5.03 DOLUTEGRAVIR with RILPIVIRINE
Tablet containing dolutegravir 50 mg with rilpivirine 25 mg, Juluca®,
ViiV Healthcare Pty Ltd

Preface

To improve the readability of this document, brand names are generally used to identify fixed dose combination (FDC) antiretroviral products. Where the form of the drug within a brand is described, the minutes use the Australian Medicines Terminology medicinal product unit of use (MPUU).

1 Purpose of Application

1.1 Section 100 (Highly Specialised Drugs Program – Community Access) listing for dolutegravir/rilpivirine fixed dose combination (Juluca) for treatment of virologically suppressed human immune deficiency virus (HIV) infected patients. This is the first submission for Juluca.

1.2 The listing was requested on the basis of a cost-minimisation analysis against the individual components dolutegravir and rilpivirine (DTG+RPV; primary comparator) and a basket of comparators (secondary comparator). Table 1 summarises the key components of the clinical issue addressed by the submission.

Table 1: Key components of the clinical issue addressed by the submission

Component	Description
Population	Virologically suppressed HIV patients
Intervention	One tablet daily of fixed dose combination tablet containing dolutegravir 50mg with rilpivirine 25mg (DTG/RPV FDC), taken with food
Comparator	Primary: dolutegravir 50mg plus rilpivirine 25 mg, taken concomitantly (DTG+RPV) Secondary: basket of comparators that references relevant treatments used in switch populations (EVG/c/FTC/TAF, DTG+FTC/TAF, RPV/FTC/TAF, DTG/ABC/3TC, RAL+FTC/TAF, DTG+RPV)
Outcomes	Proportion of patients who maintain virological suppression (HIV-1 RNA <50c/mL)
Clinical claim	In virologically suppressed patients with HIV, the DTG/RPV FDC is bioequivalent to dolutegravir plus rilpivirine (DTG+RPV) taken concomitantly, and is as effective as a basket of comparator HIV medicines at maintaining virological suppression following treatment switch.

Source: Table 1, p15 of the submission.
3TC = lamivudine; ABC = abacavir; DTG = dolutegravir; EVG/c = elvitegravir with cobicistat; FTC = emtricitabine; RPV = rilpivirine; TAF = tenofovir alafenamide

2 Requested listing

Name, restriction, manner of administration, form	Max. Qty (packs)	Max. Qty (units)	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
Dolutegravir 50mg (as sodium) with rilpivirine 25mg (as hydrochloride), tablets, 30	2	60	5	$[redacted]	Juluca® ViiV Healthcare

Episodicity:	Chronic
Severity:	
Condition:	HIV infection
PBS Indication:	Chronic HIV infection
Treatment phase:	Initial and Continuing
Restriction:	☐ Restricted benefit ☐ Authority Required - In Writing ☐ Authority Required - Telephone ☐ Authority Required – Emergency ☐ Authority Required - Electronic ☒ Streamlined
Treatment criteria:	Patients must be virologically suppressed on a previous HIV regimen prior to treatment initiation

Source: Table 16 and Table 17, p36 and 37 of the submission.
mg = milligram

Secretariat suggested wording for the restriction:

Suggestions and additions proposed by the Secretariat to the requested listing are added in italics and suggested deletions are crossed out with strikethrough.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
DOLUTEGRAVIR WITH RILPIVIRINE Tablet containing dolutegravir 50 mg (as sodium) with rilpivirine 25 mg (as hydrochloride), 30	2	5	$[redacted]	Juluca®	Viiv Healthcare Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Community Access)
Prescriber type:	☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐ Midwives
Episodicity:	~~Chronic~~
Condition:	HIV infection
PBS Indication:	HIV infection
Treatment phase:	Initial
Restriction Level / Method:	☐ Restricted benefit ☐ Authority Required - In Writing ☐ Authority Required - Telephone ☐ Authority Required - Emergency ☐ Authority Required - Electronic ☒ Streamlined

Treatment criteria:	Patient must be *stable and* virologically suppressed on ~~previous~~ *current* HIV *treatment regimen for at least 6 months* ~~prior to treatment initiation.~~
Clinical criteria:	*The treatment must be the sole PBS subsidised therapy for this condition.*

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
DOLUTEGRAVIR WITH RILPIVIRINE Tablet containing dolutegravir 50 mg (as sodium) with rilpivirine 25 mg (as hydrochloride), 30	2	5	$[redacted]	Juluca®	Viiv Healthcare Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Community Access)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Episodicity:	~~Chronic~~
Condition:	HIV infection
PBS Indication:	HIV infection
Treatment phase:	Continuing
Restriction Level / Method:	☐Restricted benefit ☐Authority Required - In Writing ☐Authority Required - Telephone ☐Authority Required - Emergency ☐Authority Required - Electronic ☒Streamlined
Clinical criteria:	*Patient must have previously received PBS-subsidised therapy with this drug for this condition* *AND* *The treatment must be the sole PBS-subsidised therapy for this condition.*

2.1 No special pricing arrangement was proposed.

2.2 The Secretariat proposed alternative restriction wording to align the restriction with the clinical evidence and likely conditions of TGA registration, and divided the requested listing into initial and continuing restrictions to reflect differences in the initiation and continuation criteria, consistent with other ART regimens for HIV infection. The Pre-Sub-Committee Response (PSCR) agreed with the Secretariat proposal to split the restriction into initial and continuing restrictions, and the addition of the requirement that patients be stable on prior therapy for at least 6 months before switching to DTG/RPV, consistent with the proposed TGA indication.

2.3 The PSCR acknowledged the criterion 'The treatment must be the sole PBS-subsidised therapy for this condition' was proposed by the Secretariat to ensure that DTG/RPV is prescribed as a standalone regimen, as per the SWORD clinical data. However, the PSCR stated that there may be a very small group of highly experienced patients who are currently taking DTG and RPV as part of a multi-drug

salvage regimen. The PSCR argued that DTG/RPV simplifies their complex treatment regimen and it would be inequitable to exclude this very small group of patients from access to the FDC DTG/RPV, however agreed it would be amenable to this addition if considered appropriate by the PBAC. The PBAC considered it would be appropriate to include this criterion to ensure the listing was consistent with the clinical evidence which used DTG/RPV as a standalone therapy.

