300 mg (99.06% of services)	60	1	60	\$ █
Ritonavir 100 mg	720	1	720	\$ █
Total Commonwealth Expenditure (weighted by services)				\$ █
Darunavir 800 mg + cobicistat 150 mg FDC	60	1	60	\$ █

Source: Table 1.5 of the submission. DPMQ = dispensed price maximum quantity; FDC = fixed dose combination. Please refer to Sheet 'CMin Calculations', Darunavir FDC Section D cost Minimisation.xls in Appendices

- 6.18 Assuming a treatment naïve weighting of █%, the proposed approved ex-manufacturer price is \$681.65 (i.e. █% at \$ █ and █% at \$ █), with a DPMQ of \$1,410.24.

- 6.19 The comparators, including darunavir, ritonavir and atazanavir will have a statutory 5% price reduction, effective on 1 April 2016.

**Estimated PBS usage & financial implications**

- 6.20 The resubmission estimates that, at the price proposed, the financial implications to the PBS and RPBS of listing darunavir with cobicistat are as follows:

**Table 4: Overall net cost to the PBS/RPBS over the first five years of PBS listing**

	Year 1	Year 2	Year 3	Year 4	Year 5
If DRV + COBI FDC is listed	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
If DRV + COBI FDC is not listed	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
<b>INCREMENTAL PBS/RPBS NET COST OF LISTING DRV + COBI FDC</b>	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

DRV = darunavir; COBI = cobicistat; FDC = fixed dose combination. Table 1.8 of the resubmission.

- 6.21 The financial estimates in minor resubmission have been updated to include the amended proposed price and replacement of atazanavir + ritonavir in treatment-naïve patients, while assumptions around replacement of darunavir 800 mg + ritonavir remains consistent with previous submission.
- 6.22 The incremental Commonwealth Government health budget impact of listing the darunavir + cobicistat FDC on the PBS is less than \$10 million in Year 1, increasing to less than \$10 million in Year 5, driven by the loss of patient co-payments associated with ritonavir.

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

**7 PBAC Outcome**

- 7.1 The PBAC recommended the Section 100 Highly Specialised Drugs Program (HSD) listing of darunavir with cobicistat fixed dose combination for the treatment of HIV. The PBAC recommended the special arrangements under the HSD Community Access Program, Authority Required (STREAMLINED).
- 7.2 The PBAC recommended the listing of darunavir with cobicistat on a cost-minimisation basis with atazanavir plus ritonavir provided concomitantly in the treatment naïve setting and darunavir plus ritonavir provided concomitantly in the treatment experience setting. The equi-effective doses are: darunavir 800 mg with cobicistat 150 mg in the FDC once daily is equivalent to darunavir 800 mg with ritonavir 100 mg taken concomitantly once daily (treatment experienced patients); and darunavir 800 mg + cobicistat 150 mg in the FDC once daily is equivalent to atazanavir 300 mg with ritonavir 100 mg taken concomitantly once daily (treatment naïve patients).

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- 7.3 The PBAC considered that this resubmission proposed a listing for darunavir/cobicistat which reflects the status of darunavir as the preferred protease inhibitor for use in treatment naïve patients in the most recent US Department of Health and Human Services Guidelines for the use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents (August 2015). Overall, the PBAC considered the listing of the darunavir with cobicistat FDC in treatment naïve and treatment experience settings was appropriate.
- 7.4 The PBAC noted that TGA-approved indication for treatment-experienced patients for the darunavir + cobicistat FDC and the darunavir 800 mg (with ritonavir) requires patients to have no darunavir resistance-associated mutations. The sponsor proposed a NOTE: Patient must not have demonstrated darunavir resistance-associated mutations detected on resistance testing, which the Secretariat suggested to be an Administrative Advice. While the PBAC agreed with the sponsor that this Administrative Advice should only appear in the listing for treatment-experienced patients for consistency with the TGA approved indication, the PBAC recommended that this NOTE may not be required as clinicians experienced in prescribing antiretroviral treatments would select the best treatment regimen for the specific patient circumstances.
- 7.5 The PBAC recalled that the Committee accepted in November 2015 the two nominated comparators, darunavir and ritonavir, taken concomitantly and darunavir and cobicistat, taken concomitantly. The PBAC accepted atazanavir 300 mg co-administered with ritonavir 100 mg as the main comparator in treatment-naïve setting. The PBAC recalled that atazanavir with cobicistat FDC was recommended at the November 2015 meeting and could be considered an appropriate comparator also.
- 7.6 Based on the evidence presented in the November 2015 submission, the PBAC recalled there appears to be no difference in benefits and harms between darunavir with cobicistat FDC and darunavir plus cobicistat or ritonavir. The PBAC acknowledged the limited evidence available to compare the darunavir with cobicistat FDC and atazanavir with ritonavir taken concomitantly in treatment naïve patients. Though not identified in the submission, the PBAC considered that the ACTG 5257 study, taken together with the submitted pharmacokinetic data from Study 1001, supported a view that darunavir with cobicistat FDC would provide, on balance, the same clinical benefits as ritonavir-boosted atazanavir.
- 7.7 The PBAC noted the cost-minimisation analysis provided in the resubmission and the proposed weighting between treatment naïve and treatment experienced patients which was numerically different to the analysis of patients using atazanavir provided in the resubmission. While the PBAC did not accept the reasoning in the submission, the PBAC considered that the assumption that 30% of patients treated with the darunavir + cobicistat FDC are treatment naïve and 70% are treatment experienced was likely to be realised in clinical practice.
- 7.8 At the November 2015 meeting, the PBAC agreed with ESC that darunavir/cobicistat could be used in place of other protease inhibitors (PI) such as lopinavir/ritonavir FDC and atazanavir plus ritonavir (or cobicistat) taken concomitantly in those whom PI-based therapy is preferred and that this could potentially increase the estimated

