AWMSG Secretariat Assessment Report – Limited submission

Dolutegravir/lamivudine (Dovato®▼) 50 mg/300 mg film-coated tablets

Company: ViiV Healthcare UK Ltd

Licensed indication under consideration: treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adults and adolescents above 12 years of age weighing at least 40 kg, with no known or suspected resistance to the integrase inhibitor class, or lamivudine.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Marketing authorisation date: 1 July 2019

Comparator(s)

The comparators included in the company's submission are combination antiretroviral three-medicine regimens:

- dolutegravir/abacavir/lamivudine (Triumeq®)
- efavirenz/emtricitabine/tenofovir disoproxil fumarate (Atripla®)
- emtricitabine/tenofovir disoproxil fumarate (Truvada®) plus dolutegravir (Tivicay®)
- emtricitabine/tenofovir disoproxil fumarate (Truvada®) plus darunavir/cobicistat (Rezolsta®)
- emtricitabine/tenofovir disoproxil fumarate (Truvada®) plus nevirapine
- emtricitabine/elvitegravir/cobicistat/tenofovir alafenamide fumarate (Genvoya®)
- emtricitabine/tenofovir disoproxil fumarate (Truvada®) plus raltegravir (Isentress®).

Limited submission details

The limited submission criteria were met based on:

- new formulation with a pro-rata or lower cost per treatment
- anticipated usage in NHS Wales is considered to be of minimal budgetary impact
- estimated small difference in cost compared to comparators.

Clinical effectiveness

- Dovato® is the first two-medicine single tablet regimen licensed for the treatment of HIV-1 in treatment-naïve and treatment-experienced patients.
- The individual components of Dovato® are licensed in combination with other antiretroviral medicines for the treatment of HIV-1 infection in adults and children: dolutegravir (Tivicay®) was previously recommended as an option for use by the All Wales Medicines Strategy Group (AWMSG); lamivudine did not meet the criteria for appraisal by AWMSG as it was granted marketing authorisation before 1 October 2010.

- Two pivotal phase III, randomised, double-blind studies (GEMINI 1 & GEMINI 2) evaluated the efficacy and safety of the two-medicine regimen (dolutegravir and lamivudine; n = 716) compared with a three-medicine regimen (dolutegravir and emtricitabine/tenofovir disoproxil fumarate; n = 717) for the treatment of HIV-1 infection in antiretroviral therapy-naive adults (≤ 10 days of previous treatment with any antiretroviral therapy). The two-medicine regimen showed non-inferior virological efficacy to the three-medicine regimen, based on the proportion of participants with HIV-1 RNA < 50 copies/ml, a standard measure of HIV-1 control, at week 48.
- A phase III, randomised, open-label study (TANGO) assessed the efficacy and safety of switching from a three-medicine, tenofovir alafenamide-based regimen (n = 372), to Dovato® (n = 369) in treatment-experienced adults with HIV-1 infection. The proportion of participants with HIV-1 RNA < 50 copies/ml at week 48 was similar in both arms and demonstrated non-inferiority.
- In a phase I, open-label, single-dose, crossover study, Dovato® was found to be bioequivalent to dolutegravir and lamivudine single agents.
- There are no clinical study data with Dovato® in the adolescent population. The Committee for Medicinal Products for Human Use (CHMP) confirmed that previous studies showed that dolutegravir and lamivudine pharmacokinetic exposures in adolescents are sufficiently similar to those in adults. The CHMP concluded that data from the bioequivalence study and supportive studies allowed extrapolation of the safety and efficacy data from the GEMINI studies and supports the adolescent indication for Dovato®.
- The company conducted a systematic literature review and Bayesian network meta-analysis to compare the efficacy and safety of dolutegravir and lamivudine to 13 existing antiretroviral triple-medicine regimens. The results suggested that dolutegravir and lamivudine was similar in efficacy and safety to the three-medicine regimens, however there was considerable between-study heterogeneity and the analysis was of treatment-naïve patients only.
- The safety profile of dolutegravir and lamivudine is well-established and supported by the GEMINI studies. The CHMP concluded that no new specific safety concerns for the dual treatment of dolutegravir plus lamivudine have been identified, and this is supported by the TANGO study.
- Clinical experts indicate the use of two medicines in the treatment of HIV-1 infection has potential benefits in terms of toxicity compared to the traditionally used three-medicine regimens.

Budget impact

- The company estimates that in Year 1 there are 2,282 patients in Wales eligible for treatment with Dovato® increasing to 2,625 patients in Year 5. This is based on 2017 HIV prevalence and incidence data for Wales reported by Public Health England.
- Based on the company's market share estimations, 205 patients will receive treatment with Dovato® in Year 1 increasing to 840 patients in Year 5.
- The budget impact analysis is based on Dovato® partly displacing all seven comparators. The company estimates the introduction of Dovato® would lead to a cost saving of [commercial in confidence figure removed] in Year 1 increasing to a cost saving of [commercial in confidence figure removed] in Year 5. This is based on Wales Patient Access Scheme (WPAS) prices for Dovato®, Triumeq® and Tivicay® and the list prices for the other comparators.
- The company conducted sensitivity analyses exploring price discounts for Genvoya® as it is associated with a WPAS. On the overall budget impact, varying

the list price of Genvoya® [confidential text removed] showed that Dovato® is likely to be cost-saving in all years.
- There are limitations to the company's budget impact calculations: estimates vary depending on which comparator is displaced and the budget impact is limited to the comparators included in the company's submission only (other available three-medicine regimens are not included). Dovato® is associated with a cost saving compared with the two individual components.

Additional information

- AWTTC is of the opinion that, if recommended, dolutegravir/lamivudine (Dovato®) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.
- The company anticipates that dolutegravir/lamivudine (Dovato®) may be supplied by a home healthcare provider.

Evidence search

Date of evidence search: 24 October 2019
Date of range of evidence search: No date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Dolutegravir/lamivudine (Dovato®) 50 mg/300 mg film-coated tablets. Reference number: 3659. January 2020.