Fostemsavir

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Approved indication: HIV-1 infection

Rukobia (ViiV Healthcare)
600 mg film-coated tablets

Despite the wide availability of antiretroviral drugs for patients with HIV infection, treatment failure continues to occur because of problems such as antiretroviral drug resistance and drug intolerance. There is therefore a need for drugs that evade resistance and are well tolerated when multiple standard treatment regimens have been unsuccessful. Fostemsavir is the first of a new class of antiretroviral drugs called attachment inhibitors. It is approved for use, in combination with other anti-HIV drugs, for heavily treatment-experienced patients when viral suppression has not been possible with other regimens.

Fostemsavir is a prodrug of temsavir. The active drug works by binding to the HIV-1 virus, thereby inhibiting its interaction with CD4 receptors on T cells. This prevents the virus from entering and infecting T cells.

Fostemsavir is available as extended-release tablets. One tablet is taken orally twice daily with or without food. It is metabolised in the small intestine to temsavir, which has its peak plasma concentration two hours after oral administration with an absolute bioavailability of 26.9%. As temsavir is partly metabolised by cytochrome P450 (CYP) 3A4, fostemsavir should not be taken concomitantly with strong CYP3A inducers, including carbamazepine, phenytoin, rifampicin and St John's wort. Doses do not need to be adjusted in patients with renal or hepatic impairment. Temsavir has a terminal half-life of about 11 hours.

In a phase III multicentre trial of fostemsavir in patients with multidrug-resistant HIV-1 infection, the mean concentration of HIV-1 RNA decreased, from a median of 4.7 $\log_{10}$ copies/mL, by 0.79 $\log_{10}$ copies/mL after eight days of fostemsavir treatment in 203 patients, compared with a decrease of 0.17 $\log_{10}$ copies/mL after eight days of a placebo in 69 patients. Beyond eight days, the patients received an optimised background therapy plus open-label fostemsavir. After 48 weeks, 115 of 203 patients (57%) in the fostemsavir group and 31 of 69 patients (45%) in the placebo group showed a sustained virological response. Compared to the baseline median of 99 cells/mm^3, the mean CD4$^+$ T-cell counts increased by 139 cells/mm^3 in the fostemsavir group and 64 cells/mm^3 in the placebo group at 48 weeks.[1] The virologic response was further sustained with an increase in the CD4$^+$ T-cell count through 96 weeks.[2] A subgroup analysis of these results based on overall susceptibility scores revealed a lower virologic response in patients with high antiretroviral resistance compared to patients with partial resistance (34% at 24 weeks and 31% at 96 weeks vs 65% at 24 weeks and 88% at 96 weeks).[3]

Although most adverse events in the phase III trial were related to complications of advanced HIV infection, 92% of the participants reported experiencing at least one adverse effect, which was typically mild or moderate in severity.[1,2] In the analysis at 96 weeks, 7% of the patients had withdrawn because of adverse events, but only 3% were considered to be drug-related effects.[2] The most common adverse effects of fostemsavir include diarrhoea, headache, nausea, rashes and vomiting. Immune reconstitution inflammatory syndrome can occur in the first six months of administration in more than one in 100 individuals, which is a state of dysregulated hyperinflammation that occurs rapidly after the recovery of immune function. Liver chemistry monitoring is recommended in patients with hepatitis B or C co-infection. Fostemsavir should be used with caution in patients taking drugs with a known risk of torsade de pointes, with a history of QT interval prolongation or with cardiac disease.

There are limited data available on the use of fostemsavir in patients 65 years of age and older, and the safety and efficacy of fostemsavir are unknown in pregnant women. The medicine is not recommended in patients younger than 18 years of age due to a lack of safety and efficacy data.

Fostemsavir taken with other HIV medicines suppresses the viral load with a sustained long-term response in patients with multidrug-resistant HIV-1 infection who have few remaining options for active therapy due to resistance, intolerance or safety considerations. Fostemsavir does not cure HIV-1 infection or acquired immunodeficiency syndrome, but it can minimise deterioration of the immune system in heavily treatment-experienced patients.

T manufacturer provided useful information

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The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.