ZIDOVUDINE (AZT, Retrovir®)

Benefits of zidovudine:

- Zidovudine (ZDV) is an antiretroviral drug that slows the growth of the HIV virus. It has shown in a large randomized, multicentre study to decrease the rate of perinatal transmission of HIV when it is taken by the mother during pregnancy and delivery and by the infant for up to 6 weeks after birth
- The use of ZDV has greatly reduced the risk of the infant becoming infected with HIV; however it does not prevent all HIV infections.

Dose and administration:

- There are two ZDV preparations in this Prevention of Perinatal HIV Transmission Kit, 10 parenteral vials (10 mg/mL) and 240 mL oral liquid (10 mg/mL).

  Mother:

  - During labour and delivery, ZDV is given intravenously (IV) to the mother as a loading dose of 2 mg/kg over one hour followed by an infusion of 1 mg/kg/hour until the cord is clamped (see IV Zidovudine Administration Protocol for details on mixing and administration).
  - Begin administration of ZDV at the onset of labour, rupture of membranes, at least 2 hours prior to cesarean section, at time of induction of labour if rapid progression is anticipated, or in any situation when delivery is anticipated.
- If labour stops and the ZDV infusion is discontinued for more than 6 hours, readminister the loading dose and resume the IV infusion when labour recommences.

  Infant:
- The recommended dose and duration of ZDV therapy for the infant will depend on the level of risk for perinatal HIV transmission (low, moderate, high) and the infant's gestational age.
  - Infants born in LOW risk situations will receive a total of 4 weeks of ZDV monotherapy with the first dose of ZDV given within 6 hours of birth
  - Infants born in MODERATE or HIGH risk situations will receive 6 weeks of ZDV as part of combination therapy with nevirapine and lamivudine, with the first dose given within 90 minutes of birth.
  - *Refer to Treatment algorithms and/or Prescriber's orders for further information (www.oaktreeclinic.bc.ca)*
- Reduced doses are recommended for preterm infants and an IV preparation is available for infants unable to tolerate oral intake (Tables 1 and 2).

Table 1. Zidovudine dosing for LOW Risk Situations (4 weeks total therapy)

≥ 35 weeks gestation	4 mg/kg/dose PO every 12 hours for total 4 weeks	3 mg/kg/dose IV every 12 hours for total 4 weeks
30-34 weeks gestation	2 mg/kg/dose PO every 12 hours for 2 weeks, then 3 mg/kg/dose PO every 12 hours until 4 weeks	1.5 mg/kg/dose IV every 12 hours for 2 weeks, then 2.3 mg/kg/dose IV every 12 hours until 4 weeks
≤ 29 weeks gestation	2 mg/kg/dose PO every 12 hours for 4 weeks	1.5 mg/kg/dose IV every 12 hours for 4 weeks

Table 2. Zidovudine dosing for MODERATE or HIGH Risk Situations (6 weeks total therapy taken as part of combination antiretroviral prophylaxis)

≥ 35 weeks gestation	4 mg/kg/dose PO every 12 hours for total 6 weeks	3 mg/kg/dose IV every 12 hours for total 6 weeks
30-34 weeks gestation	2 mg/kg/dose PO every 12 hours for 2 weeks, then 3 mg/kg/dose PO every 12 hours until 6 weeks	1.5 mg/kg/dose IV every 12 hours for 2 weeks, then 2.3 mg/kg/dose IV every 12 hours until 6 weeks
≤ 29 weeks gestation	2 mg/kg/dose PO every 12 hours for 4 weeks then 3 mg/kg/dose PO every 12 hours until 6 weeks	1.5 mg/kg/dose IV every 12 hours for 4 weeks then 2.3 mg/kg/dose IV every 12 hours until 6 weeks

- Zidovudine liquid is a 10 mg/mL syrup. Zidovudine syrup may be stored at room temperature.
- Zidovudine can be given before, during or after a feed. Gently place the oral syringe in the infant's mouth just inside the cheek and give 4 or 5 gentle pushes on the plunger of the syringe to administer the dose.

