VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

RETROVIR (Zidovudine)

Effective Date: 1/28/14

Date Developed: 1/28/14 by Catherine Sanders, MD

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Retrovir is an Antiretroviral Agent, Reverse Transcriptase Inhibitor (Nucleoside) used in the treatment of HIV-1 infections. Zidovudine is a thymidine analog which interferes with the HIV viral RNA-dependent DNA polymerase resulting in inhibition of viral replication.

Pre-Authorization Criteria:
Retrovir is to be used for the treatment of HIV-1 infection in combination with at least two other antiretroviral agents. Retrovir is also used for the prevention of maternal/fetal HIV transmission.
Patients should receive I.V. therapy only until oral therapy can be administered.
Use for postexposure prophylaxis is an unlabeled use and is not covered.

VCHCP requires that Retrovir be prescribed by an Immunology Clinic physician with current American Academy of HIV Medicine (AAHIVM) certification or a physician boarded in Infectious Disease.

Dosing: Adult:
Note: Patients should receive I.V. therapy only until oral therapy can be administered.
Prevention of maternal-fetal HIV transmission: Dose adjustment not required in pregnant women. Begin oral therapy with usual recommended dose based on current treatment guidelines. Zidovudine should be administered by continuous I.V. infusion near delivery regardless of antepartum regimen or mode of delivery in women with HIV RNA >400 copies/mL or unknown HIV RNA status. If oral zidovudine was part of the antepartum regimen, discontinue during intrapartum I.V. infusion. Other antiretroviral agents should be continued orally. Zidovudine I.V. is not required in women receiving combination antiretroviral therapy who have HIV RNA <400 copies/mL near delivery (DHHS [perinatal], 2012).
During labor and delivery, administer zidovudine I.V. at 2 mg/kg as loading dose followed by a continuous I.V. infusion of 1 mg/kg/hour until delivery. For scheduled cesarean delivery, begin I.V. zidovudine 3 hours before surgery.

HIV infection:
Oral: 300 mg twice daily or 200 mg 3 times/day
I.V.:
U.S. labeling: 1 mg/kg/dose administered every 4 hours around-the-clock (5-6 doses/day)
Postexposure prophylaxis (unlabeled use): Oral: 300 mg twice daily or 200 mg 3 times daily in combination with lamivudine or emtricitabine. A third agent may be added for high risk exposures. Therapy should be started within hours of exposure and continued for 4 weeks (CDC, 2005).

Dosing: Pediatric:
Note: Patients should receive I.V. therapy only until oral therapy can be administered.

Prevention of maternal-fetal HIV transmission (in neonates): Note: Start as soon as possible after birth, preferably within 6-12 hours of delivery. Continue dose from birth through 6 weeks of age. Use zidovudine in combination with nevirapine in select situations (eg, infants born to mothers with only intrapartum therapy or no therapy) (DHHS [perinatal], 2012).
Oral:
Manufacturer's labeling: Full-term infants: 2 mg/kg every 6 hours
DHHS [perinatal], 2012:
Infants ≥35 weeks: 4 mg/kg/dose twice daily
Infants ≥30 weeks and <35 weeks gestation at birth: 2 mg/kg/dose every 12 hours; at 15 days of age, advance to 3 mg/kg/dose every 12 hours
Infants <30 weeks gestation at birth: 2 mg/kg/dose every 12 hours; at 4 weeks of age, advance to 3 mg/kg/dose every 12 hours
I.V. (infants unable to receive oral dosing): Start as soon as possible after birth, preferably within 6-12 hours of delivery; continue dose from birth through 6 weeks of age: DHHS [perinatal], 2012:
Infants ≥35 weeks: 3 mg/kg/dose every 12 hours
Infants ≥30 weeks and <35 weeks gestation at birth: 1.5 mg/kg/dose every 12 hours; at 15 days of age, advance to 2.3 mg/kg/dose every 12 hours
Infants <30 weeks gestation at birth: 1.5 mg/kg/dose every 12 hours; at 4 weeks of age, advance to 2.3 mg/kg/dose every 12 hours