3 Background

Registration status

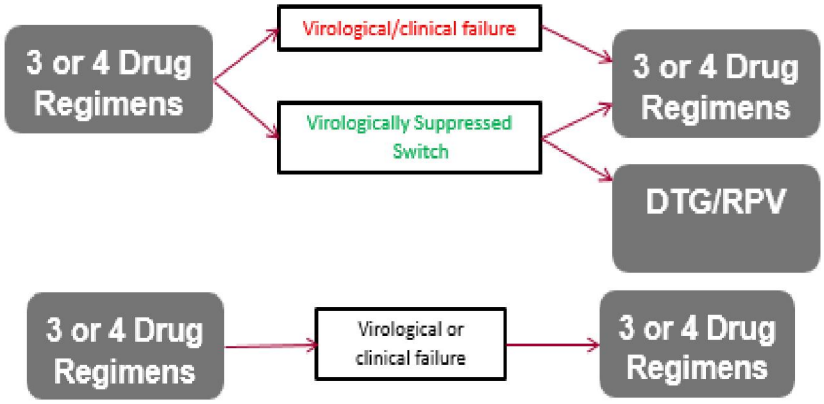
3.1 The submission was made under TGA/PBAC Parallel Process. TGA status at time of PBAC consideration: Juluca was TGA registered on 20 June 2018.

4 Population and disease

4.1 The human immunodeficiency virus (HIV) infects cells of the immune system, destroying or impairing their function. As the infection progresses, the immune system becomes weaker and the infected person becomes more susceptible to infections. HIV infection can progress to acquired immunodeficiency syndrome (AIDS), which leads to complications, opportunistic infections and death.

4.2 The submission noted that the PBAC has previously accepted the treatment algorithm to be linear. When a patient fails treatment due to virological or clinical failure they progress to another three or four drug regimen. The submission considered that this algorithm does not recognise the large proportion of switches due to issues such as toxicity, avoidance of drug-drug interactions (DDIs) or comorbidities ('virologically suppressed' switch group). The submission stated that this patient group is fundamentally different to those experiencing 'clinical failure' as previously defined by the PBAC.

Figure 1: Proposed clinical management algorithm



Source: Figure 2, p33 of the submission.

4.3 While the submission was correct in noting that previously the PBAC had primarily considered treatment switches on the basis of virological failure, it was indicated this was the first two-drug FDC to support those patients virologically suppressed and clinically appropriate for switching. The submission suggested the listing of Juluca would significantly change the clinical management of HIV patients however, this should be tempered by, firstly, the fact the individual components of the fixed dose combination are already PBS-listed; and secondly, existing PBS-listed regimens are currently being switched for reasons other than virological failure. The PSCR reiterated that Juluca was the first regimen indicated solely for use in virologically-suppressed patients only and could change the clinical management of HIV patients as current use of concomitant DTG and RPV is off-label in Australia and the SWORD studies represents the first extensive randomised controlled trials to support use of this regimen.

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

5 Comparator

5.1 The submission nominated the individual components (dolutegravir 50mg and rilpivirine 25mg, taken concomitantly) as the primary comparator. The main argument provided in support of this nomination was that the use of a two drug regimen containing dolutegravir and rilpivirine was incorporated in the clinical guidelines in October 2017, recommending that the combination of dolutegravir and rilpivirine is 'a reasonable option when the use of nucleoside reverse transcriptase inhibitors (NRTIs) is not desirable and when resistance to either DTG or RPV is not expected' (DHHS guidelines).

5.2 The submission nominated a basket of comparators as the secondary comparator. The rationale for the basket of comparators was that the selection of a single comparator that reflects the 'market leader' for this specific patient population (i.e. virologically suppressed patients) would be flawed and would not reflect the variability in patient needs and prescriber decision making. The submission argued that, alternatively, a basket of comparators that accounts for the heterogeneous nature of HIV treatment switch more accurately captures diverse patient treatment requirements.

5.3 The PSCR argued that if necessary to nominate a single 'most appropriate' comparator, that ODEFSEY® (rilpivirine + tenofovir alafenamide + emtricitabine) was the most appropriate as it is also an RPV based regimen and the majority of its use is the result of treatment switches from other regimens, most frequently tenofovir disoproxil fumarate (TDF) containing regimens.

5.4 The submission excluded three classes of comparators in the SWORD trials from the basket of comparators. These were TDF-, efavirenz- and nevirapine- containing regimens. The submission's reasoning for these exclusions was that they were not represented in the *Australian* switch population due to low utilisation owing to an

inferior safety profile according to ASHM. The submission also stated that this is validated by the Expert opinion provided in Appendix A to the submission.

5.5 The submission stated that boosted PI regimens are considered second line treatments in Australian HIV guidelines. These treatments are represented to a small degree (<3% for any regimen) in treatment switch patients. These treatments are used primarily in cases of virological failure- a population for which Juluca is not indicated.

5.6 The PBAC noted that a non-exhaustive list of relevant regimens from these excluded classes is as follows:

- TDF/emtricitabine/efavirenz (ATRIPLA® DPMQ: *$1,709.43*);
- TDF/emtricitabine/elvitegravir + cobicistat (STRIBILD® DPMQ: $1,784.25); and
- TDF/emtricitabine/rilpivirine (EVIPLERA® DPMQ: $1,784.25)

5.7 The submission relied on expert opinion for rationale behind excluding these comparators, the expert opinions generally agreed that TDF regimens would not be switched to Juluca due to the availability of TAF regimens, that switching to efavirenz regimens was not preferred to other options and that darunavir regimens would only be switched to for specific reasons (adherence issues, possibly for planning pregnancy, complex resistance profile).

5.8 At the March 2018 meeting, the PBAC considered a submission for a fixed dose combination tablet containing bictegravir with emtricitabine and tenofovir alafenamide, for the treatment of patients with HIV infection.

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.

Consumer comments

6.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

6.3 The submission was based on:

- one bioequivalence study comparing the DTG/RPV FDC to DTG+RPV, Study 201676 (N= 118), and
- two head to head trials comparing dolutegravir and rilpivirine taken concomitantly (DTG+RPV) to remaining on current antiretroviral (CAR) therapy, the SWORD 1 & 2 trials; N = 508 and 516, respectively;

- a sub study to the SWORD 1 & 2 trials (DEXA; N = 102).

The submission also included several non-randomised studies as supplementary evidence.

