

**6.03 DOLUTEGRAVIR with LAMIVUDINE,
Tablet containing dolutegravir 50 mg (as sodium) with
lamivudine 300 mg,
Dovato[®],
ViiV Healthcare Pty Ltd**

For improved readability, tradenames for fixed-dose combination (FDC) therapies and other combination therapies for the treatment of human immunodeficiency virus (HIV) are used in this public summary document (PSD). In some cases, generic names may be used for clarity.

Table 1 presents a summary of the FDCs, indicating their components, abbreviations for each drug and their associated tradenames.

Table 1: Summary of fixed-dose combinations (their components, abbreviations for each drug and their associated tradenames)

Fixed-dose combination (FDC) or other combination components	Abbreviations	Tradename
Darunavir / cobicistat / emtricitabine / tenofovir alafenamide	DRV/c/FTC/TAF	Symtuza [®]
Elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide	ELV/c/FTC/TAF	Genvoya [®]
Rilpivirine / emtricitabine / tenofovir alafenamide	RPV/FTC/TAF	Odefsey [®]
Bictegravir / emtricitabine / tenofovir alafenamide	BIC/FTC/TAF	Biktarvy [®]
Elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil fumarate	ELV/c/FTC/TDF	Stribild [®]
Efavirenz / emtricitabine / tenofovir disoproxil fumarate	EFV/FTC/TDF	Atripla [®]
Rilpivirine / tenofovir disoproxil fumarate / emtricitabine	RPV/FTC/TDF	Eviplera [®]
Dolutegravir / abacavir / lamivudine	DTG/ABC/3TC	Triumeq [®]
Dolutegravir / lamivudine	DTG/3TC	Dovato [®]
Dolutegravir / rilpivirine	DTG/RPV	Juluca [®]
Emtricitabine / tenofovir disoproxil fumarate	FTC/TDF	Truvada [®]
Emtricitabine / tenofovir alafenamide	FTC/TAF	Descovy [®]

1 Purpose of submission

- 1.1 The submission requested an extension to the existing Section 100 (Highly Specialised Drugs Program – Community Access) streamlined authority listing for dolutegravir/lamivudine (DTG/3TC, Dovato[®]) for the treatment of HIV in treatment-naïve patients, to include anti-retroviral (ART) treatment-experienced (i.e. switch) patients.
- 1.2 Listing was requested on the basis of a cost-minimisation analysis versus the individual components in the FDC (DTG and 3TC).
- 1.3 Table 2 presents the key components of the clinical issue addressed by the submission.

Table 2: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Treatment of HIV infection in adults and adolescents
Intervention	Dolutegravir 50 mg/ lamivudine 300 mg (DTG/3TC) fixed-dose combination (FDC); Dovato®
Comparator	1. Individual components (dolutegravir 50 mg and lamivudine 300 mg) taken concomitantly 2. Therapies that prescribers would most likely replace in practice ^a
Outcomes	Virologic failure, defined as proportion of patients with HIV-1 RNA \geq 50 c/mL at week 48
Clinical claim	<ul style="list-style-type: none"> • Bioequivalence: The PBAC has previously accepted that evidence from Study 204994, supported bioequivalence of the individual components (DTG 50 mg + 3TC 300 mg) and the FDC (DTG/3TC 50/300 mg, Dovato PSD; paragraph 7.2, August 2019 meeting). • Efficacy ^b: DTG/3TC is non-inferior in terms of effectiveness in comparison to Biktarvy, Genvoya, Odefsey, Juluca, and Triumeq for the treatment of HIV infection. • Safety ^b: DTG/3TC is non-inferior in terms of safety in comparison to Biktarvy, Genvoya, Odefsey, Juluca, and Triumeq for the treatment of HIV infection.

Source: Table 3, p15 of the submission

3TC = lamivudine; c = copies; DTG = dolutegravir; FDC = fixed-dose combination; HIV = human immunodeficiency virus; PBAC = Pharmaceutical Benefits Advisory Committee; PBS = Pharmaceutical Benefits Scheme; RNA = ribonucleic acid; RPV = rilpivirine; TBR = tenofovir alafenamide based regimen

^a FDCs currently listed on the PBS (Biktarvy, Genvoya, Odefsey, Juluca, and Triumeq) indicated for use in patients with HIV who are treatment-experienced

^b The submission considered that prior PBAC recommendations on the basis of cost-minimisation and therapeutic relativity sheets confer non-inferiority across the 3DR FDCs (including TBRs) and DTG/RPV in the treatment-experienced setting

2 Background

Registration status

2.1 The submission was made under the TGA/PBAC Parallel Process and was not TGA registered at the time of the PBAC meeting. The Clinical Evaluation Report containing the first and second round recommendations was obtained prior to PBAC consideration. The registration pertains to the treatment-experienced patient population; DTG/3TC FDC was previously TGA-registered in December 2019 in the treatment-naïve population. Advice from the TGA Delegate is as follows:

“I have no reason to say, at this time, that the application for DOVATO should not be approved for the following indication: DOVATO (a fixed dose combination of dolutegravir and lamivudine) is indicated for the treatment of Human Immunodeficiency Virus-1 (HIV-1) infection in adults and adolescents (from 12 years of age weighing at least 40kg):

- in antiretroviral treatment-naïve patients with no antiretroviral treatment history who have no known or suspected resistance to either antiretroviral component; or
- to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure with no known or suspected resistance to the integrase inhibitor class or lamivudine.”

- 2.2 DTG/3TC has been previously evaluated by the TGA for the treatment-experienced population. In 2018-2019, the sponsor sought to register DTG/3TC FDC for the proposed indication: treatment of human immunodeficiency virus (HIV) infection in adults and adolescents from 12 years of age weighing at least 40 kg, who have no known or suspected resistance to either antiretroviral component (pp8-12, DTG/3TC AusPAR). During the evaluation, the Advisory Committee on Medicines (ACM) recommended restriction to treatment-naïve patients only – citing insufficient data and concern over potential drug resistance in patients switching therapy. The ACM was of the view that a decision regarding the ‘switch’ indication should be deferred until 48 week data from the TANGO trial are available and formal evaluation of the study is conducted, including an assessment of resistance (p30, DTG/3TC AusPAR, November 2019). The TGA Delegate outlined their intention to align the Product Information, following advice from the ACM regarding the indication, with the TGA-registered indication to exclude patients who are treatment-experienced (paragraph 11.3, DTG/3TC Public Summary Document (PSD), July 2019 PBAC meeting with August and September 2019 addenda).
- 2.3 At the time of these minutes, DTG/3TC was approved for use in treatment-naïve and treatment-experienced patients in the European Union and restricted to treatment-naïve patients in the United States (US).

