PUBLIC SUMMARY DOCUMENT
Product: Maraviroc, tablets, 150 mg and 300 mg, Celsentri®
Sponsor: ViiV Healthcare
Date of PBAC Consideration: November 2012

1. Purpose of Application

An application requesting MBS listing of genotypic tropism testing and PBS listing of maraviroc in combination with other antiretroviral agents for the targeted treatment of all patients with CCR5-tropic HIV-1 infection.

To seek an extension of the current Section 100 (Highly Specialised Drugs Program) Private Hospital Authority Required and Public Hospital Authority Required (Streamlined) listing to include first line treatment, in combination with other antiretroviral agents, of a patient with CCR5-tropic HIV-1 infection, who meets certain criteria.

Highly Specialised Drugs are medicines for the treatment of chronic conditions, which, because of their clinical use or other special features, are restricted to supply to public and private hospitals having access to appropriate specialist facilities.

2. Background

Maraviroc was considered at the November 2008 and November 2009 PBAC meetings for treatment in combination with other antiretrovirals, of antiretroviral experienced adult patients infected with only CCR5-tropic HIV-1 (i.e. treatment experienced patients).

Maraviroc has not been considered by the MSAC or PBAC for all adult patients infected with only CCR5-tropic HIV-1.

Genotypic tropism testing has not been considered by the MSAC or PBAC for treatment experienced adult patients infected with HIV-1. Genotypic tropism testing was funded for treatment experienced patients in Australia by the sponsor under a risk-share agreement at time of submission. The submission noted that if genotypic tropism testing was listed on the MBS, external funding of the test by the sponsor would cease.

3. Registration Status

The TGA has not approved a proprietary genotypic tropism test for detecting the presence of X4-using viruses.

Maraviroc, in combination with other antiretroviral medicinal products, is indicated for adult patients infected with only CCR5-tropic HIV-1. The use of other active agents with maraviroc is associated with a greater likelihood of treatment response.

4. Listing Requested and PBAC's View

Section 100 (Highly Specialised Drugs Program)
Authority required (Private Hospital)
Authority required (STREAMLINED) (Public Hospital)
Initial treatment of CCR5-tropic HIV-1 infection in combination with other antiretroviral agents in a patient with a CD4 count of less than 500 per cubic millimetre or symptomatic HIV-1 disease;

Continuing treatment of HIV-1 infection in combination with other antiretroviral agents where the patient has previously received PBS-subsidised therapy for HIV-1 infection.

A tropism assay to determine CCR5 only strain status is required prior to initiation. Individuals with CXCR4-tropism demonstrated at any time point are not eligible.

For PBAC's view, see Recommendation and Reasons.

5. Clinical Place for the Proposed Therapy

Human Immunodeficiency Virus (HIV) is an infectious disease which can progress to Acquired Immunodeficiency Syndrome (AIDS). There are currently 21 individual drugs available to treat these patients, of which 17 are available for initial treatment. Most Highly Active Antiretroviral Therapy (HAART) regimens consist of three drugs: two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and either a non-nucleoside reverse transcriptase inhibitor (NNRTI), protease inhibitor (PI), integrase inhibitor (e.g. raltegravir), or an entry inhibitor (e.g. maraviroc). The proposed listings were claimed by sponsor to provide another alternative which achieves similar outcomes.

For PBAC's view, see Recommendation and Reasons.

6. Comparator

The submission nominated the phenotypic tropism test Enhanced Sensitivity Trofile Assay (ESTA) as the main comparator for genotypic tropism testing, for both treatment-experienced and treatment-naïve patients. Although neither the original *Trofile*® phenotypic tropism test nor the ESTA phenotypic tropism test is available in Australia, both were identified during application process as relevant analytical comparators to estimate the implications of using genotypic tropism testing in predicting the variation in treatment effect of maraviroc for use in Australia. The PBAC has requested MSAC advice about genotypic tropism testing.

The sponsor nominated efavirenz as the main comparator for the proposed maraviroc listing based on Australian HIV Treatment Guidelines, a survey of 14 HIV physicians and the March 2010 raltegravir Public Summary Document.

For PBAC's view, see Recommendation and Reasons.

7. Clinical Trials

Treatment-naïve patients

Treatment effectiveness was assessed by the MERIT randomised trial, which compared maraviroc with efavirenz in a HIV-1 treatment-naïve population identified as R5-tropic by the *Trofile* assay and subsequently reanalysed after subgroups were identified using different tropism tests.

