Zidovir ®

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Zidovir ®

Zidovir is indicated for the treatment of HIV infection when antiZIDOVIRal therapy is warranted. ZIDOVIR in combination with other antiZIDOVIRal agents is indicated for the treatment of HIV infection. ZIDOVIR does not cure HIV infection/AIDS or prevent passing HIV to others.

Zidovir-100 Capsules
Zidovir-300 Tablets
Zidovir Oral Solution

Warning
ZIDOVIR (ZIDOVUDINE) MAY BE ASSOCIATED WITH HEMATOLOGIC TOXICITY INCLUDING GRANULOCYTOPENIA AND SEVERE ANAEMIA PARTICULARLY IN PATIENTS WITH ADVANCED HIV DISEASE (See Warnings and Precautions). PROLONGED USE OF ZIDOVIR HAS BEEN ASSOCIATED WITH SYMPTOMATIC MYOPATHY SIMILAR TO THAT PRODUCED BY HUMAN IMMUNODEFICIENCY VIRUS.

RARE OCCURRENCES OF POTENTIALLY FATAL LACTIC ACIDOSIS IN THE ABSENCE OF HYPOXEMIA, AND SEVERE HEPATOMEGALY WITH STEATOSIS HAVE BEEN REPORTED WITH THE USE OF CERTAIN ANTIZIDOVIRAL NUCLEOSIDE ANALOGUES (See Warnings and Precautions).

Composition
Zidovir-100 Capsules
Each capsule contains Zidovudine 100 mg
Zidovir-300 Tablets
Each tablet contains Zidovudine 300 mg
Zidovir Oral Solution
Each 5 ml contains Zidovudine 50 mg

Description
Zidovudine, a thymidine analogue, is an anti-ZIDOVIRal drug acting against human immunodeficiency virus (HIV).
Indications
Zidovir is indicated for the treatment of HIV infection when antiZIDOVIRal therapy is warranted. The duration of clinical benefit from antiZIDOVIRal therapy may be limited. Alteration in antiZIDOVIRal therapy should be considered if disease progression occurs during treatment. Maternal Foetal HIV Transmission: Zidovir is also indicated for the prevention of maternal foetal HIV transmission. The safety of zidovudine for the mother or foetus during the first trimester of pregnancy has not been assessed.
g per day in divided doses in combination with other antiZIDOVIRal agents and 500 mg (100 mg every 4 hours while awake) or 600 mg per day in divided doses for monotherapy. The effectiveness of this dose compared to higher dosing regimens in improving the neurologic dysfunction associated with HIV disease is unknown.

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Dosage and Administration

The recommended total oral daily dose of Zidovir is 600 mg per day in divided doses in combination with other antiZIDOVIRal agents and 500 mg (100 mg every 4 hours while awake) or 600 mg per day in divided doses for monotherapy. The effectiveness of this dose compared to higher dosing regimens in improving the neurologic dysfunction associated with HIV disease is unknown.
Paediatrics: The recommended dose in children 3 months to 12 years of age is 180 mg/m2 every 6 hours (720 mg/m2 per day), not to exceed 200 mg every 6 hours.

Maternal Foetal HIV Transmission: The recommended dosing regimen for administration to pregnant women (>14 weeks of pregnancy) and their neonates is:

Maternal dosing: 100 mg orally 5 times per day until the start of labour. During labour and delivery, intravenous zidovudine should be administered at 2 mg/kg (total body weight) over 1 hour followed by a continuous intravenous infusion of 1 mg/kg/h (total body weight) until clamping of the umbilical cord.
Infant dosing: 2 mg/kg orally every 6 hours starting within 12 hours after birth and continuing through 6 weeks of age. Infants unable to receive oral dosing may be administered zidovudine intravenously at 1.5 mg/kg, infused over 30 minutes, every 6 hours.
Patient Monitoring
Haematologic toxicities appear to be related to pre treatment bone marrow reserve and to dose and duration of therapy. In patients with poor bone marrow reserve, particularly in patients with advanced symptomatic HIV disease, frequent monitoring of hematologic indices is recommended to detect serious anaemia or granulocytopenia (See Warnings and Precautions). In patients who experience hematologic toxicity, reduction in hemoglobin may occur as early as 2 to 4 weeks, and neutropenia usually occurs after 6 to 8 weeks.
Dose adjustment: Significant anaemia (hemoglobin of <7.5 g/dL or reduction of >25% of baseline) and/or significant granulocytopenia (granulocyte count of <750 cells/mm3 or reduction of >50% from baseline) may require a dose interruption until evidence of marrow recovery is observed (See Warnings and Precautions). For less severe anaemia or neutropenia, a reduction in daily dose may be adequate. In patients who develop significant anaemia, dose modification does not necessarily eliminate the need for transfusion. If marrow recovery occurs following dose modification, gradual increases in dose may be appropriate depending on hematologic indices and patient tolerance.
In end-stage renal disease patients maintained on hemodialysis or peritoneal dialysis, recommended dosing is 100 mg every 6 to 8 hours.
There are insufficient data to recommend dosage adjustment of Zidovir in patients with impaired hepatic function.

Contraindications

Patients who exhibit potentially life-threatening allergic reactions to any of the components of the formulation.

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Warnings and Precautions

Before combination therapy with Zidovir is initiated, consult the complete prescribing information for each drug. The safety profile of Zidovir plus other antiZIDOVIRal agents reflects the individual safety profiles of each component.
The incidence of adverse reactions appears to increase with disease progression, and patients should be monitored carefully, especially as disease progression occurs.