Previous PBAC consideration

- 2.4 DTG/3TC was first considered by the PBAC at its July 2019 meeting for both treatment-naïve and treatment-experienced patients. The PBAC deferred making a recommendation for the listing of DTG/3TC FDC for the treatment of HIV in both treatment-naïve and -experienced adult and adolescent patients as it was unclear if the TGA registration would permit use in patients who are treatment-experienced. For treatment naïve patients, the PBAC was of a mind to recommend DTG/3TC, however considered it was appropriate to await further clarity on the likely TGA outcome prior to making a recommendation for listing on the PBS (paragraph 7.1, DTG/3TC PSD, July 2019 PBAC meeting).
- 2.5 In August 2019, the PBAC recommended listing DTG/3TC FDC for the treatment of HIV in treatment-naïve patients who have a baseline viral load of < 500,000 copies/ml and no suspected resistance to either antiretroviral component (paragraph 13.1, DTG/3TC PSD, July 2019 PBAC meeting with August and September 2019 addenda). The PBAC did not recommend listing of DTG/3TC for patients who are treatment-experienced. The PBAC advised that it will not consider other indications until such time as the TGA registration is amended to include such indications (paragraph 13.3, DTG/3TC PSD, July 2019 PBAC Meeting with August and September 2019 addenda).

- 2.6 In September 2019, the PBAC recommended a change to the recommended listing of DTG/3TC to not include the criterion, ‘Patient must have a baseline viral load < 500,000 copies/ml’ as the final TGA approved indication did not include this requirement (paragraph 19.1, DTG/3TC PSD, July 2019 PBAC meeting with August and September 2019 addenda).

3 Requested listing

Name, restriction, manner of administration, form	Max. qty (packs)	Max. qty (units)	No. of Rpts	Dispensed price for max. qty	Available brands
Dolutegravir 50 mg + lamivudine 300 mg, tablet, 30	2	60	5	\$1,442.95	Dovato

Category/Program: Section 100 – Highly Specialised Drugs Program (Community Access)
Restriction type / method: <input checked="" type="checkbox"/> Authority Required – Streamlined (9934)
PBS indication: HIV infection
Treatment phase: Continuing treatment
Clinical criteria:
<ul style="list-style-type: none"> ▪ Patient must have previously received PBS-subsidised therapy with this drug for this condition for HIV infection

- 3.1 DTG/3TC is listed as a FDC for patients who are treatment-naïve. The submission sought an extension to include patients who are treatment-experienced by removing the requirement for previous therapy “with this drug for this condition” from the continuing treatment clinical criteria restriction. The submission did not propose changes to the existing listing of DTG/3TC with respect to initial or grandfathered treatment.
- 3.2 The price of DTG/3TC remained unchanged compared with the previous submission and the currently listed price for treatment-naïve patients. No special pricing arrangements were proposed.

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

4 Population and disease

- 4.1 The proposed place in therapy for DTG/3TC in the submission was for patients with HIV who are treatment-experienced. The current listing of DTG/3TC is restricted to treatment-naïve patients. The submission was based on evidence from the TANGO trial, which included treatment-experienced patients.
- 4.2 In 2017, there were 24,646 people living with HIV in Australia. The majority were treatment-experienced, with 21,560 people receiving antiretroviral therapy (ART).
- 4.3 HIV is an enveloped single-stranded RNA retrovirus that attaches to CD4 receptors expressed on the surface of T-lymphocytes, destroying or impairing the function of the immune system.

- 4.4 If left untreated, patients experience a gradual decline in CD4 cell count which results in damage to, and deterioration of, immune function. Progression to Acquired Immunodeficiency Syndrome (AIDS), marked by the development of opportunistic infections or specific malignancies, occurs at a median of 10 years after initial infection with HIV. At this time, the CD4 cell count usually falls below 200 cells/mm³ and patients are severely immunocompromised.
- 4.5 The development and use of combination ARTs since 1996 has successfully delayed disease progression such that life expectancy is closer to the general population (median survival age of 78 years in a patient diagnosed between 2008 and 2010). However, the prolonged immunodeficiency, chronic immune activation, and side effects of ART polypharmacy may be associated with earlier development of cardiovascular, bone, renal and liver diseases, cancers and neurocognitive decline.
- 4.6 In its July 2019 consideration of DTG/3TC, the PBAC agreed with the expert clinician's advice that with the emergence of comorbidities and polypharmacy in an aging prevalent population, some virologically suppressed patients might express a desire to switch to a regimen with fewer agents if suppression is maintained (paragraph 7.5, DTG/3TC PSD, July 2019 PBAC meeting).

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

5 Comparator

- 5.1 The submission nominated the component products, dolutegravir 50 mg and lamivudine 300 mg (DTG + 3TC), taken concomitantly, as a comparator. The PBAC considered during the previous submission that the cost-effectiveness of DTG/3TC would be acceptable if it were cost-minimised against the individual components (paragraph 13.4, DTG/3TC PSD, July 2019 PBAC meeting with August and September 2019 addenda). The PBAC also considered the evidence presented supported the claims of bioequivalence with concomitantly administered DTG and 3TC (paragraph 7.2 DTG/3TC PSD, July 2019 PBAC meeting).
- 5.2 The submission nominated a basket of 3 drug regimen (DR) FDCs (Biktarvy[®], Genvoya[®], Odefsey[®], and Triumeq[®]) as well as the 2DR FDC of dolutegravir/rilpivirine (Juluca[®]), as comparators most likely to be replaced by DTG/3TC in practice if use were expected to vary from the concomitant individual components. The submission argued that previously considered cost-minimisation analyses and therapeutic relativity sheets imply non-inferiority across the nominated basket of comparators in the treatment-experienced setting (paragraphs 6.24, 6.25, and 10.3, Biktarvy PSD, March 2018 PBAC meeting; paragraph 7.3, Juluca PSD, July 2018 PBAC meeting; and paragraph 7.2, DTG/3TC PSD, August 2019 PBAC meeting). The submission appropriately excluded Stribild[®] and Eviplera[®] following delisting in March 2020.