- If the infant vomits within 15 minutes of the dose, give another dose if possible. If it is more than 15 minutes after the dose, do NOT give another dose, and give the next dose when scheduled.
  - ***Ensure that the entire bottle of zidovudine oral liquid is sent home with the infant. It is more than enough to complete the six weeks of therapy.***

Adverse effects:

- Parenteral zidovudine is generally well tolerated. Initial adverse effects may include weakness, headache, dizziness, insomnia, anorexia, vomiting, malaise and myalgia. These symptoms seldom require lowering the dosage or stopping the drug.

- Mild anemia and neutropenia have been noted in some infants receiving zidovudine. Reductions in hemoglobin or neutrophils may occur as early as 2-4 weeks. These conditions are usually mild and resolve when the dose is reduced or the drug is discontinued.

NEVIRAPINE (Viramune®)

Benefits of nevirapine:

- Nevirapine is an antiretroviral drug that slows the growth of the HIV virus. In the absence of maternal antenatal antiretroviral therapy, nevirapine has been shown to decrease the risk of a mother passing the HIV virus to her infant when it is taken by the mother as a single oral dose at delivery followed by administration of nevirapine to the infant (current dosing recommendation is to administer three oral doses to the infant).
- Nevirapine can reduce the risk of the infant being infected; however it does not prevent all infections.

Dose and administration

- There are two nevirapine preparations in this Prevention of Perinatal HIV Transmission Kit, oral tablets (two tablets of 200 mg each) and oral liquid (10 mL of 10 mg/mL liquid). There is no IV formulation of nevirapine available.

Mother:

- Nevirapine 200 mg orally should be administered as a *single-dose* as soon as possible after arrival at the hospital to the pregnant woman who is in labour if:
  - She is known to be HIV positive and *has not received any* antiretroviral therapy during pregnancy, or
  - She is thought to be at high risk of HIV infection but her HIV status is unknown and HIV serology results (Rapid HIV test or EIA) is *preliminary positive* or *pending* or her HIV serology is negative BUT she has engaged in any high risk activity in the previous 3 weeks (i.e., she could be in the seroconversion window period)
- If the nevirapine tablet is vomited within 15 minutes of administration it should be re-administered.
- In addition to nevirapine, thewoman should **also receive** zidovudine intravenously as 2 mg/kg loading dose over 1 hour followed by 1 mg/kg/hour until delivery.
- All women who received single-dose oral nevirapine should **also receive** oral Combivir® (lamivudine-zidovudine) 1 tablet orally twice daily for 7 days postpartum to reduce the risk of developing nevirapine resistance.

Infant:

- Nevirapine 12 mg (8 mg if infant weighs ≤ 2 kg) by mouth is given for a *total of 3 doses* to an infant born to:
  - A mother who is known HIV positive and considered at moderate or high risk of HIV transmission
  - A mother whose HIV status is unknown/considered at high risk of HIV infection whose HIV serology results were preliminary positive, pending, or negative BUT considered to be in the seroconversion window period of infection as described above.
  - The first dose of nevirapine should be given immediately at birth (day 0). The second dose is given at 2 days of age. The third dose is given at 6 days of age.

- Nevirapine liquid is a 10 mg/mL syrup. Each dose for the infant will be either 12 mg (1.2 mL) if infant weight is > 2 kg, or 8 mg (0.8 mL) if infant weight is ≤2 kg.
- Nevirapine liquid can be stored at room temperature.
- Nevirapine can be given before, during or after a feed. Gently place the oral syringe in the infant's mouth just inside the cheek and give 4 or 5 gentle pushes on the plunger of the syringe to administer the dose.
- If the infant vomits within 15 minutes of the dose, give another dose if possible. If it is more than 15 minutes after the dose, do NOT give another dose, and give the next dose when scheduled.
- The infant should **also receive** oral zidovudine (recommended dose for gestational age) for the first six weeks of life **and** lamivudine 6 mg (4 mg if infant weighs ≤ 2 kg) orally every twelve hours for the first two weeks of life.
  - ***Ensure that an adequate volume of nevirapine oral liquid to complete the three-dose nevirapine regimen is sent home with the infant.***