BONE MARROW SUPPRESSION

Zidovir should be used with caution in patients who have bone marrow compromise evidenced by granulocyte count <1000 cells/mm3 or hemoglobin <9.5 g/dL. There have been reports of pancytopenia associated with the use of zidovudine, which was reversible in most instances after discontinuance of the drug.
Frequent blood counts are strongly recommended in patients with advanced HIV disease who are treated with zidovudine. For patients with asymptomatic or early HIV disease, periodic blood counts are recommended. If anaemia or neutropenia develops, dosage adjustments may be necessary (See Dosage and Administration).

MYOPATHY

Myopathy and myositis with pathological changes, similar to that produced by HIV disease, have been associated with prolonged use of zidovudine.

LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS

Rare occurrences of potentially fatal lactic acidosis in the absence of hypoxemia, and severe hepatomegaly with steatosis have been reported with the use of certain antiZIDOVIRal nucleoside analogues. Therapy with Zidovir should be suspended until the diagnosis of lactic acidosis has been excluded. Caution should be exercised when administering Zidovir to any patient, particularly obese women, with hepatomegaly, hepatitis, or other known risk factors for liver disease. Treatment with zidovudine should be suspended in the setting of rapidly elevating aminotransferase levels, progressive hepatomegaly, or metabolic/lactic acidosis of unknown aetiology.

OTHER SERIOUS ADVERSE REACTIONS

Reports of pancreatitis, sensitization reactions, vasculitis and seizures have been rare. These adverse events, except for sensitization, have also been associated with HIV disease. Changes in skin and nail pigmentation have been associated with the use of zidovudine.

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DRUG INTERACTIONS

Ganciclovir, interferon alpha: Use of zidovudine in combination with either ganciclovir or interferon alpha increases the risk of hematologic toxicities in some patients with advanced HIV disease. Hematologic parameters should be monitored frequently in all patients receiving either of these combinations.

Bone Marrow Suppressive Agents/Cytotoxic Agents: Co administration of zidovudine with drugs that are cytotoxic or which interfere with RBC/WBC number or function (e.g. dapsone, flucytosine, vincristine, vinblastine or adriamycin) may increase the risk of hematologic toxicity.

Probenecid: Limited data suggests that probenecid may increase zidovudine levels by inhibiting glucuronidation and/or by reducing renal excretion of zidovudine.

Phenytoin: Phenytoin plasma levels have been reported to be low in some patients receiving zidovudine. In one study, a 30% decrease in oral zidovudine clearance was observed with phenytoin.

Methadone: No adjustments in methadone maintenance requirements were reported in a study of nine HIV positive patients receiving methadone maintenance.

Fluconazole: The co administration of fluconazole with zidovudine has been reported to interfere with the oral clearance and metabolism of zidovudine.

Atovaquone: A decrease in zidovudine oral clearance was observed.
Valproic Acid: Data suggests that valproic acid increases the oral bioavailability of zidovudine through inhibition of first pass hepatic metabolism. Patients should be monitored for a possible increase in zidovudine related adverse events.
Lamivudine: Co-administration of zidovudine with lamivudine resulted in an increase in the maximum concentration (Cmax) of zidovudine.

Other nucleoside analogues: Experimental nucleoside analogues affecting DNA replication such as ribavirin antagonize the in vitro antiviral activity of zidovudine against HIV.

PREGNANCY

Category C. Congenital abnormalities were found to occur with similar frequency between infants born to mothers who received zidovudine and infants born to mothers who received placebo. Abnormalities were either problems in embryogenesis (prior to 14 weeks) or were recognised on ultrasound before or immediately after initiation of study drugs.

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NURSING MOTHERS

HIV infected women are advised not to breast feed to avoid postnatal transmission of HIV to a child who may not yet be infected. Zidovudine is excreted in human milk.

IMPAIRED RENAL AND HEPATIC FUNCTION

Zidovudine is eliminated from the body primarily by renal excretion following metabolism in the liver. In patients with severely impaired renal function, dosage reduction is recommended. Although very little data are available, patients with severely impaired hepatic function may be at greater risk of toxicity (See Dosage and Administration).

Side Effects

MONOTHERAPY

Adults
The frequency and severity of adverse events associated with the use of zidovudine in adults are greater in patients with more advanced infection at the time of initiation of therapy.
The anaemia reported in patients with advanced HIV disease receiving zidovudine appeared to be the result of impaired erythrocyte maturation. Thrombocytopenia has also been reported in patients with advanced disease. Mild drug-associated elevations in total bilirubin levels have been reported as an uncommon occurrence in patients treated for asymptomatic HIV infection.

Clinical adverse events or symptoms which occurred in at least 5% of all patients with advanced HIV disease treated with 1,500 mg/day of zidovudine were: fever, headache, nausea, vomiting, anorexia, myalgia, insomnia, dizziness, paraesthesia, dyspnoea and rash. Malaise, gastrointestinal pain, dyspepsia, and taste perversion were also reported.
Paediatrics

Anaemia and granulocytopenia among paediatric patients with advanced HIV disease receiving zidovudine occurred with similar incidence to that reported for adults with AIDS or advanced AIDS-Related complex. Macrocytosis was frequently observed.
Other adverse events were similar to that observed in adults.
Maternal-Foetal Transmission
The most commonly reported adverse experiences were anaemia and neutropenia. The long-term consequences of in vitro and infant exposure to zidovudine are unknown.

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Overdosage

No reported cases of acute overdosage (up to 50 gms) in both children and adults have been fatal. The consistent finding in these cases was spontaneous or induced nausea and vomiting. Hematologic changes were transient and not severe. Hemodialysis and peritoneal dialysis appear to have a negligible effect on the removal of zidovudine while elimination of its primary metabolite is enhanced.

Presentation

Zidovir 100
Strip of 10 capsules and container of 100 capsules

Zidovir 300
Strip of 10 tablets and container of 60 tablets

Zidovir
Bottle of 100 ml Oral Solution with syringe