- 5.3 For the current item in July 2020, the PBAC considered that the comparator of DTG + 3TC, taken concomitantly, and/or a basket of three- or two-drug FDCs most likely to be replaced in practice was reasonable.
- 5.4 The submission excluded Atripla[®] (EFV/TDF/FTC) and Symtuza[®] (DRV/c/FTC/TAF) as comparators. The PBAC previously considered that therapies containing efavirenz (i.e. Atripla) are of inferior safety to non-efavirenz containing therapies (paragraph 6.41, DTG/3TC PSD, July 2019 PBAC meeting; paragraph 7.8, Juluca PSD, July 2018 PBAC meeting). The exclusion of Symtuza was reasonable as the treatment guidelines from the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) state that in general, boosted protease inhibitor regimens are only recommended for certain clinical situations. Its exclusion did not affect the cost-minimisation analysis.
- 5.5 Among the therapies nominated as relevant comparators by the submission, none of the alternative therapies are less costly than the requested price for DTG/3TC based on PBS prices current in April 2020. Other multi-drug treatment combinations for the treatment of HIV infection that could be considered as alternatives may be less costly than DTG/3TC. If treatment with DTG/3TC is substantially more costly than an alternative therapy or alternative therapies, the PBAC could only recommend listing of DTG/3TC if it is satisfied that the FDC provides, for some patients, a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies (National Health Act 1953, Section 101(3B)).

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 a 48-week US Food and Drug Administration (FDA) snapshot analysis of a randomised open-label trial comparing switching from a current tenofovir alafenamide (TAF)-based regimen (TBR) to DTG/3TC, versus remaining on TBR in virologically suppressed patients with uninterrupted TBR for at least 6 months prior to screening, with no evidence or history of ART drug resistance (TANGO: N = 743). Table 3 presents the details of TANGO and associated reports.

Table 3: Trial and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
TANGO	Study 204862 (TANGO): A Phase III, randomized, multicentre, parallel-group, non-inferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus lamivudine in HIV 1 infected adults who are virologically suppressed- Week 48. (Sept 2019)	CSR. 25 September 2019
	Van Week J, Ajana F, Bisshop F, De Wit S, Osiyemi O, Portilla J, et al. (2020) Efficacy and Safety of Switching to Dolutegravir/Lamivudine Fixed-Dose Two-Drug Regimen Versus Continuing a Tenofovir Alafenamide-Based Three- or Four-Drug Regimen for Maintenance of Virologic Suppression in Adults With HIV-1: Phase 3, Randomized, Non-inferiority TANGO Study.	Clinical infectious diseases; Published online: 06 Jan 2020; Article in press February 2020; doi: 10.1093/cid/ciz1243.

Source: Table 18, p35 of the submission

CSR = clinical study report; HIV = human immunodeficiency virus;

6.4 Table 4 presents the key features of the TANGO trial.

Table 4: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcomes
DTG/3TC vs. TBR					
TANGO	743	R, OL, MC/ 48-week FDA snapshot	Low	Treatment-experienced, virologically suppressed patients with HIV infection on TBR for ≥6mths	Virologic failure; HIV-1 RNA < 50; changes from baseline in CD4+ counts and CD4+/CD8+ ratio; disease progression (HIV associated conditions, AIDS, death); EQ-5D-5L; Safety

Source: Table 20, p37, Table 21, p39, of the submission

3TC = lamivudine; AIDS = acquired immunodeficiency syndrome; CD4 = cluster of differentiation 4; DTG = dolutegravir; EQ-5D-5L = EuroQol-five dimension-five level; FDA = Food and Drug Administration; HIV = human immunodeficiency virus; MC = multi-centre; OL = open label; R = randomised; RNA = ribonucleic acid; TBR = tenofovir alafenamide based regimen

6.5 Although the TANGO trial was open-label, the overall risk of bias was considered low as the trial utilised objective outcome measures that were mostly defined by HIV-1 RNA copies.

6.6 Results from the 24-week snapshot of TANGO were included in the July 2019 submission to support listing of DTG/3TC in treatment-experienced patients (paragraph 6.5, DTG/3TC PSD, July 2019 PBAC meeting). During the previous TGA evaluation, the ACM concluded that evaluation of DTG/3TC in treatment-experienced patients, although the data looked promising, should be deferred pending results from the 48-week snapshot of TANGO, including an assessment of resistance (p30, DTG/3TC AusPAR, December 2019).

6.7 The submission did not present evidence from the DOLAM and ASPIRE trials which were included as supporting studies in the July 2019 submission. This was reasonable as the previous evaluation considered the trials had a small sample size and short follow-up; had a high risk of bias; and in ASPIRE, utilised a non-inferiority margin which was not consistent with the pivotal trial.

Comparative effectiveness

- 6.8 Results from the TANGO trial supported the clinical claim of non-inferiority for DTG/3TC compared with TBR in patients who are treatment-experienced. The results were consistent with the 24-week TANGO snapshot analysis presented in the July 2019 submission.
- 6.9 Table 5 presents results for the primary outcome, the proportion of participants with virologic failure at 48-weeks (Day 295 to 378) using the FDA snapshot algorithm. The FDA snapshot algorithm conservatively determines patients to have virologic failure for any of the following:
- HIV-1 RNA \geq 50 c/mL at 48 weeks,
 - change in ART (other than the pharmacokinetic booster) at any time, or
 - discontinuation for other reason while HIV RNA \geq 50 c/mL prior to the week 48 window.

Table 5: Proportion of participants with virologic failure at the 48-week snapshot

Study population	n/N (%; 95%CI)		RD, % (95% CI)	
	DTG/3TC	TBR	Unadjusted ^a	Adjusted ^b
ITT-E population	1/369 (0.3; 0.0, 0.8)	2/372 (0.5; 0.0, 1.3)	-0.3 (-1.2, 0.6)	-0.3 (-1.2, 0.7)
PP population	0/352	2/358 (0.6; 0.0, 1.3)	-0.6 (-1.3, 0.2)	-0.6 (-1.3, 0.2)

Source: Table 28, p48 of the submission

3TC = lamivudine; DTG = dolutegravir; CI = confidence interval; ITT-E = intent to treat-exposed; n = number of participants with event; N = total participants in group; PP = per protocol; RD = risk difference; TBR = tenofovir alafenamide-based regimen;

^a Difference: Proportion for DTG/3TC – Proportion for TBR

^b Adjusted based on Cochran Mantel Haenszel stratified analysis adjusting for baseline third agent class (protease inhibitor, integrase strand transfer inhibitor, non-nucleoside reverse-transcriptase inhibitors).