6.4 Details of the trials presented in the submission are provided in Table 2.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Key Randomised trials		
SWORD 1 & 2	A Phase III, randomized, multicentre, parallel group, non-inferiority study evaluating the efficacy, safety and tolerability of switching to dolutegravir plus rilpivirine from current INI-, NNRT- or PI-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed. 48 week results. 3 May 2017. 2016N287382_00.	3 May 2017
	A Phase III, randomized, multicentre, parallel group, non-inferiority study evaluating the efficacy, safety and tolerability of switching to dolutegravir plus rilpivirine from current INI-, NNRT- or PI-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed. 48 week results. 3 May 2017. 2016N287539_00	3 May 2017
	Llibre JM et al.. Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies.	The Lancet. 2018.
	Llibre JM et al.. Phase III sword 1&2: Switch to DTG+RPV maintains virologic suppression through 48 wks.	Topics in Antiviral Medicine 2017. 25:1 Supplement 1 (19s-20s)
DEXA* (SWORD sub-study)	An Evaluation of Bone Mineral Density in HIV-1-Infected Adult Subjects Switching from a Tenofovir-Containing Antiretroviral Therapy Regimen to a Dolutegravir plus Rilpivirine Regimen. 48 week results.	3 May 2017
202094	An Open-label, Randomized, Two-way Crossover, Single dose, Pivotal Bioequivalence Study of a Fixed-dose Combination of Dolutegravir and Rilpivirine in Healthy Volunteers	22 March 2017.
Supplementary evidence:		
Capetti 2016	Capetti, A. et al.. Switch to Dolutegravir plus Rilpivirine Dual Therapy in cART-Experienced Subjects: An Observational Cohort.	PLOS ONE, 2016; 11(10), p.e0164753..
Capetti 2016	Capetti, A. et al. Dolutegravir plus rilpivirine in cART-experienced subjects: an observational cohort.	J Int AIDS Soc 2016; 19(suppl 7), p.81.
Palacios 2016	Palacios, R., Mayorga, M. & González-Domenech, C.-M. Safety and efficacy of dolutegravir plus rilpivirine (DTG/RPV) in treatment-experienced HIV-infected patients: preliminary results at 24 weeks of the DORIVIR study.	J Int AIDS Soc, 2016 19(suppl 7): 54.
Gantner 2017	Gantner, P. et al. Efficacy and safety of dolutegravir and rilpivirine dual therapy as a simplification strategy: a cohort study.	HIV Medicine 2017; 18(19): 704–708.
Revuelta-Herrero 2018	Revuelta-Herrero J.L., et al. 2018. Effectiveness, Safety, and Costs of a Treatment Switch to Dolutegravir Plus Rilpivirine Dual Therapy in Treatment-Experienced HIV Patients.	The Lancet 2015; 385(9980): 1873-1883.
Ruiz Martinez 2016	Ruiz Martinez, C et al., 2016. Effectiveness and safety of switching to dual antiretroviral therapy in a treatment experienced HIV cohort. European Journal of Hospital Pharmacy. 23 Supplement 1 (A97).	Annals of Pharmacotherapy 2016; 52(1): 11-18

Trial ID	Protocol title/ Publication title	Publication citation
Gabuvu 2016	Gabuvu C et al., 2016. Dolutegravir-based monotherapy or dual therapy maintains a high proportion of viral suppression even in highly experienced HIV-1-infected patients.	Journal of Antimicrobial Chemotherapy 2016 71(4) : 1046-1050
Togami 2016	Togami H, Kato M, Fukushima N, Hirano A, Imamura J, Hachiya A et al. Treatment outcome for NRTI sparing regimen consisting of dolutegravir and rilpivirine	[abstract] Asia Pacific AIDS and Co-infections Conference (APACC). 2016.
Diaz 2016	Diaz, A. et al., 2016. Dolutegravir plus rilpivirine in suppressed heavily pretreated HIV-infected patients.	In AIDS Conference.
Grabmeier Pfistershammer 2017	Grabmeier-Pfistershammer, K., 2017. Maintenance Therapy with Dolutegravir/Rilpivirine is efficient and well tolerated in a real-life setting.	NR
Saling 2016	Saling, C.F., Szabela, M.E. & Johnson, T., 2016. Dolutegravir 50 mg + Rilpivirine 25 mg (DTG+RPV) Daily in Treatment-Experienced HIV-Infected Patients.	DSA Conference.

Source: Table 20, p43-44 of the submission.

6.5 The key features of the direct randomised trial are summarised in Table 3.

Table 3: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)
Dolutegravir + rilpivirine vs. CAR					
SWORD 1	508	R, MC OL 148 weeks*	Low**	Patients with HIV, virologically suppressed for at least 6 months.	Virological Success and Failure (FDA snapshot)
SWORD 2	516				
DEXA	102	SS; MC; OL 48 weeks	High	SWORD patients receiving TDF containing regimen at screening	Total hip BMD; lumbar spine BMD
Dolutegravir/rilpivirine FDC vs dolutegravir + rilpivirine					
201676	118	R, SC, OL	Low	Patients treated with dolutegravir/rilpivirine or dolutegravir + rilpivirine	Bioequivalence outcomes

BMD = bone mineral density; CAR = current antiretrovirals; DB=double blind; FDA = Food and Drug Administration; HIV = human immunodeficiency virus; MC=multi-centre; OL=open label; R=randomised. SC = single centre; SS = sub study; TDF = tenofovir disoproxil fumarate

* Ongoing- only 48 week data available in CSR form, and 100 week data available as summary results.

** Although open-label, the outcome of virological success or failure was objective

Source: pp 46-51 and pp74-77 the submission

Comparative effectiveness

6.6 The results of Study 201676 showed that for both dolutegravir and rilpivirine, the 90% CIs for the ratios of the adjusted geometric means for Cmax and AUCs, derived using either actual or nominal sampling times, were all fully contained within the bioequivalence limits (0.80, 1.25) and indicated that the FDC tablet formulation of dolutegravir 50mg/rilpivirine 25mg was bioequivalent to the co-administration of the separate tablet formulations of dolutegravir 50 mg + rilpivirine 25 mg. In addition, there was no difference in the median t_{lag} or t_{max} for either dolutegravir or rilpivirine between the FDC tablet formulation of dolutegravir 50mg/rilpivirine 25mg versus co-

administration of the separate tablet formulations of dolutegravir 50 mg + rilpivirine 25 mg.

6.7 Table 4 and Table 5 present the results for the primary outcome of virological success and a key secondary outcome of virological failure from the SWORD trials, respectively.