Treatment-experienced patients

Treatment effectiveness was assessed by the MOTIVATE randomised trials, which were presented in the 2009 PBAC submission. They compared maraviroc with placebo in a HIV 4th-line population identified as R5-tropic by the *Trofile* assay and subsequently reanalysed after subgroups were identified using different tropism tests.

Patients enrolled in both MERIT (treatment naïve) and MOTIVATE (4th line) were initially screened for R5-tropic virus using the phenotypic *Trofile* test, however were subsequently re-screened using ESTA (reported in clinical trial reports) to create one subgroup and genotypic tropic testing to create other subgroups. Genotypic tropism testing was conducted with population based sequencing for MOTIVATE and deep sequencing for MERIT, and results were variously reported for both the clonal model and the clinical model of the geno2pheno algorithm and for various false positive rates (reported in McGovern 2010, Swenson 2011, and McGovern 2012). Hence there was evidence regarding the effectiveness of maraviroc in subgroups of patients originally deemed negative for X4-tropism by *Trofile* who were subsequently deemed negative for X4-tropism by ESTA or by various approaches to genotypic tropism testing.

The following published trials were presented in the submission.

Trial ID/First Author	Protocol title/ Publication title	Publication citation
Linked evidence – prognostic studies		
Shepherd et al	Emergence and persistence of CXCR4-tropic HIV-1 in a population of men from the multicentre AIDS cohort study.	*Journal of Infectious Diseases* (2008)*;* 198:1104-12.
Waters et al	The impact of HIV tropism on decreases in CD4 cell count, clinical progression, and subsequent response to a first antiretroviral therapy regime.	*Clinical Infectious Diseases* (2008)*; 46:1617-1623.*
Moyle et al	Epidemiology and predictive factors for chemokine receptor use in HIV-1 infection.	*The Journal of Infectious Diseases* (2005); *191:866-872.*
Brumme et al	Molecular and clinical epidemiology of CXCR4-using HIV-1 in a large population of antiretroviral-naïve individuals.	*The Journal of Infectious Diseases* (2005); *192:466-474*
de Mendoza et al	Prevalence of X4-tropic viruses in patients recently infected with HIV-1 and lack of association with transmission of drug resistance.	*Journal of Antimicrobial Chemotherapy* (2007); *59:698-704.*
Poveda et al	Prevalence of X4-tropic HIV-1 variants in patients with differences in disease stage and exposure to antiretroviral therapy.	*Journal of Medical Virology* (2007); *79:1040-1046.*
Linked evidence – diagnostic or predictive accuracy studies		
Swenson et al	Deep V3 sequencing for HIV type 1 tropism in treatment naïve patients: A reanalysis of the MERIT trial of maraviroc.	*Clinical Infectious Diseases* (2011); 53:732-742.
Svitcher et al	Performance of genotypic tropism testing in clinical practice using the enhanced sensitivity version of Trofile as reference assay: Results from the OSCAR Study Group.	*New Microbiologica* (2010); 33:195-206
Sanchez et al	Performance of genotypic algorithms for predicting HIV-1 tropism measured against the enhanced sensitivity Trofile co-receptor tropism assay.	*Journal of Clinical Microbiology* (2010)*;* 48:4135-4139

Trial ID/First Author	Protocol title/ Publication title	Publication citation
Prosperi et al	Comparative determination of HIV-1 co-receptor tropism by Enhanced Sensitivity Trofile, gp120 V3-loop RNA and DNA genotyping.	*Retrovirology* (2010); 7:56
Sanchez et al	A highly sensitive and specific model for predicting HIV-1 tropism in treatment experienced patients combining interpretation of V3 loop sequences and clinical parameters.	*Journal of Acquired Immune Deficiency Syndromes* (2011); 56:51-58.
McGovern et al	Population-based V3 genotypic tropism assay: a retrospective analysis using screening samples from the A4001029 and MOTIVATE studies	*AIDS* (2010); 24:2517-2525
Linked evidence – treatment randomised trials		
MERIT (Study A4001026)		
Cooper et al.	Maraviroc versus Efavirenz, Both in Combination with Zidovudine-Lamivudine, for the Treatment of Antiretroviral-Naïve Subjects with CCR5-Tropic HIV-1 Infection.	*The Journal of Infectious Disease* (2010); 201:803-813.
Sierra-Madero et al.	Efficacy and Safety of Maraviroc Versus Efavirenz, Both with Zidovudine/Lamivudine: 96-Week Results from the MERIT Study.	*HIV Clinical Trials* (2010); 11(3):125-132.
Craig et al.	Week 48 Results from the Phase III study A4001026 (MERIT) – Time to loss of virologic response (TLOVR) virology analysis of failures in the enhanced Trofile-censored population.	*Antiviral Therapy* (2009); 14(5 Suppl.1):A50.