- 6.10 The adjusted treatment difference for virologic failure met the nominated non-inferiority margin of -4%. The submission highlighted that the non-inferiority margin of -4% was consistent with the FDA guidance on HIV trials (FDA, 2015¹) and previously accepted by the PBAC for the two-drug regimen Juluca (paragraph 6.8, Juluca PSD, July 2018 PBAC meeting).
- 6.11 Table 6 presents the disaggregated results of the FDA snapshot analysis at 48 weeks.

¹ FDA 2015, Human Immunodeficiency Virus-1 Infection: Developing Antiretroviral Drugs for Treatment Guidance for Industry <https://www.fda.gov/media/86284/download>

Table 6: Snapshot analysis at 48 weeks (ITT-E population)

Virological data at Week 48	DTG/3TC (N = 369), n (%)	TBR (N = 372), n (%)
HIV-1 RNA < 50 c/mL (virologic success)	344 (93.2)	346 (93.0)
Unadjusted RD, % (95% CI)	0.2 (-3.4, 3.9)	
Adjusted RD, % (95% CI) ^a	0.2 (-3.4, 3.9)	
HIV-1 RNA ≥ 50 c/mL (virologic failure)	1 (0.3)	2 (0.5)
Data in window & HIV-1 RNA ≥ 50 c/mL	0	0
Discontinued due to lack of efficacy	0	2 (0.5)
Discontinued for reason other than efficacy (HIV-1 RNA ≥ 50 c/mL)	1 (0.3)	0
Change in ART	0	0
No virological data	24 (6.5)	24 (6.5)
Discontinued trial due to AE/Death	12 (3.3)	1 (0.3)
Discontinued trial for other reasons	12 (3.3)	22 (5.9)
Discontinued trial but missing data in window	0	1 (0.3)

Source: Table 31, p48 of the submission

3TC = lamivudine; AE = adverse event; ART = antiretroviral therapy; c = copies; CI = confidence interval; DTG = dolutegravir; HIV = human immunodeficiency virus; ITT-E = intent to treat-exposed; RD = risk difference; RNA = ribonucleic acid; TBR = tenofovir alafenamide-based regimen

^a Adjusted using the Cochran-Mantel Haenszel test, stratified by baseline third agent class (Protease Inhibitor, Integrase strand transfer inhibitor, or Non-nucleoside reverse transcriptase inhibitor).

- 6.12 The lower confidence bound for the risk difference for proportion of participants with plasma HIV-1 RNA ≥ 50 c/mL met the nominated non-inferiority margin of -8%.
- 6.13 Resistance testing was conducted on one participant (from the TBR treatment arm) who met confirmed virological withdrawal (CVW) criteria - two consecutive on-treatment viral load measurements ≥ 50 c/mL, with the second measurement being ≥ 200 c/mL (the second being the confirmatory virology sample). No integrase strand transfer inhibitor (INSTI), reverse transcriptase- or protease inhibitor-associated resistance mutations were detected. No participants in the DTG/3TC treatment arm met the criteria for CVW. The PBAC has previously considered the introduction of two-drug regimens represented a potential change from longstanding treatment practice (paragraph 6.15, DTG/3TC PSD, July 2019 PBAC meeting); as such, longer-term data on effectiveness, safety, and resistance (particularly as no resistance information in the DTG/3TC population was available at the time) would be informative.
- 6.14 Table 7 presents EQ-5D results from the 48-week snapshot analysis.

Table 7: Change from baseline in EQ-5D at Week 48 (ITT-E population)

EQ-5D-5L		Utility Score		Thermometer Score	
		DTG/3TC	TBR	DTG/3TC	TBR
n: baseline; week 48		369; 364	372; 370	369; 364	372; 370
Baseline	Mean score (SD)	0.9497 (0.0950)	0.9483 (0.0876)	87.5 (11.32)	87.5 (12.21)
Week 48	Mean score (SD)	0.9533 (0.0917)	0.9519 (0.0886)	88.7 (11.39)	89.2 (10.72)
	Adjusted mean change (SE) ^a	0.0037 (0.0041)	0.0023 (0.0037)	1.1 (0.52)	1.7 (0.43)
	Difference (95% CI); p value	0.0015 (-0.0094, 0.00123); p=0.792		-0.5 (-1.9, 0.8), p=0.414	

Source: Table 36, p52 of the submission

3TC = lamivudine; AE = adverse event; ART = antiretroviral therapy; CI = confidence interval; CSR = clinical study report; DTG = dolutegravir; EQ-5D-5L = EuroQol-five dimension-five level; HIV = human immunodeficiency virus; ITT-E = intent to treat-exposed; LOCF = last observation carried forward; RD = risk difference; RNA = ribonucleic acid; SD = standard deviation; SE = standard error; TBR = tenofovir alafenamide-based regimen

^a Adjusted mean calculated using the LOCF dataset as the estimated mean change from baseline at each visit in each arm from a repeated measures model, with Visit as the repeated factor, adjusting for: Treatment, Visit, Baseline Third Agent Class, Baseline EQ-5D Utility or Thermometer (continuous), Treatment by Visit interaction, and Baseline EQ-5D Utility or Thermometer by Visit interaction.

Note: The tariffs used to calculate EQ-5D-5L scores were not described in the submission or attached CSR.

6.15 Overall, no meaningful differences in change in EQ-5D could be observed between the two treatment groups.

Comparative harms

6.16 Table 8 presents the summary of adverse events (AEs) at 48 weeks in the TANGO trial. The incidence and severity of any AEs was similar between treatment groups and consistent with those observed during the July 2019 submission.