Table 4: Results of virological suppression success (HIV-1 RNA <50c/mL at Week 48 - ITT-E)

Trial ID	DTG+RPV n/N (%)	CAR n/N (%)	Difference in proportion (95% CI)	Adjusted difference in proportion (95% CI)
Pooled	486/513 (95%)	485/511 (95%)	-0.2 (-2.9, 2.5)	-0.2 (-3.0, 2.5)
SWORD 1	240/252 (95%)	245/256 (96%)	-0.5 (-4.1, 3.2)	-0.6 (-4.3, 3.0)
SWORD 2	246/261 (94%)	240/255 (94%)	0.1 (-3.9, 4.2)	0.2 (-3.9, 4.2)

Source: Table 36, p65 of the submission.
CAR = current antiretroviral; CI = confidence interval; DTG = dolutegravir; ITT=E = intention to treat exposed; n = number of participants with event; N = total participants in group; RPV = rilpivirine

Table 5: Results of virological failure (HIV-1 RNA >50c/mL at Week 48 - ITT-E)

Trial ID	DTG+RPV n/N (%)	CAR n/N (%)	Difference in proportion (95% CI)	Adjusted difference in proportion (95% CI)
Pooled	3/513 (<1%)	6/511 (1%)	-0.5 (-1.7, 0.6)	-0.5 (-1.4, 0.5)
SWORD 1	2/252 (<1%)	2/256 (<1%)	0.0 (-1.5, 1.5)	0.0 (-1.3, 1.4)
SWORD 2	1/261 (<1%)	4/255 (2%)	-1.2 (-2.9, 0.5)	-1.0 (-2.4, 0.5)

Source: Table 38, p66 of the submission.
CAR = current antiretroviral; CI = confidence interval; DTG = dolutegravir; ITT=E = intention to treat exposed; n = number of participants with event; N = total participants in group; RPV = rilpivirine

6.8 The pre-specified non-inferiority margin in each SWORD study for HIV-1 RNA <50c/ML at week 48 was -10%. For the pooled analysis (SWORD 1 and 2) a pre-specified non-inferiority margin of -8% was nominated. The submission noted that the non-inferiority margin of -10 % had been previously accepted by the PBAC (most recently in the Odefsey® Public Summary Document (PSD), July 2016) and was aligned to a 10-12% margin supported by the previous and current FDA guidance on HIV clinical trials for standard design trials (FDA, 2002, FDA, 2015). The submission also noted that a pre-specified non-inferiority margin of -4% for snapshot virological failures at week 48 (the alternative endpoint) was assessed, which was supported by the updated FDA guidance on HIV trials (FDA, 2015).

6.9 Overall, the SWORD trials' selection of primary endpoints and non-inferiority margins was consistent with both regulatory guidance and previous PBAC considerations and were met by the SWORD trials.

6.10 The results indicated that the non-inferiority margins were met for all analyses and outcomes.

Comparative harms

6.11 Table 6 presents a summary of AE data in the SWORD trials and Study 201676.

Table 6: Summary of key adverse events in the randomised trials

Trial ID	DTG+RPV n with event/N (%)	CAR n with event/N (%)
SWORD 1&2		
Any AE	395/513 (77%)*	364/511 (71%)
Drug related AE	97/513 (19%)	9/511 (2%)
AE leading to discontinuation	21/513 (4%)	3/511 (<1%)
Serious AEs	27/513 (5%)	21/511 (4%)
Study 201676	**FDC DTG/RPV**	**DTG + RPV**
Any AE	20/115 (17%)	21/116 (18%)
Headache	5/115 (4%)	2/116 (2%)
Upper respiratory tract infection	2/ 115 (2%)	1/116 (<1%)
Dermatitis contact	1/115 (<1%)	2/116 (2%)
Arthropod bite	2/115 (2%)	0

Source: Tables 41, 42, 43, 44, and 47, pp69-71 and 73 of the submission.
AE = adverse event; CAR = current antiretroviral; CI = confidence interval; DTG = dolutegravir; FDC = fixed dose combination; n = number of participants reporting data; N = total participants in group; RD = risk difference; RPV = rilpivirine; RR = relative risk
*the submission noted that multiple adverse events could be recorded for a single treatment discontinuation, and that in the DTG+RPV arm, 21 adverse events resulted in withdrawal of 17 patients from study. This may suggest that the difference in proportions of AEs leading to discontinuation was somewhat underestimated.

6.12 The TGA evaluator noted that "greater proportions of subjects in DTG + RPV group compared with those in the CAR group reported AEs (77% vs 71%), drug-related AEs (19% vs 2%) and AEs leading to withdrawal (4% vs <1%), which is expected when comparing an open label switch arm to subjects continuing their current tolerated treatment".

6.13 The TGA evaluator noted there was no data beyond the 48 weeks but noted that the SWORD trials were ongoing and that results from the ongoing SWORD trials (up to week 148) should provide information on long term safety of proposed DTG/RPV FDC treatment. Recent 100-week safety data was presented in the submission, which was consistent with the 48 week data.

6.14 The clinical evaluator considered that "Overall, the safety profile seen for DTG + RPV in Studies 201636 and 201637 [SWORD 1 & 2] is consistent with current labelling and the established safety profile for DTG and RPV. There is no predicted additive or synergistic effect on the risk of hepatic disorders, psychiatric AEs, depression or suicide in patients taking the DTG/RPV FDC tablet beyond that expected for the SEs".

6.15 The submission also included a comparison of bone mineral density (BMD) outcomes between SWORD patients who remained on TDF-containing regimens compared to patients who switched from TDF-containing regimens to DTG+RPV (DEXA sub study). Mean change from baseline to week 48 in total hip BMD was greater for subjects in

the DTG+RPV group compared with the CAR group, and that there was almost no change in mean BMD in the total hip in the CAR group. An alternative of the difference between the 2 treatment groups in the percent change from baseline at Week 48 in total hip BMD, using an ANCOVA model adjusted for age at study entry, BMI at baseline and BMD at baseline demonstrated a statistically significant improvement in total hip BMD for the DTG+RPV group. The submission stated that the change in BMD for patients who switched to DTG+RPV from a TDF regimen was numerically comparable to those short-term data noted for TAF containing regimens in comparison to TDF containing regimens. The submission also noted that PBAC had previously acknowledged difference in surrogate bone markers between these treatments but remained uncertain of the clinical relevance of these differences (Genvoya® PSD, November 2015).