8. Results of Trials

The antiviral activity at week 48 as measured using *Trofile* met the criteria for noninferiority for <400 copies but not for less than 50 copies/mL (using the Primary analysis). The analysis based on patients confirmed as R5-tropic using ESTA had better outcomes than the patients screened using *Trofile* and, when using the cohort confirmed as R5-tropic using ESTA, the noninferiority criteria was achieved. The results of antiviral activity (viral load HIV-1 RNA less than 400 copies/mL and/or less than 50 copies/mL) at Week 48 and 96 in R5-tropic patients enrolled in MERIT are shown below.

Study ID	Maraviroc 300 mg BID n with event/N (%)	Efavirenz 600 mg QD n with event/N (%)	Stratified Difference (%) (Lower 97.5% Confidence Bound)	Raw Risk Difference RD* (%) (95% CI)	Raw Relative risk RR* (95% CI)
WEEK 48					
<400 copies/mL, (Primary analysis), Trofile	254/360 (70.6)	264/361 (73.1)	-3.0 (-9.5)	-2.6 (-9.1, 4.0)	0.96 (0.88, 1.06)
<400 copies/mL, post-hoc reanalysis (ESTA)	228/311 (73.3)	219/303 (72.3)	0.6 (-6.4)	1.0 (-6.0, 8.1)	1.01 (0.92, 1.12)
<50 copies/mL, (Primary analysis), Trofile	***235/360 (65.3)***	***250/361 (69.3)***	***-4.2 (-10.9)***	***-4.0 (-10.8, 2.9)***	***0.94 (0.85, 1.04)***

Study ID	Maraviroc 300 mg BID n with event/N (%)	Efavirenz 600 mg QD n with event/N (%)	Stratified Difference (%) (Lower 97.5% Confidence Bound)	Raw Risk Difference RD* (%) (95% CI)	Raw Relative risk RR* (95% CI)
<50 copies/mL, post-hoc reanalysis (ESTA)	213/311 (68.5)	207/303 (68.3)	-0.2 (-7.4)	0.2 (-7.2, 7.5)	1.00 (0.90, 1.12)
WEEK 96					
<50 copies/mL, ESTA R5 reanalysis	***183/311 (58.8)***	***190/303 (62.7)***		***-4.0 (-11.6, 3.9)***	***0.94 (0.83, 1.07)***

*Indicate figures calculated during the evaluation and not provided by the sponsor; Bolded italics indicates that the prespecified noninferiority margin of -10% was not satisfied
BID: twice daily, QD: once daily

The antiviral activity at week 96 based on patients confirmed as R5-tropic using ESTA had better outcomes than the patients screened using *Trofile*. Stratified percentage difference for the <400 copies/mL measured by *Trofile*, <400 copies/mL measured by ESTA in post-hoc reanalysis and <50 copies/mL measured by *Trofile* subject groups, all favoured efavirenz over maraviroc.

The submission also reported antiviral activity (viral load < 50 copies/mL) at 48 weeks based on the re-analysis in Swenson (2011) reporting genotype tropism testing with deep sequencing compared with the original *Trofile* and also the ESTA-based re-analysis.

Results of antiviral activity (viral load HIV-1 RNA <50 copies/mL) at Week 48 in R5-tropic patients enrolled in MERIT whose virus was also examined by genotypic tropism testing using geno2pheno with deep-sequencing are shown in the table below.