Table 8: Summary of AEs (Safety population)

	DTG/3TC (N = 369), n (%)	TBR (N = 371), n (%)	RR (95% CI) ^a	RD% (95% CI) ^a
Any AE	295 (79.9)	292 (78.7)	1.02 (0.94, 1.09)	1.2 (-4.6, 7.1)
Grade 1 AE	102 (27.6)	94 (25.3)	1.09 (0.86, 1.39)	2.3 (-4.1, 8.7)
Grade 2 AE	170 (46.1)	177 (47.7)	0.97 (0.83, 1.13)	-1.6 (-8.8, 5.6)
Grade 3 AE	19 (5.1)	15 (4.0)	1.27 (0.66, 2.47)	1.1 (-1.9, 4.1)
Grade 4 AE	3 (0.8)	6 (1.6)	0.50 (0.13, 2.00)	-0.8 (-2.4, 0.8)
Most common AEs (n ≥ 2% of participants) with a significant difference in incidence between treatment groups				
Bronchitis	8 (2.2)	20 (5.4)	0.40 (0.18, 0.90)	-3.2 (-6.0, -0.5)
Fatigue	20 (5.4)	3 (0.8)	6.70 (2.01, 22.36)	4.6 (2.1, 7.1)
Seasonal allergy	12 (3.3)	3 (0.8)	4.02 (1.14, 14.13)	2.4 (0.4, 4.5)
Any DR-AE	45 (12.2)	5 (1.3)	9.05 (3.63, 22.54)	10.8 (7.3, 14.4)
Grade 1 AE	28 (7.6)	2 (0.5)	14.08 (3.38, 58.66)	7.0 (4.2, 9.9)
Grade 2 AE	17 (4.6)	3 (0.8)	5.70 (1.68, 19.28)	3.8 (1.5, 6.1)
Grade > 2 AE	-	-	-	-
AE leading to withdrawal	13 (3.5)	2 (0.5)	6.54 (1.49, 28.76)	3.0 (1.0, 5.0)
DR-AE leading to withdrawal	9 (2.4)	1 (0.3)	9.05 (1.15, 71.07)	2.2 (0.5, 3.8)
Any SAE	21 (5.7)	16 (4.3)	1.32 (0.70, 2.49)	1.4 (-1.8, 4.5)
DR-SAE	0	0	-	0.0 (0.0, 0.0)
Fatal AE	1 (0.3)	0	-	0.3 (-0.3, 0.8)
DR fatal AE	0	0	-	0.0 (0.0, 0.0)

Source: Table 37-39, pp52-53 of the submission

3TC = lamivudine; AE = adverse events; CI = confidence interval; DR = drug related; DTG = dolutegravir; RD = risk difference; RR = relative risk; SAE = serious adverse event; TBR = tenofovir alafenamide based regimen; **Bold** = statistical significance

^a Ad-hoc analyses

- 6.17 Discontinuations due to AEs were more common with DTG/3TC (13 vs. 2 participants) whereas discontinuations due to “other” reasons were more common with TBR (12 vs. 22 participants). The PBAC noted imbalance in drug-related AEs was expected from an open-label trial design comparing a treatment switch with a continuing therapy treatment arm (paragraph 6.12, Juluca PSD, July 2018 PBAC meeting). Viral load tests were conducted on participants discontinuing due to the reason “other” with at least one on-treatment assessment (9 and 21 participants, in the DTG/3TC and TBR arms, respectively). All demonstrated plasma HIV-1 RNA < 40 c/mL at their last visit.
- 6.18 The submission noted that treatment with DTG/3TC was associated with significantly higher incidence of fatigue and seasonal allergy and a significantly lower incidence of bronchitis compared with TBR. The incidence of serious AEs (SAEs) were low and comparable between treatment groups. No treatment-related deaths were observed in either treatment group.

Clinical claim

- 6.19 The submission described DTG/3TC as non-inferior in terms of effectiveness compared to the TBRs Biktarvy, Genvoya, Odefsey and non-TBRs Triumeq and Juluca. This claim was adequately supported if PBAC accept that the TBRs in the TANGO trial could act as a proxy for the other two or three-drug regimens. Biktarvy and Juluca were not used by patients in the TBR arm in the TANGO trial. At its July 2019 consideration of DTG/3TC for treatment-naïve patients, the PBAC considered that the claim of non-inferior comparative effectiveness was reasonable for the treatment-naïve population (paragraph 6.31, DTG/3TC PSD, July 2019 PBAC meeting). The PBAC was previously satisfied that a regimen of DTG + Truvada® (the comparator in the GEMINI trial) could be a reasonable proxy for other similar three-drug regimens (3DRs) in treatment-naïve patients (paragraph 7.2, DTG/3TC PSD, July 2019 PBAC meeting).
- 6.20 The submission described DTG/3TC as non-inferior in terms of safety compared to Biktarvy®, Genvoya®, Odefsey®, Triumeq®, and Juluca®. This claim was adequately supported. At its July 2019 consideration of DTG/3TC for treatment-naïve patients, the PBAC considered the data supported a conclusion of non-inferior comparative safety versus a regimen of DTG + Truvada, and by extension other similar 3DR regimens in treatment-naïve patients (paragraph 7.4, DTG/3TC PSD, July 2019 PBAC meeting).
- 6.21 The PBAC considered the clinical claims of non-inferior comparative efficacy and safety to its component drugs taken concomitantly and to the nominated TBRs and non-TBRs were reasonable and accepted the TBRs were a reasonable proxy for comparative efficacy and safety to the nominated non-TBRs. The PBAC noted this was consistent with its view that a regimen of DTG + Truvada was a reasonable proxy for other 3DRs when it considered DTG/3TC at its July 2019 meeting.

Economic analysis

- 6.22 The submission presented a cost-minimisation analysis (CMA) for DTG/3TC based on the lowest cost methodology according to the individual components (Part 1) or the nominated comparators (Part 2). The CMA, other than nominated comparators, was unchanged from the previous submission.
- 6.23 Table 9 presents the key components of the CMA.

Table 9: Key components and assumptions of the cost-minimisation analysis

Component	Claim or assumption
Therapeutic claim: bioequivalence	Based on bioequivalence between DTG/3TC and individual components previously considered appropriate during the July 2019 submission (paragraphs 6.19 and 7.2, July 2019 DTG/3TC PSD)
Therapeutic claim: effectiveness	Based on evidence presented, DTG/3TC is non-inferior in terms of effectiveness in comparison to Biktarvy, Genvoya, Odefsey, Juluca and Triumeq for the treatment of HIV infection.
Therapeutic claim: safety	Based on evidence presented, DTG/3TC is non-inferior in terms of safety in comparison to Biktarvy, Genvoya, Odefsey, Juluca and Triumeq for the treatment of HIV infection
Evidence base	<ul style="list-style-type: none"> Direct randomised trial: TANGO: 48 week analyses <ul style="list-style-type: none"> Extended assessment of harms: DTG/3TC July 2019 PBAC submission and DTG, Triumeq, DTG/3TC PBRER 2019
Equi-effective doses	Individual components: DTG/3TC (50/300 mg) equivalent to DTG 50 mg + 3TC 300 mg
Direct medicine costs	<ul style="list-style-type: none"> Part 1 (individual components): cost-minimised to DTG +3TC; Part 2 (alternative FDC triple therapy): cost-minimised to Biktarvy, Triumeq, Genvoya, Odefsey, Juluca
Other costs or cost offsets	<ul style="list-style-type: none"> ABC: HLA-B*5701 testing prior to the commencement (MBS Item 71203/73323); Tenofovir: assessment of urinary protein and glucose every 6 months (DHHS 2018; MBS Item: 66503)