6.16 The TGA evaluator made the following comment regarding the DEXA sub study:

> "The number of patients (n=81) evaluated in this DEXA sub study should be mentioned. Furthermore, the long term clinical significance of these changes in BMD is not known. The exploratory endpoint of WHO Fracture Risk Assessment Tool (FRAX) score did not show any difference between the DTG+RPV and CAR groups in the 10-year probability of hip or osteoporotic fracture. The actual incidence of fractures in the sub study was not provided" .

6.17 The submission claimed that patients may switch to Juluca for avoidance of potential long-term toxicities. There is no comparative long-term toxicity evidence for Juluca, and according to the SWORD trials, the various comparators have different but non-inferior toxicity profiles.

Clinical claim

6.18 The submission described Juluca as bioequivalent to DTG+RPV. The TGA has accepted this claim.

6.19 The submission also described Juluca as non-inferior compared to a basket of comparators representative of the current treatment switch landscape in Australian HIV patients. The evaluation considered this claim (assumed to be in regards to comparative effectiveness and comparative safety) was reasonable; however, noted that the SWORD 1&2 trials indicated non-inferiority to current-antiretroviral therapy, including multiple comparators that the submission excluded from the nominated "basket of comparators."

6.20 Additionally, the SWORD trials showed non-inferiority between Juluca and current antiretroviral therapy, suggesting that the claim of non-inferiority did not apply to switch patients specifically, but rather in successfully virologically suppressed patients in general.

6.21 The PBAC considered that the claim of non-inferior comparative effectiveness with alternative therapies was reasonable and supported by the data.

6.22 The PBAC considered that the claim of non-inferior comparative safety with alternative therapies was reasonable and supported by the data.

Economic analysis

6.23 The submission conducted a cost-minimisation analysis against the primary comparator of dolutegravir 50mg + rilpivirine 25mg taken concomitantly, and the secondary comparator of a basket of antiretrovirals.

6.24 For the primary comparator, the submission estimated that one FDC tablet of dolutegravir 50mg/rilpivirine 25mg was equivalent to one tablet each of dolutegravir 50mg (Tivicay®) + rilpivirine 25mg (Edurant®).

6.25 For the basket of comparators, the submission estimated that one FDC tablet of dolutegravir 50mg/rilpivirine 25mg was equivalent to :

- one tablet each of dolutegravir 50mg + rilpivirine 25mg;
- one tablet of dolutegravir 50mg/abacavir 600mg/lamivudine 300mg (Triumeq®);
- one tablet rilpivirine 25mg/emtricitabine 200mg/tenofovir alafenamide 25mg (Odefsey®);
- one tablet elvitegravir 150mg boosted with cobicistat 150mg/ emtricitabine 200mg/tenofovir alafenamide 10mg (Genvoya®);
- one tablet of dolutegravir 50mg + one tablet of emtricitabine 200mg /tenofovir alafenamide 25mg (Tivicay® + Descovy®); and
- one tablet of raltegravir 400mg + one tablet of emtricitabine 200mg/ tenofovir alafenamide 25mg (Isentress® + Descovy®).

6.26 The submission claimed that Prospection data (Q2Q3, 2017) was the only dataset which included all available alternatives, and therefore was chosen to represent the appropriate weighting for the basket. Table 7 presents the submission's cost-minimisation analysis.

Table 7: Results of the cost-minimisation analysis, *as of 1 June 2018.*

Treatment:			**AEMP**	**DPMQ**
DTG/RPV (requested)			$[redacted]	$[redacted]
Primary comparator				
DTG+RPV			$665.55* + $258.00** = $923.55	$1378.25 + $543.79 = $1922.04
Differential (saving)			-	$[redacted]
Secondary comparator (basket)				
Treatment	**Switch to, n**	**Weighting**	**AEMP**	**DPMQ**
DTG+RPV	[redacted]	[redacted]% ([redacted]%)	$923.55	$1922.04
DTG+FTC/TAF	[redacted]	[redacted]% ([redacted]%)	$1365.61	*$2825.52* ~~*$2879.10*~~
EVG/c/FTC/TAF	[redacted]	[redacted]% ([redacted]%)	$958.06	*$1963.27* ~~*$2016.85*~~
RPV/FTC/TAF	[redacted]	[redacted]% ([redacted]%)	$958.06	*$1963.27* ~~*$2016.85*~~
DTG/3TC/ABC	[redacted]	[redacted]% ([redacted]%)	$900.34	$1847.83
RAL+FTC/TAF	[redacted]	[redacted]% ([redacted]%)	$1332.33	*$2758.96* ~~*$2812.54*~~
Weighted CMA price of DTG/RPV (DMPQ 60)			*$[redacted] = (DPMQ-$[redacted]-$[redacted])/[redacted]* *$[redacted] (weighted AEMP)$[redacted] = (DPMQ-$[redacted]-$[redacted])/[redacted]*	*$[redacted]* ~~*$[redacted] (weighted)*~~
Differential (saving)			*$[redacted] (or $[redacted]**)* ~~*$[redacted]*~~	*$[redacted]* ~~*$[redacted]*~~

Source: Tables 71 and 72, p99 of the submission, *updated with DPMQs as of 1 June 2018. .*
~~*Strikethrough*~~ *= pre-1 June values presented in the lodged submission*
*Tivicay (DTG) AEMP & DPMQ, **Edurant (RPV) AEMP (1 pack) & DPMQ (2 packs)
/c = cobicistat; 3TC = lamivudine; ABC = abacavir; AEMP = Australian ex-manufacturer price; CMA = cost-minimisation analysis; DPMQ = dispensed price per maximum quantity; DTG = dolutegravir; EVG = elvitegravir; FTC = emtricitabine; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide.

Note: Some antiretrovirals met the criteria for a statutory price reduction (SPR) on 1 June 2018 under sections 99ACF and 99ACL(1) of Division 3A of Part VII of the National Health Act 1953 (Anniversary Price Reductions). In the 'Attachment 5_Juluca Cost Min Weighted Basket.xlsx lodged with the submission', the tab 'Weighted basket' included the DPMQ that corresponded with prices at the time of lodgement (March 2018), but the AEMP corresponded to prices equal to those on 1 June 2018 following the SPR on comparator products. The weighted AEMP of $1107.76 presented in the lodged submission was calculated directly from the DPMQ and corresponds to the pre-1 June prices.
***: weighted AEMP was calculated by the applying the weightings in the spreadsheet to the 1 June 2018 AEMPs.*

6.27 The requested price was equal to that of the two individual components dolutegravir and rilpivirine, with cost savings attributed to the reduction in fees associated with the DPMQ.