Treatment of HIV infection:
Children 4 weeks to <18 years (U.S. labeling) or 3 months to ≤12 years (Canadian labeling):
Oral: Dose should be calculated by body weight (in kg) or body surface area and should not exceed the recommended adult dose. Note: Doses calculated by body weight may not be the same as those calculated by body surface area.
Dosing based on body surface area: 240 mg/m^2 twice daily (maximum: 300 mg twice daily) or 160 mg/m^2/dose 3 times daily (maximum: 200 mg 3 times daily)
Dosing based on weight (Note: 3 times daily dose is approved but rarely used in clinical practice):
4 to <9 kg: 12 mg/kg/dose twice daily or 8 mg/kg/dose 3 times/day
≥9 to <30 kg: 9 mg/kg/dose twice daily or 6 mg/kg/dose 3 times/day
≥30 kg: 300 mg twice daily or 200 mg 3 times/day
Children 3 months to ≤12 years (Canadian labeling): *I.V. intermittent infusion:* 120 mg/m^2/dose every 6 hours
Children ≥12 years: *I.V. intermittent infusion:* 1 mg/kg/dose every 4 hours around-the-clock

Administration:
Oral: Administer around-the-clock to promote less variation in peak and trough serum levels; may be administered without regard to meals
I.M.: Do not administer I.M.
I.V.: Avoid rapid infusion or bolus injection
Neonates: Infuse over 30 minutes
Adults: Infuse over 1 hour; in pregnant women, infuse loading dose over 1 hour followed by continuous infusion
Hazardous agent; use appropriate precautions for handling and disposal (NIOSH, 2012).

Dosing: Geriatric:
Refer to adult dosing.

Dosing: Renal Impairment
Cl_{cr} <15 mL/minute including hemo-/peritoneal dialysis (administer dose after dialysis on dialysis days [DHHS, 2012]):
Oral: 100 mg every 6-8 hours (manufacturers labeling); 100 mg 3 times daily or 300 mg once daily (DHHS [adult], 2012)
I.V.: 1 mg/kg every 6-8 hours
Continuous renal replacement therapy (CRRT): No adjustment needed (Aronoff, 2007)
Dosing: Hepatic Impairment
Insufficient data to make dosing recommendation. The risk of hematologic toxicity may be increased.
Dosing: Adjustment for Toxicity
Consider dose interruption for significant anemia (hemoglobin <7.5 g/dL or >25% reduction from baseline) and/or neutropenia (granulocyte count <750 cells/mm^3 or >50% reduction from baseline) until evidence of recovery. Anemia associated with chronic zidovudine may warrant dose reduction.
Dosage Forms: U.S.
Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
Capsule, Oral:
Retrovir: 100 mg [contains soybean lecithin]
Generic: 100 mg
Solution, Intravenous [preservative free]:
Retrovir: 10 mg/mL (20 mL)
Syrup, Oral:
Retrovir: 50 mg/5 mL (240 mL) [contains sodium benzoate; strawberry flavor]
Generic: 50 mg/5 mL (240 mL)
Tablet, Oral:
Generic: 300 mg
Generic Equivalent Available: U.S.
May be product dependent

Exclusions:
Retrovir is not to be used as monotherapy.
Retrovir use for postexposure prophylaxis is an unlabeled use and is therefore not covered.

Adverse Reactions:
>10%: headache, malaise, fever, rash, nausea, anorexia, vomiting, macrocytosis, anemia, hepatomegaly, cough.
Other Serious Less Common Reactions: lactic acidosis, pancreatitis, neutropenia, pancytopenia, myopathy, rhabdomyolysis, Stevens-Johnson syndrome, toxic epidermal necrolysis, immune reconstitution syndrome, autoimmune disorders, fat distribution,

U.S. BOXED WARNING:
Zidovudine-associated hematologic toxicity, including neutropenia and severe anemia, especially in patients with advanced HIV, has been reported with use.
Symptomatic myopathy and myositis has been associated with prolonged zidovudine use.

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, has been associated with nucleoside analogue use alone or in combination; suspend treatment if clinical or laboratory findings suggest lactic acidosis or hepatotoxicity.

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