Source: Table 45, p63 of the submission

3TC = lamivudine; ABC = abacavir; BIC = bictegravir; DHHS = Department of Health and Human Services; DTG = dolutegravir; ELV/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FTC = emtricitabine; HIV = human immunodeficiency virus; HLA = human leukocyte antigen; MBS = Medicare Benefits Schedule; PBAC = Pharmaceutical Advisory Committee; PBRER = Periodic Benefit Risk Evaluation Report; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

- 6.24 The equi-effective doses were derived from the recommended adult daily dose (TGA-approved/draft product information) for the intervention (Dovato) and the individual component medicines (DTG + 3TC).
- 6.25 A difference in MBS costs for monitoring requirements was expected between DTG/3TC and the alternative FDC triple therapies containing abacavir (ABC) and tenofovir (Biktarvy, Triumeq, Genvoya, Odefsey):
- Abacavir (ABC): human leukocyte antigen (HLA)-B*5701 testing prior to the commencement (MBS Item 71203/73323; \$34.50)
 - Tenofovir: urinary protein and glucose at baseline and every 6 months (MBS Item: 66503; \$9.95 at baseline, 6 months, and 12 months)
- 6.26 The CMA approach for DTG/3TC versus cost of individual components was reasonable as the TGA has accepted they are bioequivalent. The CMA approach versus the alternative ART regimens relied on the PBAC accepting that TBRs could act as a proxy for other three-drug FDCs.

6.27 Part 1 of the CMA, DTG/3TC cost-minimised against the individual components, demonstrated the lowest cost method for DTG/3TC. The CMA included prices current as of April 2020 and was consistent with the current PBS price for treatment naïve patients. DTG/3TC was less costly than Symtuza, which was not included as a comparator in the submission. Table 10 presents the results of the cost-minimisation analysis.

Table 10: Results of CMA

	Drug costs (AEMP)				Additional monitoring costs	Total costs	
	Treatment		30 days	1 year	1 year	1 year	
Part 1: Individual components	DTG (50 mg)	Tivicay	\$632.27	\$697.78	\$8,495.50	NA	\$8,495.50
	3TC (300 mg)	lamivudine	\$65.51				
Part 2: Alternative FDC triple therapy	DTG/ABC/3TC (50/600/300 mg)	Triumeq	\$830.03	\$10,105.62	MBS Item 71203/73323: \$34.50 at commencement	\$10,140.12	
	BIC/TAF/FTC (50/25/200 mg)	Biktarvy	\$900.34	\$10,961.64	MBS Item 66503: \$9.95 every 6 months (baseline, month 6, month 12) = \$29.85	\$10,991.49	
	ELV/c/TAF/FTC (150/150/10/200 mg)	Genvoya	\$958.06	\$11,644.38		\$11,694.28	
	RPV/TAF/FTC (25/25/200 mg)	Odefsey	\$958.06	\$11,644.38		\$11,694.28	
	DTG/RPV (50/25 mg)	Juluca	\$842.43	\$10,265.59	NA	\$10,256.59	

Source: Table 47, p64 of the submission, submission cost-minimisation and financial impact worksheets.

3TC = lamivudine; ABC = abacavir; AEMP = approved ex-manufacturer price; BIC = bictegravir; c = cobicistat; DRV = darunavir; DTG = dolutegravir; ELV/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FTC = emtricitabine; HIV = human immunodeficiency virus; NA = not applicable; RPV = rilpivirine; TAF = tenofovir alafenamide

Drug cost/patient/year

6.28 The drug cost per patient per year is \$8,783.96 based on an DPMQ of \$1,442.95, a pack size of 60 tablets and 365.25 days in a year ($\$1,442.95/60 \times 365.25 = \$8,783.96$). This compares with \$8,860.84 (DPMQ dolutegravir [$\$1,311.93$] + DPMQ for lamivudine [$\$143.65$])/60 x 365.25) for DTG + 3TC taken concomitantly. Treatment is ongoing; it is expected that patients would remain on ART treatment for the duration of their life.

Estimated PBS usage & financial implications

6.29 This submission was not considered by DUSC.

6.30 The submission used a hybrid epidemiological and market share approach to estimate use in patients who are treatment-experienced, derived from the prevalent HIV treated population, overlaid with the proportion of patients who are virologically suppressed and switching therapy. The approach was consistent with the July 2019 submission for treatment-experienced patients, however some of the inputs were updated. Table 11 presents the key inputs for the financial estimates.

Table 11: Key inputs for financial estimates

Parameter	Value applied, source, and change from July 2019	Comment
Comparator market share data	Dec 2018 to Nov 2019 PBS/RPBS services for: Triumeq Tivicay, Descovy, Truvada (TDF/FTC several brands) ^a , Biktarvy, Genvoya, Odefsey, and Juluca Delisted TDF/FTC based 3DRs appropriately distributed to Genvoy and Odefsey	Appropriate. Uptake from DTG and 3TC taken concomitantly not considered.
Estimated DTG/3TC uptake		
Prevalent treated population	20,000 to < 30,000 (Year 1) to 30,000 to < 40,000 (Year 6) Forecast from Kirby Institute data and PBS 10% sample. Similar to July 2019 submission (prevalent – incident) population.	Growth of prevalent population potentially overestimated due to PrEP
Proportion switching ART	43% (Year 1) and 24% (Years 2-6) Based on 10% PBS sample data for switching after Biktarvy listing (limited detail provided) and long-term average. Increased from July 2019 submission: 34.9% (Year 1) and 20.4% (Years 2-6)	Potentially overestimated. Advisory board reported 19% of patients switched to optimise ART.
Proportion virologically suppressed	95% (Kirby Institute 2018). Unchanged	Appropriate
Eligible for DTG/3TC	60% (Advisory board 2018). Unchanged	Unchanged. Mean was 55%. Ranged from 10% to 90%. Uncertain as survey question poorly worded.
Uptake	25% (Year 1) and 33% (Year 2-6). Increased from July 2019 submission 19.9% (Year 1) and 11.6% (Years 2-6)	Likely overestimated. Uncertain desirability of 2DRs in practice. Relatively small number of patients would seek to change regimen. Juluca [®] absorbed a portion of switch patients willing to use 2DR (para 7.9, July 2019 PSD). Increased from July 2019 submission (19.1% in Year 1, then 11.6%).
Persistence to therapy	92% (Triumeq [®] discontinuation in PBS 10% sample) Decreased from 94.4% in July 2019 submission	Appropriate
% comparator market eligible for DTG/3TC	24.36% (Year 1) to 48.17% ^b	Appropriate
DTG/3TC uptake	25% (Year 1) to 30.83% (Year 6) ^c	Likely overestimated
Treatment-related monitoring costs	ABC hypersensitivity testing (MBS Item 73323) Urine protein and urine glucose (MBS Item 66503): (Year 1: 3 tests; Year 2 and beyond: 2 tests per year) for TAF/TDF based regimens. Unchanged	Appropriate