6.28 The requested price was less than the weighted price of the basket of comparators, with Triumeq being the only comparator included in the basket that was less expensive.

6.29 The ESC noted the individual patient regimens could not be identified from the reports for the SWORD studies. The ESC noted the comparable HIV regimens

(derived from possible SWORD regimens) which are in DHHS/ASHM Guidelines and which are PBS (see Table 8).

Table 8: Possible comparative regimens based on SWORD CAR component data and DHHS/ASHM Guidelines

Comparable Regimen (derived from possible SWORD regimens)	AEMP	DPMQ
DTG/RPV requested price	$923.55	$1,894.25
Single-box FDCs		
Tenofovir disoproxil/emtricitabine backbone		
TDF/FTC/EFV (Atripla®)	$831.14	$1,709.43
TDF/FTC/EVG/c (Stribild®)	$868.55	$1,784.25
TDF/FTC/RPV (Eviplera®)	$868.55	$1,784.25
Tenofovir alafenamide/emtricitabine backbone		
TAF/FTC/EVG/c (Genvoya®)	$958.06	$1,963.27
TAF/FTC/RPV (Odefsey®)	$958.06	$1,963.27
Abacavir/lamivudine backbone		
ABC/3TC/DTG (Triumeq®)	$900.34	$1,847.83
Other DHHS/ASHM Guidelines recommended initial regimens		
TDF/FTC (Truvada®)* + DTG (Tivicay®)	($610.55 + $665.55) = $1,276.10	($1,268.25 + $1,378.25) = $2,646.50
TAF/FTC (Descovy®) + DTG (Tivicay®)	($700.06 + $665.55) = $1,365.61	($1,447.27 + $1,378.25) = $2,825.52
TDF/FTC (Truvada®) + RAL (Isentress®)	($610.55 + $632.27) = $1,242.82	($1,268.25 + $1,311.69) = $2,579.94
TAF/FTC (Descovy®) + RAL (Isentress®)	($700.06 + $632.27) = $1,332.33	($1,447.27 + $1,311.69) = $2,758.96
Other DHHS/ASHM Guidelines A or B evidence level regimens (in certain clinical situations) (AI, AII, BI or BII)		
TDF/FTC (Truvada®) OR TAF/FTC (Descovy®) + DRV/r **(AI)**	N/A – DRV/r not PBS listed or high cost (concomitant ritonavir)	
TDF/FTC (Truvada®) + DRV/c (Prezcobix®) **(AII)**	($610.55 + $606.08) = $1,216.63	($1,268.25 + $1,259.31) = $2,527.59
TAF/FTC (Descovy®) + DRV/c (Prezcobix®) **(AII)**	($700.06 + $606.08) = $1,306.14	($1,447.27 + $1,259.31) = $2,706.58
TDF/FTC (Truvada®) OR TAF/FTC (Descovy®) + ATV/r (**BI**)	N/A – ATV/r not PBS listed or high cost (concomitant ritonavir)	
TDF/FTC (Truvada®) + ATV/c (Evotaz®) (**BI**)	($610.55 + $485.13) = $1,095.68	($1,268.25 + $1,016.23) = $2,284.48
TAF/FTC (Descovy®) + ATV/c (Evotaz®) (**BI**)	($700.06 + $485.13) = $1,185.19	($1,447.27 + $1,016.23) = $2,463.50

Source: Compiled by the PBAC Secretariat from PBS-listed FDCs and DHHS/ASHM 'What to Start' Guidelines, available at https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/11/what-to-start

Abbreviations: FDC = fixed-dose combination; TDF = tenofovir disoproxil fumarate; FTC = emtricitabine; EFV = efavirenz; EVC/c = elvitegravir (cobicistat boosted); RPV = rilpivirine; TAF = tenofovir alafenamide; ABC = abacavir; 3TC = lamivudine; DTG = dolutegravir; RAL = raltegravir; DRV/r = darunavir (ritonavir boosted); DRV/c = darunavir (cobicistat boosted); ATV/r = atazanavir (ritonavir boosted); ATV/c = atazanavir (cobicistat boosted)

*TDF/FTC (Truvada®) prices based on 1 March 2018 pricing prior to listing of PrEP

Drug cost/patient/year:

6.30 $[redacted] at the submission's requested price, based on six 60-day scripts with a DPMQ of $[redacted].

Estimated PBS usage & financial implications

6.31 This submission was not considered by DUSC. The submission reasonably took a market share approach to estimating use and financial impact.

6.32 Table 9 presents the estimated use and financial implications for Juluca, based on the DPMQs of the antiretrovirals when the submission was lodged.

Table 9: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated financial implications of dolutegravir/rilpivirine FDC						
Number of scripts dispensed[a]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost to PBS/RPBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Co-payments	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]
Cost to PBS/RPBS less co-payments	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Estimated financial implications for other medicines						
Number of scripts dispensed[a]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost to PBS/RPBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Co-payments	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]
Cost to PBS/RPBS less co-payments	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net financial implications						
Net cost to PBS/RPBS	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]

[a] Assuming 6 per year as estimated by the submission. A higher number of scripts for the comparators was estimated due to some regimens (e.g. dolutegravir + rilpivirine) requiring multiple separate scripts.

Source: Table 83, p109-110, Table 85, p111-112 and Table 86, p113

6.33 The submission estimated net savings to the PBS/RPBS of less than $10 million in Year 1 increasing to less than $10 million in Year 6 for a total of $30 - $60 million over the first 6 years of listing.

6.34 The ESC agreed that estimating the likely utilisation and net cost to the PBS was inherently uncertain as it is difficult to estimate the proportion of patients who may pre-emptively switch as the available data would not account for or provide a baseline for comparison. The ESC considered there was no reliable basis on which to estimate the proportion of these patients who are virologically suppressed and not currently experiencing toxicity or adverse events would likely have remained on their current regimen in the absence of Juluca.

Quality Use of Medicines

6.35 The submission claimed that the listing of Juluca would result in improved quality use of medicines by reducing polypharmacy and tablet burden. The submission considered that the evidence shows that improvements in both these QUM issues result in improved quality of life and reduced health care utilisation for patients with HIV.