	Maraviroc 300 mg BID n with event/N (%)	Efavirenz 600 mg QD n with event/N (%)	Raw Risk Difference RD (%)	Stratified Difference (%) (Lower 97.5% Confidence Bound)
Original Trofile assay				
R5	227/347 (65.42)	238/346 (68.79)	-3.37	-3.73 (-10.61)
Re-analysis using deep sequencing of V3 loop and geno2pheno with FPR 3.5%				
R5	210/312 (67.3)	217/316 (68.67)	-1.36	-1.48 (-8.67)
Non-R5	17/35 (48.6)	21/30 (70.0)	-21.43	-42.19 (-60.71)
Re-analysis using ESTA				
R5	205/300 (68.3)	196/290 (67.59)	0.75	0.17 (-7.21)
Non-R5	22/47 (46.8)	42/56 (75.0)	-28.19	-31.15 (-48.87)

Antiviral activity (viral load <50 copies/mL) at 48 weeks was also reanalysed following re-testing with ESTA and genotype tropism testing with population based sequencing and reported by McGovern (2012).

Results of antiviral activity (viral load HIV-1 RNA <50 copies/mL) at Week 48 in R5-tropic patients enrolled in MERIT whose virus was also examined by genotypic tropism testing using geno2pheno with population-based sequencing are shown in the table below.

	Maraviroc 300mg BID n with event/N (%)	Efavirenz 600mg QD n with event/N (%)	Stratified Difference (%) (Lower 97.5% Confidence Bound)	Raw Risk Difference RD (%)

	Maraviroc 300mg BID n with event/N (%)	Efavirenz 600mg QD n with event/N (%)	Stratified Difference (%) (Lower 97.5% Confidence Bound)	Raw Risk Difference RD (%)
Population-based sequencing of V3 loop and geno2pheno with FPR 5.75%				
R5	215/323 (66.6)	221/324 (68.2)	NR (-8.95)	-1.6
X4-using	14/29 (48.3)	23/29 (79.3)	NR (-61.4)	-31.0
Trofile assay				
R5	235/360 (65.3)	250/361 (69.3)	-4.2 (-10.9)	-4.0
ESTA assay				
R5	213/311 (68.5)	207/303 (68.3)	-0.2 (-7.4)	0.2
X4-using	22/49 (44.9)	43/58 (74.1)	NR (-49.4)	-29.2

The results illustrated the importance of the accuracy of testing in identifying patients with X4-using virus so that they received an effective HAART regimen. The submission noted that, based on the data above, ESTA and the geno2pheno algorithm in combination with deep sequencing performed similarly in predicting virological response to maraviroc. The PBAC noted the trial was not powered to test for differences in antiviral activity when different tests were utilised.

For PBAC's view, see Recommendation and Reasons.

9. Clinical Claim

The submission claimed that genotypic sequencing followed by bio-informatic tropism prediction represented an acceptable substitute for phenotypic tropism determination in treatment-naïve patients.

The submission made no claim regarding the superiority or non-inferiority of genotype tropism testing and phenotype tropism testing in treatment-experienced HIV-1 patients.

The submission described maraviroc as non-inferior in terms of comparative effectiveness and superior in terms of comparative safety over efavirenz in HIV-1 treatment-naïve R5-tropic patients.

The submission also stated that those patients obtaining false negative results (i.e. X4-using patients identified as R5-tropic) will experience no negative consequences as a result of inappropriate treatment with maraviroc.

For PBAC's view, see Recommendation and Reasons.

10. Economic Analysis

The submission presented two economic evaluations; one in treatment-naïve patients and one in treatment-experienced patients.

Treatment-naive model:

The model was a single-cohort Markov model that compared costs and outcomes of maraviroc available from first-line compared to maraviroc available only in fourth-line treatments, using genotypic testing to assess tropism status. In the comparator arm, people move through a typical sequence of three lines of therapy. At the end of the third-line they are allocated either to a fourth-line that includes maraviroc, or proceed directly to the salvage state, depending on the results of the genotypic tropism test. In the proposal arm, people start

with a genotypic tropism test and depending on the result of the test they are either allocated to the same treatment sequence modelled in the comparator arm or to a typical treatment sequence that consists of four lines of therapy with maraviroc as first-line therapy.

The submission claimed that the proposed scenario (maraviroc available from first-line) dominates the current scenario (maraviroc available only after the failure of third-line therapy). The basis of this claim was a stepped economic evaluation (cost-utility analysis) using rates of virologic failure from the MERIT trial, the MOTIVATE trial, and from the included literature. The treatment effect of maraviroc on virologic failure was assumed to apply across a 30 year time horizon. Utility weights were applied based on the literature (Schackman et al 2002).

During evaluation two errors were identified in the structure of the model which, when corrected, had the effect of reversing the results. The sponsor acknowledged these errors, and presented a revised model incorporating corrections to these errors. The results in the revised model were consistent with the original submission.