Source: Table 49, pp65-66 of the submission; July 2019 DTG/3TC submission and Section 4 spreadsheet
 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; DR = drug regimen; DTG = dolutegravir; FTC = emtricitabine; HIV = human immunodeficiency virus; MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme; PrEP = pre-exposure prophylaxis; PSD = public summary document; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate
^a The brand Truvada was delisted from the PBS on 1 April 2020 but generic versions are PBS-listed
^b Calculated as eligible virologically suppressed patients switching ART/prevalent treated population
^c Calculated as DTG/3TC treated patients (eligible virologically suppressed patients switching ART × uptake × persistence)/ eligible virologically suppressed patients switching ART

6.31 Compared with the July 2019 submission, the submission removed assumptions of any switching from Stribild and Eviplera which were delisted from the PBS. The submission did not include Atripla.

- 6.32 Compared with the July 2019 submission, the submission estimated that a higher proportion of treatment-experienced patients would switch ART regimens. The submission calculated revised switch rate using 10% PBS sample data in the six months following the listing of Biktarvy (March 2019 to September 2019). The financial estimates utilised switch rates of 43% for Year 1 (corresponding to the first 6 months of listing for Biktarvy) and 24% for Years 2-6 (based on the long-term average). It is likely that patients would have a greater preference for a new 3DR (e.g. Biktarvy) compared with a 2DR (e.g. DTG/3TC). Hence the use of Biktarvy as a proxy likely resulted in an overestimated switch rate for DTG/3TC. The submission also increased the estimated uptake of DTG/3TC from the July 2019 submission. The PBAC previously considered the eligible treatment-experienced population and uptake in this group was likely overestimated (paragraph 7.9, DTG/3TC PSD, July 2019 PBAC meeting).
- 6.33 There was uncertainty associated with estimates for the proportion of patients applicable for DTG/3TC (unchanged from July 2019) and DTG/3TC uptake (increased since July 2019) as they were derived from Advisory Board advice. Assuming the PBS and TANGO eligibility criteria are similar, the Advisory Board may have underestimated the proportion of patients eligible for DTG/3TC (60% vs. 81%).
- 6.34 Table 12 presents the estimated use and financial implications of DTG/3TC.

Table 12: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
DTG/3TC switch patients						
July 2019 submission						
Scripts replaced						
July 2019 submission						
Estimated financial implications of DTG/3TC						
Cost to PBS/RPBS less co-payments	\$	\$	\$	\$	\$	\$
Estimated financial implications for replaced ARTs						
Cost to PBS/RPBS less co-payments	-\$	-\$	-\$	-\$	-\$	-\$
Net financial implications						
Net cost to PBS/RPBS	-\$	-\$	-\$	-\$	-\$	-\$
Net cost to MBS	-\$	-\$	-\$	-\$	-\$	-\$
Net cost to PBS/RPBS/MBS	-\$	-\$	-\$	-\$	-\$	-\$

Source: Tables 92-94, pp126-127, Tables 97-98, p 129, and Table 102, p131 of the submission; Section 4 of the July 2019 DTG/3TC submission

3TC = lamivudine; DTG = dolutegravir; MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Schedule of Pharmaceutical Benefits

Note: The July 2019 submission projected financial impact from 2019 to 2024 (Years 1 to 6). The current submission projected financial impact from 2021 to 2026.

The redacted table shows that at Year 6, the estimated number of DTG/3TC switch patients was 500 to < 5,000 (compared to 500 to < 5,000 for the July 2019 submission); the number of scripts replaced was 10,000 to < 20,000 (compared to 10,000 to < 20,000 for the July 2019 submission); and the net cost to the PBS would be a net cost saving.

- 6.35 The submission likely overestimated the utilisation of DTG/3TC. The estimated number of DTG/3TC prescriptions was higher in the current submission than the July 2019 estimates for the treatment-experienced population. This was due to the current submission assuming a higher proportion of patients switching treatment and higher uptake of DTG/3TC. In its July 2019 consideration:
- The PBAC advised that the use of 3DRs in practice is well-established and it is unclear how many patients will seek to switch to a regimen with fewer drugs;
 - The PBAC considered the eligible treatment-experienced population and likely uptake of DTG/3TC in this group was likely overestimated. The PBAC considered there is a place for 2DRs in treatment-experienced patients and while some patients may realise a safety benefit, it was likely a relatively small number of patients would seek to change regimen; and,
 - The PBAC noted Juluca was already listed on the PBS and considered it may have already absorbed a portion of the treatment-experienced market willing to switch to a 2DR (paragraph 7.9, DTG/3TC PSD, July 2019 PBAC meeting).
- 6.36 The Pre-PBAC Response argued that the populations that may switch to DTG/3TC or Juluca were different populations and DTG/3TC was expected to be suitable for more patients, as Juluca was contraindicated for patients who take a proton pump inhibitor (which was approximately 12% of the Australian population, based on Daniels 2020²). The Sponsor also noted that DTG/3TC was associated with fewer drug-drug interactions.
- 6.37 The submission estimated the listing of DTG/3TC would result in a net cost saving in Year 6, and a total net cost saving in the first 6 years of listing. The total savings including MBS cost offsets over the first 6 years was \$40 million to < \$50 million. The estimated savings to the PBS/RPBS were based on DTG/3TC replacing more expensive therapies. The PBAC agreed with the evaluation that these savings could be substantially lower if the estimated population treated with DTG/3TC were smaller due to lower uptake or smaller proportion of patients being eligible for treatment.