Adverse effects:

- Nevirapine given as either a single or three-dose regimen is well tolerated. Only mild adverse effects on mother and infant were seen during the research trials for prevention of perinatal HIV transmission. These included mild skin rash and mild anemia.
- An allergic reaction (shortness of breath, closing of the throat, swelling of lips, tongue or face) is extremely rare after a single or three-dose regimen, and requires immediate medical attention.
- Adverse effects seen with long-term use of nevirapine include rash, altered liver function, nausea, vomiting, diarrhea, abdominal pain, headache, numbness, tingling or muscle pain, but these have not been reported following either a single or three-dose regimen.

LAMIVUDINE (3TC®) or LAMIVUDINE-ZIDOVUDINE (COMBIVIR®)

Benefits of lamivudine:

- Lamivudine is an antiretroviral drug that slows the growth of the HIV virus. The reason lamivudine and lamivudine-zidovudine (Combivir®) is included in the Prevention of Perinatal HIV Transmission Kit is to prevent the emergence of HIV drug resistance in mothers and babies *who received* either the *single-dose or three-dose nevirapine* regimen respectively.

Dose and administration:

- The Prevention of Perinatal HIV Transmission Kit contains oral lamivudine-zidovudine (Combivir®) tablets (14 tablets of combination lamivudine 150 mg + zidovudine 300 mg) and oral lamivudine liquid (25 mL of 10 mg/mL liquid). There is no IV formulation of lamivudine available.

Mother:

  - Lamivudine-zidovudine (Combivir®) *1 tablet orally twice daily for seven days* should be administered to women who received single-dose oral nevirapine during labour and delivery.
- The first dose should be given as soon as the woman is able to tolerate oral intake.
  - ***Ensure that the oral lamivudine-zidovudine (Combivir®) tablets are sent home with the mother.***

Infant:

  - Lamivudine 6 mg (4 mg if infant weighs ≤ 2 kg) by mouth every 12 hours for *two weeks.* The first dose of lamivudine should be given immediately after birth.
  - Lamivudine liquid is a 10 mg/mL solution. Each dose for the infant will be either 6 mg (0.6 mL) if infant weight > 2kg, or 4 mg (0.4 mL) if infant weight ≤ 2 kg.
  - Lamivudine liquid can be stored at room temperature.
  - Lamivudine can be given before, during, or after a feed. Gently push the oral syringe in the infant's mouth just inside the cheek and given 4 or 5 gentle pushes on the plunger of the syringe to administer the dose.
  - If the infant vomits within 15 minutes of the dose, give another dose if possible. If it is more than 15 minutes after the dose, do NOT give another dose, and give the next dose when scheduled.
- The infant should **also receive** oral zidovudine (recommended dose for gestational age) for the first six weeks of life **and** three-doses of nevirapine 12 mg (8 mg if infant weighs ≤ 2 kg) given at birth (day 0), two days of age and six days of age.
  - ***Ensure that an adequate volume of lamivudine oral liquid is sent home with the infant.***

Adverse effects:

  - Lamivudine-zidovudine (Combivir®) when given for 7 days is well tolerated. Possible adverse effects that may occur include nausea, headache, difficulty sleeping and fatigue.
- Mild anemia and neutropenia have been noted in some infants receiving lamivudine. Reductions in hemoglobin or neutrophils may occur as early as 2-4 weeks. These conditions are usually mild, however may be slightly greater as infants are also receiving oral zidovudine therapy, and resolve when the dose is reduced or the drug is discontinued.