Darunavir

Section: 6. Anti-infective medicines > 6.4. Antiviral medicines > 6.4.2. Antiretrovirals > 6.4.2.3. Antiretrovirals > Protease inhibitors

EMLc | ATC codes: J05AE10

Indication	Human immunodeficiency virus disease without mention of tuberculosis or malaria, clinical stage unspecified ICD11 code: 1C62.Z
INN	Darunavir
Medicine type	Chemical agent
List type	Core
Formulations	**Oral > Solid:** 75 mg ; 400 mg (EML) ; 600 mg (EML) ; 800 mg (EML)
EML status history	First added in 2015 (TRS 994)
Sex	All
Age	Also recommended for children
Age restriction	> 3 years
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Darunavir
DrugBank	Darunavir

Summary of evidence and Expert Committee recommendations

An application was submitted by Dr Marco Vitoria, WHO Department of HIV/AIDS, for addition of darunavir to the EML and EMLc for the treatment of HIV infection, in anticipation of improvements in formulation and price reduction that will place ritonavir-boosted darunavir (DRV/r) on a comparable level to existing recommended ritonavir-boosted protease inhibitors lopinavir (LPV/r) and atazanavir (ATZ/r). Expert reviews of the application were prepared by two members of the Expert Committee. Comments on the application were received from Dr Myriam Henkens, International Medical Coordinator, Medecins Sans Frontieres, and from Janssen-Cilag Ltd. The Committee noted that use of a boosted protease inhibitor in combination with two nucleoside/nucleotide reverse-transcriptase inhibitors (NRTIs) is recommended in WHO's 2013 Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection as second-line ART for adults and adolescents. It is also recommended as second-line ART for children who received first-line ART with non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens. According to the 2013 guidelines, heat-stable fixed-dose combinations (FDCs) of ATV/r or LPV/r are the preferred boosted protease inhibitor (PI) options for second-line ART. DRV/r can be used as an alternative (1). The application describes the main limitation of DRV/r: unlike the alternative ritonavir-boosted PIs, it is not currently available in a heat-stable FDC, although one is in development. The application presented results from a 2012 WHO-commissioned systematic review of data from trials that compared drugs used in second-line ART (ATV/r, LPV/r and DRV/r) to support the comparative effectiveness and safety of DRV/r when used as part of ART (2). Evidence assessment using GRADE methodology showed low- or very-low-quality evidence for using ATV/r or DRV/r (once daily) over LPV/r (twice daily) or vice versa as the

preferred boosted PI options. The Expert Committee considered that the systematic review of data suggests that DRV/r is an acceptable treatment option to ATV/r and/or LPV/r as second-line ART, as it has similar (or greater) efficacy and a similar safety profile to ATV/r and LPV/r. DRV/r is not currently a “preferred” treatment option in WHO ART guidelines because of its greater cost and unavailability as a heat-stable FDC. The Committee noted correspondence received from Janssen Sciences Ireland (sponsor of Prezista brand of darunavir) indicating their support for inclusion of darunavir on the EML and EMLc for the treatment of HIV infection because of the growing need for second-line HIV medicines in resource-limited settings. Janssen advised that the ex-factory price for the 1200 mg and 800 mg daily doses of darunavir are US$ 1.80 and US$ 1.20 respectively in sub-Saharan Africa and least-developed countries. No information was provided regarding the price and timeline for development of the heat-stable FDC. The Committee noted that the 2013 Update to the optimal list of paediatric ARV formulations. IATT Meeting Report (3) does not include any darunavir formulations in the “optimal” list of paediatric ARV formulations. Darunavir tablets 75 mg are included in the “limited-use” list for third-line use in special circumstances where appropriate, when boosting with separate ritonavir is available. Darunavir oral liquid (500 mg/5 mL) and 150 mg tablets are included in the “non-essential” list. The 75 mg tablet was considered a more suitable option for inclusion than the oral liquid on the limited-use list, as darunavir is not approved for use in children under 3 years of age and the 75 mg tablet provides dosing for all body weights above 15 kg. In consideration of the public health need for second-line treatment alternatives for HIV infection, the Expert Committee recommended addition of darunavir to the EML and EMLc as an alternative to the other listed ritonavir-boosted PIs, in anticipation of a reduction in price and of market availability of the heat-stable FDC formulation, said to be in development. The Committee advised that it would welcome an application for inclusion of the FDC when it becomes available. With regard to the formulations and strengths proposed for inclusion, the Expert Committee recommended addition to the EML of darunavir 75 mg, 400 mg, 600 mg and 800 mg tablets, and addition of darunavir 75 mg tablets to the EMLc. It was noted that darunavir is not approved for use in children under 3 years of age and that the 75 mg tablet would provide dosing for all body weights above 15 kg. The Committee did not recommend addition to either list of darunavir oral liquid 100 mg/mL or 150 mg tablets on the basis that these formulations are classified as “non-essential” for paediatric use in the IATT Meeting Report, and that more suitable dosage forms and strengths are available for adult patients. References: 1. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013. Available from: http://apps.who.int/iris/bitstream/10665/85321/1/9789241505727_eng.pdf. 2. What ARV regimen to switch to in adults, pregnant women, adolescents and children living with HIV (once-daily PI regimen) Geneva: World Health Organization; 2012. Available from: http://apps.who.int/iris/bitstream/10665/90773/1/WHO_HIV_2013.38_eng.pdf. 3. Update to the optimal list of paediatric ARV formulations. IATT Meeting Report, Geneva, Switzerland, 11-12 September 2013 Geneva: World Health Organization; 2013. Available from: http://apps.who.int/medicinedocs/documents/s21435en/s21435en.pdf.