Treatment-experienced model:
The economic model for treatment-experienced patients presented clinical outcome data previously accepted by PBAC and applied this evidence to the use of a genotypic tropism test compared to a phenotypic tropism test. The structure of the economic model was based on the model in the 2008 submission to PBAC for maraviroc in treatment-experienced patients.

The updated model began with a cohort that, based on the tropism test results, receive either maraviroc plus optimised background therapy (OBT) or OBT alone. Patients could be in one of seven health states: six health states depending on CD4+ count or death. The time horizon of the model was 26 years and the cycle length was one month.

The submission presented a stepped economic evaluation (cost-utility analysis) that compared the incremental costs and benefits of maraviroc for treatment-experienced patients with genotypic compared to phenotypic tropism testing. The submission estimated an ICER in the range of $15,000-$45,000/QALY based on the proportion of patients achieving virologic success.

For PBAC's view, see Recommendation and Reasons.

11. Estimated PBS Usage and Financial Implications

The likely number of patients per year was estimated in the submission to be less than 10,000 in Year 5, at an estimated net saving per year to the PBS of less than $10 million in Year 5.

For PBAC's view, see Recommendation and Reasons.

12. Recommendation and Reasons

The major submission sought an extension of the current Section 100 (Highly Specialised Drugs Program) Private Hospital Authority Required and Public Hospital Authority Required (Streamlined) listing to include first line treatment, in combination with other antiretroviral agents, of a patient with CCR5-tropic HIV-1 infection, who meets certain criteria

The PBAC deferred consideration of this application to obtain advice, including from MSAC, on what proportions of patients with HIV-1 infection would be considered for tropism testing in the first-, second- and third-line settings, and on the likely identifying characteristics of these patients. Possible characteristics might include patients whose genotype antiretroviral testing (GART) indicates a high likelihood of resistance or intolerance to non-nucleoside reverse transcriptase inhibitors (NNRTIs) such as efavirenz.

The PBAC also requested MSAC advice on the details of implementation of genotypic tropism testing to support clinical decisions to use maraviroc. These details include minimal test performance characteristics such as the pre-specified false positive rate for detecting X4-using virus, the associated bioinformatic algorithm(s), the information to be entered into the algorithm(s), and the minimum viral load sufficient for sequencing. It was unclear how data generated from deep sequencing would be incorporated into the current bioinformatics algorithms.

The PBAC further requested advice from MSAC on the prevalence of R5-tropism in the limited populations identified for testing; the number of tests per patient treated with earlier maraviroc, which should reflect the frequency of repeat testing under the proposed implementation of genotypic tropism testing, and therefore the costs of such testing per patient treated with earlier maraviroc; and the overall increase in the cost of testing to support earlier use compared with current testing for the existing fourth-line listing of maraviroc.

The PBAC noted that the request was to extend the current fourth-line listing of maraviroc to an allow maraviroc to be used as part of a combination antiretroviral regimen earlier in the management of patients with HIV-1 infection, including patients who have not been treated previously (treatment-naïve). The PBAC accepted that there is a clinical need in a population that is currently managed by a small group of experienced prescribers. The Committee noted that the submission's proposed earlier use of maraviroc was not matched by its projected low rates of uptake following listing or by international guidelines for managing patients with HIV infection. These guidelines recommend maraviroc in the third tier of an "acceptable" first-line regimen on the grounds of being less satisfactory than "preferred" or "alternative" but may be selected for some patients.

The PBAC accepted that efavirenz, an NNRTI also used as part of a combination antiretroviral regimen was the appropriate comparator for maraviroc.

The PBAC noted several practical disadvantages for maraviroc compared with efavirenz: it is taken twice daily rather than once daily, it is not included in any combination tablet containing other antiretroviral agents. These have the potential to reduce patient adherence to the treatment regimen. However, the most important problem is that it is ineffective in patients with even a minimal amount of X4-tropic virus. The PBAC accepted that Australian pathology laboratories using these genotypic assays mostly specify the false positive rate for genotypic tropism testing as 20% to lower the risk of falsely reporting R5-tropism when X4-tropism is present. This reduces the risk of using maraviroc when it will be ineffective, but also increases the risk of not using maraviroc when it may be effective. The PBAC also noted that the turnaround time of 2 weeks and the proposed minimal viral load of 1,000 copies per mL were also practical reasons to expect a reduced uptake of maraviroc.

