

**AWMSG Secretariat Assessment Report – Limited submission****Emtricitabine/rilpivirine/tenofovir alafenamide (Odefsey[®]▼)
200 mg/25 mg/25 mg film-coated tablets**

Company: Gilead Sciences Ltd

Licensed indication under consideration:

Emtricitabine/rilpivirine/tenofovir alafenamide (Odefsey[®]▼) for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35 kg) infected with human immunodeficiency virus-1 (HIV-1) without known mutations associated with resistance to the non-nucleoside reverse transcriptase inhibitor (NNRTI) class, tenofovir or emtricitabine and with a viral load \leq 100,000 HIV-1 RNA copies/mL.

▼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: 21 June 2016

Comparator(s)

The comparator included in the company submission was Eviplera[®]. Clinical expert opinion sought by AWTTTC (All Wales Therapeutics and Toxicology Centre) suggested that that most paediatric/adolescent patients in Wales receive abacavir with lamivudine (Kivexa[®]) plus nevirapine or Kivexa[®] plus efavirenz.

Limited submission details

The limited submission criteria were met based on an estimated small difference in cost compared to comparator and an anticipated minimal budgetary impact in NHS Wales.

Odefsey[®] differs from Eviplera[®] in having tenofovir alafenamide (TAF) in place of tenofovir disoproxil fumarate (TDF). TAF and TDF are however, both prodrugs which metabolise to generate tenofovir. Effective therapeutic concentrations of tenofovir in lymphoid cells are obtained from a much smaller dose of TAF than TDF.

Clinical effectiveness

- No data are available from clinical studies of Odefsey[®] in HIV-1 infected patients and no comparison with the main comparator, Eviplera[®], has been presented. The evidence for Odefsey[®] presented in the submission includes data from bioequivalence clinical trials of Genvoya[®] to demonstrate bioequivalence of TAF in emtricitabine/rilpivirine/tenofovir alafenamide (F/R/TAF) Odefsey[®] to TAF in elvitegravir/cobisistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) Genvoya[®]. Hence data from the Genvoya[®] clinical studies are relevant to Odefsey[®]. Bioequivalence of Odefsey[®] to the individual component rilpivirine, was also shown. This approach was accepted by the European Medicines Agency in the application

for marketing authorisation.

- Studies included in the company submission suggest the TAF component of Genvoya[®] to be at least non-inferior to the TDF component of Stribild[®], the only different component between these two products. Eviplera[®] is considered the non-nucleoside reverse transcriptase inhibitor (NNRTI) standard of care as evidenced by current British Human Immunodeficiency Virus Association (BHIVA) guidelines. Odesfey[®] differs from Eviplera[®] only in the inclusion of TAF in place of TDF. Clinical expert opinion suggests Odesfey[®] is most likely to replace Eviplera[®] in clinical practice as TAF has a better side effect profile than TDF.
- Clinical expert opinion sought by AWTTC confirmed that Odesfey[®] is likely to address an unmet need in patients with moderate or severe renal impairment (creatinine clearance < 50ml/min).
- Eviplera[®] is not licensed in children or adolescents. The use of TDF in adolescents is restricted because of safety concerns in growing adolescents, including effects on bone mineralisation.
- Due to limited data the Committee for Medicinal Products for Human Use recommends specific monitoring of adolescents in the risk management plan for Odesfey[®].

Budget impact

- Prevalence and incidence data were calculated from Public Health England HIV surveillance data tables using the estimated number of patients with HIV (1,665); annual incidence of HIV (189) and the proportion of patients who received antiretroviral (ART) therapy for HIV in Wales in 2014 (92%); an annual mortality rate of 0.43% was also applied.
- The company estimate that the number of patients eligible to receive Odesfey[®] will range from 113 patients in year one to 192 patients in year five based on a company market share projections of [commercial in confidence data removed].
- Odesfey[®] is offered at price parity to Eviplera[®] and therefore the net budget impact is zero for years one to five.
- There are uncertainties with the budget impact analysis as the company has assumed that Odesfey[®] will only displace Eviplera[®]; displacement of other antiretroviral regimens has not been considered.
- The company estimate there are approximately 16 children and adolescents eligible for treatment in Wales, of which a maximum of two would receive Odesfey[®] based on the submitted market share projections of [commercial in confidence data removed].
- The associated budget impact for this patient group is therefore in the range of £500-£1,000 per year compared to clinical expert choice of comparator regimens sought by the AWTTC (i.e. Kivexa[®] plus nevirapine or Kivexa[®] plus efavirenz).

Additional information

- In July 2016 the All Wales Medicines Strategy Group recommended Genvoya[®] as an option for use for the same indication as that assessed in this report.
- AWTTC is of the opinion that, if recommended, emtricitabine/rilpivirine/tenofovir alafenamide (Odesfey[®]) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.
- The company anticipate that emtricitabine/rilpivirine/tenofovir alafenamide (Odesfey[®]) will be supplied by a home healthcare provider.

Evidence search

Date of evidence search: 22 July 2016.

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 AW TTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Emtricitabine/rilpivirine/tenofovir alafenamide (Odefsey®) 25 mg/200 mg/25 mg film-coated tablets. Reference number: 3031. October 2016.