



Retrovir IV For Infusion רטרובר לאינפוזיה תוך ורידית

רופא/ה, רוקח/ת נכבד/ה,

- העלון לרופא עודכן ב-ינואר 2016.
- בהודעה זו מצוינים השינויים המהווים החמרה. בעלון שינויים נוספים שאינם החמרה.
- טקסט שהתווסף מסומן בקו תחת.

התוויה (ההתוויה והמינונים עודכנו באישור משרד הבריאות):

Retrovir I.V. is indicated for the short-term management of serious manifestations of Human Immunodeficiency Virus (HIV) infection in patients with Acquired Immune Deficiency Syndrome (AIDS) who are unable to take Retrovir oral formulations.

Retrovir chemoprophylaxis, is indicated for use in HIV-positive pregnant women (over 14 weeks of gestation) for prevention of maternal-foetal HIV transmission and for primary prophylaxis of HIV infection in newborn infants. Retrovir I.V. should only be used when oral treatment is not possible (except during labour and delivery – see section 4.2).

מינונים:

Dosage in adults: A dose for Retrovir I.V. of 1 or 2 mg zidovudine/kg bodyweight every 4 hours provides similar exposure (AUC) to an oral dose of 1.5 or 3.0 mg zidovudine/kg every 4 hours (600 or 1200 mg/day for a 70 kg patient). The current recommended oral dose of Retrovir is 250 or 300 mg twice daily. This current dose is used as part of a multi-drug treatment regimen.

Patients should receive Retrovir I.V. only until oral therapy can be administered.

Dosage in children: Limited data are available on the use of Retrovir I.V. in children. A range of intravenous dosages between 80-160 mg/m² every 6 hours (320-640 mg/m²/day) have been used. Exposure following the 120 mg/m² dose every 6 hours approximately corresponds to an oral dose of 180 mg/m² every 6 hours. An oral dose of Retrovir of 360 to 480 mg/m² per day approximately corresponds to an intravenous dose of 240-320 mg/m²/day.

Dosage in the prevention of maternal-foetal transmission: ...In case of planned caesarean, the infusion should be started 4 hours before the operation. In the event of a false labour, the Retrovir infusion should be stopped and oral dosing restarted.

Dosage adjustments in patients with haematological adverse reactions: Substitution of zidovudine should be considered in patients whose haemoglobin level or neutrophil count fall to clinically significant levels. Other potential causes of anaemia or neutropenia should be excluded. Retrovir dose reduction or interruption should be considered in the absence of alternative treatments (see sections 4.3 and 4.4).

הרכב וחוזק:

Zidovudine 200mg/20ml

העדכונים בעלון לרופא נעשו בסעיפים הבאים:

• Contraindications

- Retrovir is contra-indicated in newborn infants with hyperbilirubinaemia requiring treatment other than phototherapy, or with increased transaminase levels of over five times the upper limit of normal.

• Special warnings and precautions for use

- The concomitant use of rifampicin, stavudine with zidovudine should be avoided (see section 4.5).
- Patients with chronic hepatitis B or C and treated with combination antiretroviral therapy are at an increased risk of severe and potentially fatal hepatic adverse events. In case of concomitant antiviral therapy for hepatitis B or C, please also refer to the relevant product information for these medicinal products.

Patients with pre-existing liver dysfunction, including chronic active hepatitis, have an increased frequency of liver function abnormalities during combination antiretroviral therapy and should be monitored according to standard practice. If there is evidence of worsening liver disease in such patients, interruption or discontinuation of treatment must be considered (see section 4.2).

- Immune Reactivation Syndrome: In HIV-infected patients with severe immune deficiency at the time of institution of combination antiretroviral therapy (CART), an inflammatory reaction to asymptomatic or residual opportunistic pathogens may arise and cause serious clinical conditions, or aggravation of symptoms. Typically, such reactions have been observed within the first few weeks or months of initiation of CART. Relevant examples are cytomegalovirus retinitis, generalized and/or focal mycobacterial infections and Pneumocystis carinii pneumonia. Any inflammatory symptoms should be evaluated and treatment instituted when necessary. Autoimmune disorders (such as Graves' disease) have also been reported to occur in the setting of immune reactivation; however, the reported time to onset is more variable and can occur many months after initiation of treatment.
- Osteonecrosis: Although the etiology is considered to be multifactorial (including corticosteroid use, alcohol consumption, severe immunosuppression, higher body mass index), cases of osteonecrosis have been reported particularly in patients with advanced HIV-disease and/or long-term exposure to combination antiretroviral therapy (CART). Patients should be advised to seek medical advice if they experience joint aches and pain, joint stiffness or difficulty in movement.
- Latex allergy: The rubber stopper of the Retrovir I.V. vials contains dry natural latex rubber that has the potential to cause allergic reactions in latex sensitive individuals.

- **Interaction with other medicinal products and other forms of interaction**

- Limited data suggests that co-administration of zidovudine with rifampicin decreases the AUC (area under the plasma concentration curve) of zidovudine by $48\% \pm 34\%$. This may result in a partial loss or total loss of efficacy of zidovudine. The concomitant use of rifampicin with zidovudine should be avoided (see section 4.4).
- Probenecid increases the AUC of zidovudine by 106% (range 100 to 170%). Patients receiving both drugs should be closely monitored for haematological toxicity.
- Valproic acid, fluconazole or methadone when co-administered with zidovudine have been shown to increase the AUC with a corresponding decrease in its clearance. As only limited data are available the clinical significance of these findings is unclear but if zidovudine is used concurrently with either valproic acid, fluconazole or methadone, patients should be monitored closely for potential toxicity of zidovudine.

- **Undesirable effects**

- *Adverse reactions with Retrovir for the prevention of maternal-foetal transmission:*

In a placebo-controlled trial, overall clinical adverse reactions and laboratory test abnormalities were similar for women in the Retrovir and placebo groups. However, there was a trend for mild and moderate anaemia to be seen more commonly prior to delivery in the zidovudine treated women.

העלון לרופא ישלח למשרד הבריאות לצורך פרסומו במאגר התרופות שבאתר משרד הבריאות
וניתן לקבלו מודפס על-ידי פניה לחברת <http://www.health.gov.il/units/pharmacy/trufot/index.asp>
גלקסומיתקליין רח' בזל 25 פתח תקוה בטלפון: 03-9297100.

מיכל סרפר
רוקחת ממונה, Rx & CH