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net cost. The PBAC noted that utilisation of the FDC was updated in resubmission to reflect the proposed listing in both treatment naïve and experience patients. The financial impact was appropriately greater compared to the November 2015 submission where utilisation only in treatment experience patients were the basis of the estimates.

- 7.9 The PBAC recommended that the Early Supply Rule should apply to darunavir with cobicistat FDC, as recommended for all HIV treatments at the November 2015 meeting.
- 7.10 The PBAC advised that Section 100 medicines are currently considered out of scope for prescribing by nurse practitioners.
- 7.11 In accordance with subsection 101(3BA) of the Act, the PBAC advised that it is of the opinion that darunavir with cobicistat should not be treated as interchangeable on an individual patient basis with other antiretroviral therapies.

**Outcome:**

Recommended

**8 Recommended listing**

8.1 Add new item:

Name, Restriction, Manner of administration and form	Max. Qty Packs	Max. Qty Units	No. of Rpts	Proprietary Name and Manufacturer	
DARUNAVIR 800 mg + COBICISTAT 150 mg oral tablet, 30	2	60	5	Prezcobix	Janssen-Cilag Pty Ltd

***Treatment-naive***

<b>Category / Program</b>	Section 100 – Highly Specialised Drugs Program (Community Access)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Episodicity:</b>	
<b>Severity:</b>	
<b>Condition:</b>	Human immunodeficiency virus (HIV) infection
<b>PBS Indication:</b>	HIV Infection
<b>Treatment phase:</b>	Initial
<b>Restriction Level / Method:</b>	<input checked="" type="checkbox"/> Streamlined

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<b>Clinical criteria:</b>	<p>Patient must be antiretroviral treatment naive,</p> <p>AND</p> <p>The treatment must be in combination with other antiretroviral agents;</p> <p>AND</p> <p>The treatment must not be in combination with ritonavir</p>
<b>Administrative Advice:</b>	<p>NOTE:</p> <p>The cobicistat component of the darunavir + cobicistat combination product provides the necessary pharmacokinetic enhancement of darunavir to achieve therapeutic levels of darunavir.</p>

<b>Category / Program</b>	Section 100 – Highly Specialised Drugs Program (Community Access)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Episodicity:</b>	
<b>Severity:</b>	
<b>Condition:</b>	Human immunodeficiency virus (HIV) infection
<b>PBS Indication:</b>	HIV Infection
<b>Treatment phase:</b>	Continuing
<b>Restriction Level / Method:</b>	<input checked="" type="checkbox"/> Streamlined
<b>Clinical criteria:</b>	<p>Patient must have previously received PBS-subsidised therapy for HIV infection,</p> <p>AND</p> <p>The treatment must be in combination with other antiretroviral agents;</p> <p>AND</p> <p>The treatment must not be in combination with ritonavir</p>
<b>Administrative Advice:</b>	<p>NOTE:</p> <p>The cobicistat component of the darunavir + cobicistat combination product provides the necessary pharmacokinetic enhancement of darunavir to achieve therapeutic levels of darunavir.</p>

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**Treatment-experienced**

<b>Category / Program</b>	Section 100 – Highly Specialised Drugs Program (Community Access)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Episodicity:</b>	
<b>Severity:</b>	
<b>Condition:</b>	Human immunodeficiency virus (HIV) infection
<b>PBS Indication:</b>	HIV infection
<b>Treatment phase:</b>	-
<b>Restriction Level / Method:</b>	<input checked="" type="checkbox"/> Streamlined
<b>Clinical criteria:</b>	The treatment must be in addition to optimised background therapy, AND The treatment must be in combination with other antiretroviral agents; AND The treatment must not be in combination with ritonavir, AND Patient must have experienced virological failure or clinical failure or genotypic resistance after at least one antiretroviral regimen,
<b>Prescriber Instruction:</b>	Virological failure is defined as a viral load greater than 400 copies per mL on two consecutive occasions, while clinical failure is linked to emerging signs and symptoms of progressing HIV infection or treatment-limiting toxicity.
<b>Administrative Advice:</b>	NOTE: The cobicistat component of the darunavir + cobicistat combination product provides the necessary pharmacokinetic enhancement of darunavir to achieve therapeutic levels of darunavir.

**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.