



The following information is intended for medical or healthcare professionals only:

## **RETROVIR IV for Infusion 10 mg/ml SOLUTION FOR INFUSION**

### **Zidovudine**

#### **DOSAGE AND ADMINISTRATION INFORMATION ONLY**

Please refer to the Physician Leaflet for further information.

#### **Pharmaceutical form**

Solution for infusion.

Retrovir IV for Infusion is a clear, nearly colourless, sterile aqueous solution with a pH of approximately 5.5.

#### **Posology and method of administration**

The required dose of Retrovir IV for Infusion must be administered by slow intravenous infusion of the **diluted** product over a one-hour period.

Retrovir IV for Infusion must **NOT** be given intramuscularly.

**Dilution:** Retrovir IV for Infusion **must** be diluted prior to administration (see Instructions for use and handling).

#### **Dosage in adults**

A dose for Retrovir IV for Infusion 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 1,200 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 IV for Infusion only until oral therapy can be administered.

#### **Dosage in children**

Limited data are available on the use of Retrovir IV for Infusion in children. A range of intravenous dosages between 80-160 mg/m<sup>2</sup> every 6 hours (320-640 mg/m<sup>2</sup>/day) have been used. Exposure following the 120 mg/m<sup>2</sup> dose every 6 hours approximately corresponds to an oral dose of 180 mg/m<sup>2</sup> every 6 hours. An oral dose of Retrovir of 360 to 480 mg/m<sup>2</sup> per day approximately corresponds to an intravenous dose of 240-320 mg/m<sup>2</sup>/day.

#### **Dosage in the prevention of maternal-foetal transmission**

Although the optimal dosage schedule has not been identified, the following dosage regimen has been shown to be effective. Pregnant women (over 14 weeks of gestation) should be given 500 mg/day orally (100 mg five times per day) until the beginning of labour. During labour and delivery, Retrovir should be administered intravenously at 2 mg/kg bodyweight given over one hour followed by a continuous intravenous infusion at 1 mg/kg/h until the umbilical cord is clamped.

The newborn infants should be given 2 mg/kg bodyweight orally every 6 hours starting within 12 hours after birth and continuing until 6 weeks old (e.g. a 3 kg neonate would require a 0.6 ml dose of oral solution every 6 hours). Infants unable to receive oral dosing should be given Retrovir intravenously at 1.5 mg/kg bodyweight infused over 30 minutes every 6 hours.

In case of planned caesarean, the infusion should be started 4 hours before the operation. In the event of 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.

#### **Dosage in the elderly**

Zidovudine pharmacokinetics have not been studied in patients over 65 years of age and no specific data are available. However, since special care is advised in this age group due to age-associated changes such as the decrease in renal function and alterations in haematological parameters, appropriate monitoring of patients before and during use of Retrovir is advised.

#### **Dosage in renal impairment**

In patients with severe renal impairment, the recommended IV dosage is 1 mg/kg 3-4 times daily. This is equivalent to the current recommended oral daily dosage for this patient group of 300-400 mg allowing for oral bioavailability of 60-70%. Haematological parameters and clinical response may influence the need for subsequent dosage adjustment. For patients with end-stage renal disease maintained on haemodialysis or peritoneal dialysis, the recommended dose is 100 mg every 6-8 hrs (300 mg-400 mg daily).

#### **Dosage in hepatic impairment**

Data in patients with cirrhosis suggest that accumulation of zidovudine may occur in patients with hepatic impairment because of decreased glucuronidation. Dosage reductions may be necessary but, due to the large variability in zidovudine exposures in patients with moderate to severe liver disease, precise recommendations cannot be made. If monitoring of plasma zidovudine levels is not feasible, physicians will need to monitor for signs of intolerance, such as the development of haematological adverse reactions (anaemia, leucopenia, neutropenia) and reduce the dose and/or increase the interval between doses as appropriate.

#### **Overdose**

##### **Symptoms and signs:**

No specific symptoms or signs have been identified following acute oral overdose with zidovudine, apart from those listed as undesirable effects.

**Treatment:** Patients should be observed closely for evidence of toxicity and given the necessary supportive therapy.

Haemodialysis and peritoneal dialysis appear to have a limited effect on elimination of zidovudine but enhance the elimination of the glucuronide metabolite.

#### **Shelf life and special precautions for storage**

3 years when not stored above 30°C.

#### **Instructions for use and handling**

**Dilution:** Retrovir IV for Infusion must be diluted prior to administration. Since no antimicrobial preservative is included, dilution must be carried out under full aseptic conditions, preferably immediately prior to administration, and any unused portion of the vial should be discarded.

The required dose should be added to and mixed with Glucose Intravenous Infusion 5% w/v to give a final zidovudine concentration of either 2 mg/ml or 4 mg/ml. These dilutions are chemically and physically stable for up to 48 hours at both 5°C and 25°C.

Should any visible turbidity appear in the product either before or after dilution or during infusion, the preparation should be discarded.