6.36 The submission also discussed activities undertaken by the Sponsor to support the quality use of medicines. The submission included the following items summarised in the proposed risk management plan in order to ensure quality use of Juluca:

- a discussion of patient perspectives in HIV therapy. The submission stated that the benefits of dolutegravir / rilpivirine two drug regimen satisfied patient needs of maintaining virological control, reduction in risk of long term toxicities associated with alternative therapies, simplification of regimen and reduction of drug-drug interactions; and
- presented the results of three published studies (Murray 2014; Mühlbacher 2013; and Young 2017) that discussed patient insights. These included a European (Murray 2014) study in Germany and the UK to elicit patients' strengths of preference for different attributes of ARVs.

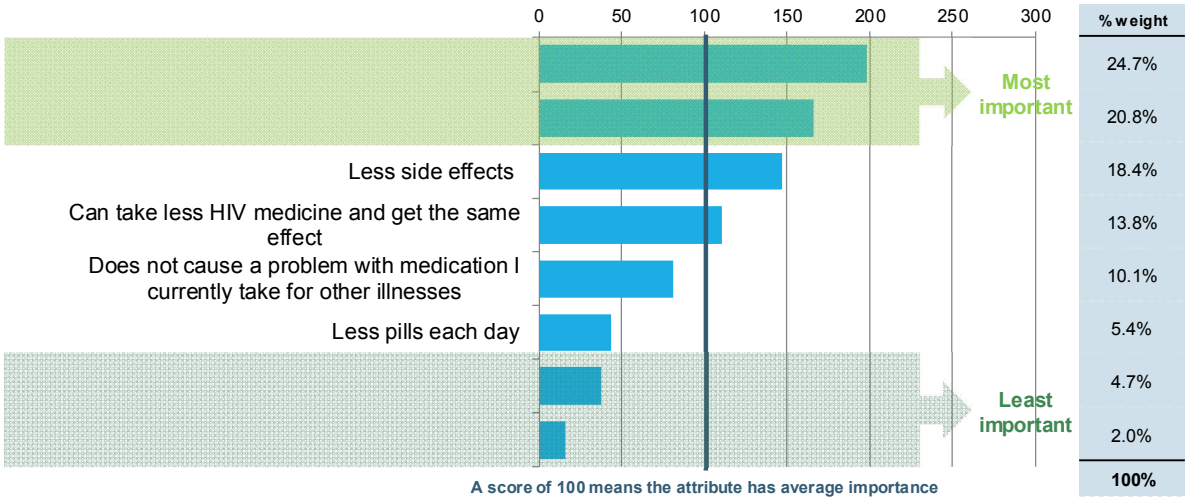
6.37 The results reported in Murray (2014) showed that:

- a rapid improvement in CD4 count and viral load were treatment attributes valued most highly by patients (UK: OR= 0.79; CI= 0.69-0.90; P<0.001. Germany: OR=0.79; CI=0.71-0.87; P<0.001).
- the absence of side effects such as diarrhoea was also valued highly (UK: OR=0.57 CI= 0.51-0.65, p<0.001. Germany: OR=0.79, CI=0.72-0.86; P<0.001), as well as lower risk of long-term toxicities such as decline in renal function and an increase of cardiovascular risk (UK: OR= 0.30 CI= 0.25- 0.35, p<0.001. Germany: OR=0.55, CI=0.48-0.63, p<0.001).
- other treatment attributes driving patient preference included reduction in treatment failure, absence of food restrictions with ARVs, and fewer DDIs. The main difference between the German and UK results is that German patients did not value the absence of DDIs, the qualitative data suggests that they felt that these issues are being managed by their clinician.

6.38 Mühlbacher (2013), another German study, revealed similar results. The top priority was marked by needs such as high efficacy, the avoidance of long term and short term side effects, but also by the improvement of emotional and social status.

6.39 Another study, supported by the Sponsor, was conducted in 8 countries in North America, Europe and Australia. (Young 2017). In depth interviews were performed to identify patient preferences for ARVs in people living with HIV (n=1,085). Figure 2 presents the results of the Young (2017) study in terms of attributes of improvement preferred in current ARVs.

Figure 2: Weight of attributes of improvement preferred in current ARVs



Source: Figure 12, p126 of the submission. ARV = antiretroviral; HIV = human immunodeficiency virus

6.40 The PBAC noted that the submission did not request a price advantage based on purported QUM advantages in the submission.

7 PBAC Outcome

7.1 The PBAC recommended the listing of the combination drug dolutegravir with rilpivirine (Juluca®) on the basis that it should be available only under special arrangements under section 100 (Highly Specialised Drugs Program – Community Access) and only in the circumstances: Authority Required (STREAMLINED) for treatment of virologically suppressed human immune deficiency virus (HIV) infected patients. The PBAC recommended the special arrangements and circumstances described in the tables in section 8 below.

7.2 For reason's explained further below, the PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of Juluca would be acceptable if it were cost-minimised against a mixed comparator of Eviplera® (TDF/FTC/RPV)/Stribild® (TDF/FTC/EVG/c) and Odefsey® (TAF/FTC/RPV)/Genvoya® (TAF/FTC/EVG/c), the latter accounting for the small patient population (6% of the total population) ineligible to receive a TDF based regimen due to moderate or severe renal impairment for which TDF is not recommended.

7.3 The equi-effective doses are one tablet of DTG 50mg/RPV 25mg FDC (Juluca®) once daily and one of either: one tablet of TDF 300mg/FTC 200mg/RPV 25mg (Eviplera®) once daily; one tablet of TDF 300mg/FTC 200mg/EVG 150mg/cobicistat 150mg (Stribild®) once daily; or, in patients with renal impairment, one tablet of TAF 25mg/FTC 200mg/RPV 25mg (Odefsey®) or one tablet of TAF 25 mg/FTC 200 mg/EVG 150mg/cobicistat 150 mg (Genvoya®) once daily.

7.4 The PBAC noted that Australian data on renal impairment, as defined by an estimated glomerular filtration rate (eGFR) of <60 mL/min, in HIV patients[1] estimated approximately 6% of patients have an eGFR below this level, and would therefore be ineligible to receive TDF-based regimens.

7.5 The PBAC noted the submission had nominated the individual components (dolutegravir 50mg and rilpivirine 25mg, taken concomitantly) as the primary comparator and a basket of comparators as the secondary comparator. The PBAC further noted that following the evaluation, the sponsor proposed that Odefsey® would also be an appropriate single comparator.