The PBAC noted difficulty in interpreting the retrospective comparisons of tropism testing methods presented in the submission because they were limited to samples from treatment-naïve patients already defined as R5-tropic using the *Trofile* assay to be recruited into the randomised trials of maraviroc. Although this is the only source of clinical data for maraviroc outcomes and for assessing the clinical utility of the tropism tests being compared, these comparisons do not reflect test performance in an Australian population which had not been pre-screened in this way. They also did not necessarily use the parameters of genotypic tropism testing which would apply in Australia.

The PBAC noted that the key randomised trial (MERIT) compared maraviroc and efavirenz as add-on to the same regimen of zidovudine and lamivudine in treatment-naïve patients identified as R5-tropic using the *Trofile* phenotypic tropism assay. The pre-specified non-inferiority margin of -10% risk difference in the proportion of patients achieving pre-specified viral load reductions was not met in the prespecified primary analysis and the numerical trends were mostly against maraviroc. Post hoc exclusion of small subgroups of X4-tropic patients identified using the "Enhanced Sensitivity Trofile Assay" (ESTA) phenotypic tropism assay or various definitions of genotypic tropism assays, and who showed substantially inferior results for maraviroc, meant that the results for maraviroc in the residual R5-tropic subgroups tended away from the non-inferiority threshold. The PBAC noted other concerns such as the high rate of drop-outs in the trial and a higher rate of resistance developing to the other components of the regimen in the maraviroc arm than in the efavirenz arm (although resistance also develops rapidly to efavirenz via a one-step mutation). Overall, the PBAC concluded that, at best and after using optimised testing to exclude patients with X4-tropic HIV, maraviroc is non-inferior to efavirenz in terms of antiviral activity.

The PBAC noted that there are effective alternative therapies in the requested earlier lines of therapy. This means that ineffective use of maraviroc-containing regimens in patients with X4-tropism would result in a net harm for patients, as indicated by the notably inferior results in the post hoc subgroups identified as being non-R5-tropic. In this regard, the PBAC noted the potentially important omission from the submission of a model that was capable of examining the consequences of varying test accuracy. Therefore the advice of MSAC was sought as to how best to implement an adequate standard of genotypic tropism testing to support clinical decisions about the use of maraviroc.

The PBAC agreed that maraviroc had a better toxicity profile than efavirenz in terms of fewer discontinuations due to adverse events and a better lipid profile, but noted that this was not translated into a discernible effect on utilities in the economic evaluation.

Although the PBAC accepted the structure of the modelled economic evaluation to compare proposed earlier use of maraviroc with current fourth-line use of maraviroc, it did not accept that the model reflected its clinical conclusion of non-inferiority at best. In particular, the PBAC agreed with the advice of the Joint ESCs, and rejected as implausible the results of the revised (but not independently evaluated model) improved QALYs and reduced costs. The PBAC noted that the Joint ESCs had listed several reasons why the model produced such implausible results favouring maraviroc:

- the choice of subsequent antiretroviral therapy regimens;
- the use of the numerically favourable open-label week 240 data rather than the numerically unfavourable blinded week 96 data for the transition from first- to second-line therapy;

- the assumption of an unchanged rate of virological failure beyond the duration of the trial period;
- the probability of virological failure per 16 weeks in the first line setting being based on data from 17 to 240 weeks, including data from the open-label phase of the trial;
- the assumption that there is no re-testing of not reportable results of the tropism test; and
- the failure to account for any false negatives for X4-tropism with genotypic tropism testing.

The financial implications reasonably assume a low uptake of testing (5% compared with 1% in the United States and 71% in the survey of experts conducted for the submission) and therefore of treatment, and project a small net cost for genotypic tropism testing and a small net saving for maraviroc by projecting substantial PBS cost offsets.

Overall, the PBAC considered that the submission failed to justify the substantial price advantage for maraviroc over efavirenz for earlier use than in the fourth-line setting. The PBAC suggested that a cost-minimisation approach would establish an acceptable price for this earlier use, noting that the maraviroc costs in this analysis would also need to include the additional costs of identifying which patients have R5-tropic HIV. Therefore the PBAC also requested a response from the applicant on the cost-minimisation analysis, which is to be considered when the other matters identified above as the basis for the deferral are provided to the Committee.

Recommendation:
Defer

13. 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.

14. Sponsor's Comment

ViiV Healthcare will respond to the requests of the PBAC in a future application.