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 (Community Access), Authority Required (STREAMLINED) listing of combination dolutegravir with lamivudine (DTG/3TC) be extended to allow use in patients with HIV infection who have previously been treated with an alternative anti-retroviral therapy (ART) regimen.
- 7.2 The PBAC's recommendation for listing was based on, among other matters, its

² Daniels, B., Pearson, S.-A., Buckley, N. A., Bruno, C., & Zoega, H. (2020). Long-term use of proton-pump inhibitors: whole-of-population patterns in Australia 2013–2016. *Therapeutic Advances in Gastroenterology*. <https://doi.org/10.1177/1756284820913743>

assessment that DTG/3TC would be acceptably cost-effective in the ART-experienced population on a cost minimisation basis with its component drugs, dolutegravir and lamivudine taken concomitantly. The equi-effective doses are 1 tablet of DTG/3TC (50 mg dolutegravir/300 mg lamivudine) once daily and one tablet each of dolutegravir 50 mg and lamivudine 300 mg once daily.

- 7.3 The PBAC considered it was reasonable to align the listing of DTG/3TC for ART-experienced patients with other ART regimens and to amend the current continuing criterion from, 'Patient must have previously received PBS-subsidised therapy with this drug for this condition' to, 'Patient must have previously received PBS-subsidised therapy for HIV infection' to permit switches between other ART regimens and DTG/3TC.
- 7.4 The PBAC reaffirmed its view there was a place for DTG/3TC (and two-drug regimens more broadly) in treatment-experienced patients. The PBAC considered that while some patients may realise a safety benefit, particularly in the context of an aging prevalent population where polypharmacy and comorbidities may lead to some interest in effective regimens with fewer drugs, it was likely that only a relatively small number of patients who are stable on current treatment would seek to change regimen.
- 7.5 The PBAC considered the nominated primary comparator of dolutegravir and lamivudine taken concomitantly was reasonable and further considered the nominated secondary basket of comparators was reasonable, consistent with its conclusions for DTG/3TC in the ART-naïve population. The Committee was satisfied the tenofovir-based regimens (TBRs) in the TANGO trial were a reasonable proxy for the non-TBRs included in the basket of secondary comparators. The PBAC reaffirmed its view from when it considered dolutegravir with rilpivirine (Juluca[®]) at its July 2018 meeting that regimens containing efavirenz were of inferior safety to non-efavirenz containing regimens. The Committee noted that since the ART-naïve recommendation of DTG/3TC in July 2019, the combination drugs Stribild (ELV/c/FTC/TDF) and Eviplera (RPV/FTC/TDF) had been delisted from the PBS, and were reasonably excluded as comparators. The PBAC considered the exclusion of protease inhibitor containing regimens (i.e. Symtuza) was also reasonable as clinical guidelines generally reserved these regimens only for certain clinical situations.
- 7.6 The PBAC noted the submission presented the 48-week results of the TANGO trial, which was specifically designed to assess the efficacy and safety of DTG/3TC in ART-experienced patients who switched from a TBR. The PBAC accepted the longer-term 48-week data from the TANGO trial presented in this submission provided greater certainty as to the comparative effectiveness and safety of DTG/3TC in ART-experienced patients compared to the 24-week FDA Snapshot analysis presented in the previous submission.

- 7.7 The PBAC considered the results of the 48-week data from the TANGO trial supported a conclusion that DTG/3TC is of non-inferior comparative effectiveness to TBRs and the other non-TBR comparators nominated in the submission.
- 7.8 With regards to comparative safety, the PBAC noted DTG/3TC was associated with a significantly higher incidence of fatigue and seasonal allergy and a significantly lower incidence of bronchitis compared with TBRs, and further noted that discontinuations due to adverse events were more frequent in the DTG/3TC arm of the TANGO trial. The PBAC considered it was reasonable to expect that patients who were stable on current treatment and switching to an alternative therapy under open label conditions may experience new adverse events associated with the new regimen. On balance, the PBAC considered the safety profile of DTG/3TC to be consistent with the known profiles of the dolutegravir and lamivudine, and likely to be non-inferior to the nominated comparators.
- 7.9 The PBAC noted the TANGO trial did not present any additional information on the potential for development of resistance as none of the patients in the DTG/3TC arm of the trial met the criteria for confirmed virologic failure.
- 7.10 The PBAC noted the submission requested listing at the same price as its component drugs (and the same price for which DTG/3TC is currently listed on the PBS for ART-naïve patients) and considered this was reasonable as DTG/3TC is currently the least costly of the nominated comparators.
- 7.11 The PBAC noted the submission assumed a higher uptake of DTG/3TC amongst treatment-experienced patients than the July 2019 submission. The PBAC reaffirmed its view that the uptake of DTG/3TC in treatment-experienced patients was likely overestimated, as the place of three-drug regimens was well established and patients and clinicians may be reluctant to switch patients who are stable on their current therapy. However, the PBAC noted that, as the least costly option amongst the nominated basket of comparators, the listing of DTG/3TC would only substitute for therapies that are more expensive. The PBAC considered that while the listing of DTG/3TC for ART-experienced patients would represent a saving to the PBS, it was likely to be less than that estimated in the submission.
- 7.12 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because DTG/3TC is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over its component drugs, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009 for Pricing Pathway A were not met.
- 7.13 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 Amend existing Continuing treatment restriction to appear as follows:

Name, strength, form, pack quantity	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
DOLUTEGRAVIR with LAMIVUDINE dolutegravir 50 mg + lamivudine 300 mg tablet, 30	11843H	2	60	5	Dovato

Restriction Summary 9910 / Treatment of Concept 9934

Concept ID (for internal Dept. use)	Category / Program: Section 100 (Highly Specialised Drugs Program) - Community Access (Code CA)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners
	Restriction Type / Method: <input checked="" type="checkbox"/> Authority Required – Streamlined (9934)
9007	Indication: HIV infection
Edit	Treatment Phase: Continuing or switching treatment
12372	Clinical criteria:
Remove 12371 Insert 9018	Patient must have previously received PBS-subsidised therapy for HIV infection

8.2 Remove Grandfather listing for 1 December 2020 (Restriction Summary 9909).

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

ViiV Healthcare welcomes the PBAC's decision to recommend Dovato for the treatment of HIV-infection in anti-retroviral (ART) treatment-experienced patients.