

**Enc 9 Appx 2****AWMSG Secretariat Assessment Report – Limited submission****Darunavir/cobicistat/emtricitabine/tenofovir alafenamide (Symtuza®)▼
800 mg/150 mg/200 mg/10 mg film-coated tablet****Company:** Janssen-Cilag Ltd**Licensed indication under consideration:** Treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and adolescents (aged 12 years and older with body weight at least 40 kg).

▼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: 26 September 2017**Comparator(s)**

- Darunavir/cobicistat (Rezolsta®) in combination with emtricitabine/tenofovir alafenamide (Descovy®)

Limited submission details

- Significant 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.
- A minor licence extension.

Clinical effectiveness

- Symtuza® is a once-daily single tablet regimen. The individual components of Symtuza® have previously been recommended by the All Wales Medicines Strategy Group (AWMSG) as the fixed dose combinations Rezolsta® (darunavir/cobicistat) and Descovy® (emtricitabine/tenofovir alafenamide).
- This submission covers a minor licence extension for darunavir/cobicistat, as Rezolsta® is currently not licensed for use in adolescents between 12–18 years old. Both darunavir and cobicistat have been previously recommended by AWMSG in combination with other medicinal products for adults and adolescents.
- The pharmacokinetics of Symtuza® have not been investigated in paediatric patients; however, there are pharmacokinetic data for the different components of Symtuza®, showing that doses of 800 mg darunavir, 150 mg cobicistat, 200 mg emtricitabine and 10 mg tenofovir alafenamide have similar exposures in adults and adolescents aged 12 years and older, weighing at least 40 kg. The clinical studies programme showed that Symtuza® is bioequivalent to its separate components.



- Although there are no clinical data available for Symtuza® in adolescents, the Committee for Medicinal Products for Human Use (CHMP) states that the individual components are approved for this population, and studies have shown other regimens containing cobicistat or darunavir to be safe and efficacious in adolescent populations who are naïve to antiretroviral therapy.
- An ongoing phase III study showed that the virological efficacy of Symtuza® is non-inferior to RezoIsta® plus Descovy® in treatment-naïve adult patients. Another ongoing phase III study showed non-inferiority in terms of virological rebound when switching to Symtuza® versus remaining on a regimen of a boosted protease inhibitor plus emtricitabine/tenofovir disoproxil fumarate.
- Symtuza® was found to be well tolerated, with similar clinical safety compared to active comparators (RezoIsta® plus Descovy® or a boosted protease inhibitor plus emtricitabine/tenofovir disoproxil fumarate). Low rates of discontinuation were reported. No serious adverse events were treatment-related in the Symtuza® arms and no safety concerns were identified. CHMP highlights that using tenofovir alafenamide instead of tenofovir disoproxil fumarate would offer an improved renal and bone safety profile.
- Symtuza® reduces pill burden compared with taking the fixed-dose combinations RezoIsta® and Descovy®.

Budget impact

- The company estimates that the eligible number of patients will be 24 in Year 1, rising to 35 patients in Year 5. The company bases these estimates on annual incidence figures from Public Health Wales, combined with mortality rate figures provided by Public Health England, and assumes that Symtuza® will only be used in patients currently taking RezoIsta® in combination with Descovy®.
- Symtuza® is cost neutral if it displaces RezoIsta® given in combination with Descovy®.
- Clinical experts state that Atripla® is the predominant treatment in Wales followed by Truvada® plus darunavir/ritonavir. If Symtuza® displaced Atripla® this would have an additional cost of £1,705 per patient annually. Symtuza® would be cost neutral if it displaced Truvada® plus darunavir/ritonavir.

Additional information

- AW TTC is of the opinion that, if recommended, Symtuza® is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.
- The company anticipates that Symtuza® may be supplied by a home healthcare provider.

Evidence search

Date of evidence search: 24 October 2017

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. Darunavir/cobicistat/emtricitabine/tenofovir alafenamide (Symtuza®) 800 mg/150 mg/200 mg/10 mg film-coated tablet. Reference number: 2418. January 2018.