7.6 The PBAC also noted the pooled analysis of the SWORD trials, with about 1,000 patients between the two trials, which examined virological success over 6 months in patients who had switched from their current antiviral regimen (CAR) to Juluca® or remained on their CAR. The PBAC noted a substantial number of patients' CARs included TDF. The PBAC agreed the results of SWORD demonstrated non-inferior comparative efficacy and safety of Juluca® versus remaining on CAR in patients who were virologically suppressed at baseline and considered that Juluca® could therefore be considered non-inferior to any of the CAR regimens in the SWORD study.

7.7 The PBAC noted that if treatment with Juluca® were to be substantially more costly than an alternative or alternative therapies, the PBAC could only recommend listing if it is satisfied Juluca® provides, for some patients, a significant improvement in efficacy or reduction in toxicity over the alternative therapy or therapies. The PBAC considered that the alternative therapies in this case may include the TDF containing drugs Eviplera, Stribild or Atripla, as well as Odefsey® and Genvoya® (amongst other therapies).

7.8 The PBAC noted there is now considerable evidence that efavirenz (a component of Atripla®) is associated with a range of moderate-to-severe central nervous system (CNS) adverse events including drowsiness, insomnia, nightmares, agitation, memory loss, hallucinations and other effects. The PBAC was therefore satisfied that therapies containing efavirenz are of inferior safety to non-efavirenz containing therapies for the treatment of HIV infection. Accordingly, the PBAC considered that Juluca offers a significant reduction in toxicity over Atripla®.

7.9 For the reasons outlined in paragraph 7.4 above, the PBAC considered that for the subgroup of patients with renal impairment TDF containing regimens should not be considered an alternative therapy to Juluca. The PBAC noted that alternative therapies to Juluca in patients with renal impairment include tenofovir alafenamide-containing regimens, including Odefsey® and Genvoya®.

[1] Gracey, D., Chan, D., Bailey, M., Richards, D. and Dalton, B., 2013. Screening and management of renal disease in human immunodeficiency virus-infected patients in Australia. Internal medicine journal, 43(4), pp.410-416.

7.10 For virologically suppressed HIV infected patients who do not have renal impairment the PBAC considered that the TDF containing regimens, Stribild and Eviplera, are alternative therapies to Juluca.

7.11 The PBAC noted that although the sponsor had dismissed TDF containing regimens as potential alternative therapies, it had accepted that the TAF containing regimen, Odefsey® was an alternative therapy (both as a single agent or in a mixed basket – see Section 5, above). The PBAC recalled that in July 2016 it had formed the view that Odefsey® was non inferior to Eviplera® in terms of effectiveness and safety (Odefsey® PSD, July 2016). The PBAC further recalled that, at that time, it had not been satisfied that Odefsey provided, for any group of patients, a significant improvement in patient compliance or in efficacy or reduction in toxicity over alternative therapies. In particular, the PBAC considered there remained uncertainty that changes in surrogate outcomes of bone and renal safety over a 96 week study period were sufficient to support the claimed significant reduction in toxicity in some patients over a lifetime. The PBAC noted the sponsor had not made a further submission seeking to change the PBAC's previously expressed view.

7.12 The PBAC noted the submission argued that some patients would switch to Juluca® to avoid longer-term adverse events associated with an NRTI-backbone based regimen, and considered this claim was difficult to quantify as it was unclear what proportion of patients would switch to Juluca to reduce extant adverse events or toxicities and what proportion would switch to avoid anticipated adverse events or toxicities. The PBAC was not satisfied that the fact a treatment regimen is NRTI-sparing is a reasonable basis to exclude one or more NRTI-containing regimens as potential alternative therapies.

7.13 With regards to the requested restriction, the PBAC agreed with the Secretariat suggestions to align the listing with the TGA indication and required patients to be stable on their previous antiviral regimen for at least six months prior to switching to Juluca®, with wording aligned with the TGA indication as requested in the Pre-PBAC Response. The PBAC also agreed it was appropriate to restrict Juluca as the sole subsidised therapy for HIV infection whilst patients remain on the drug, consistent with the clinical trial evidence.

7.14 The PBAC noted this was the first treatment for HIV infection that had requested a listing only for patients who are virologically suppressed on their current antiviral regimen. The PBAC further noted that most new regimens have been intended to be used when patients experience virological failure on current therapy or are no longer able to tolerate their current regimen.

7.15 The PBAC agreed with the ESC that the utilisation estimates were inherently uncertain as it was unclear how many patients would express a preference to switch to DTG/RPV to pre-emptively avoid adverse events associated with their current regimen as there was no data source to provide a reasonable basis on which to estimate the extent to which these switches may occur.

7.16 The PBAC advised that DTG/RPV should not be treated as interchangeable on an individual basis with any other drugs.

7.17 The PBAC advised that DTG/RPV is not suitable for prescribing by nurse practitioners, similar to other HIV antiviral regimens.

7.18 The PBAC advised that the Early Supply Rule should apply.

7.19 The PBAC noted that this submission is 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 and Manufacturer	
DOLUTEGRAVIR WITH RILPIVIRINE Tablet containing dolutegravir 50 mg (as sodium) with rilpivirine 25 mg (as hydrochloride), 30	2	5	Juluca®	Viiv Healthcare Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Community Access)
Prescriber type:	☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐ Midwives
Condition:	HIV infection
PBS Indication:	HIV infection
Treatment phase:	Initial
Restriction Level / Method:	☐ Restricted benefit ☐ Authority Required - In Writing ☐ Authority Required - Telephone ☐ Authority Required - Emergency ☐ Authority Required - Electronic ☒ Streamlined
Treatment criteria:	Patient must be virologically suppressed on a stable antiretroviral regimen for at least 6 months
Clinical criteria:	The treatment must be the sole PBS subsidised therapy for this condition.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
DOLUTEGRAVIR WITH RILPIVIRINE Tablet containing dolutegravir 50 mg (as sodium) with rilpivirine 25 mg (as hydrochloride), 30	2	5	Juluca®	Viiv Healthcare Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Community Access)

Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	HIV infection
PBS Indication:	HIV infection
Treatment phase:	Continuing
Restriction Level / Method:	☐Restricted benefit ☐Authority Required - In Writing ☐Authority Required - Telephone ☐Authority Required - Emergency ☐Authority Required - Electronic ☒Streamlined
Clinical criteria:	Patient must have previously received PBS-subsidised therapy with this drug for this condition AND The treatment must be the sole PBS-subsidised therapy for this condition.

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

ViiV Healthcare is pleased that Juluca will be made available for Australians with HIV but disagrees with the comparators chosen by the PBAC as the majority of these would not be used instead of Juluca due to concerns about long-term toxicity.