Didanosine (ddI, Videx)

Updated: May 22, 2018
Reviewed: May 22, 2018

Formulations

Pediatric Oral Solution: 10 mg/mL

Enteric-Coated (EC) Delayed-Release Capsules (EC Beadlets): 125 mg, 200 mg, 250 mg, and 400 mg

Generic Formulations

Delayed-Release Capsules: 125 mg, 200 mg, 250 mg, and 400 mg

For additional information, see Drugs@FDA.

Dosing Recommendations

Note: Didanosine is no longer recommended by the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV for use in children due to higher rates of adverse effects than other NRTIs.

Neonate/Infant Dose (Aged 2 Weeks to <3 Months)

- 50 mg/m^2 of body surface area every 12 hours. See dosing section below for justification of this dose.

Infant Dose (Aged ≥3 Months to 8 Months)

- 100 mg/m^2 of body surface area every 12 hours

Pediatric Dose of Oral Solution (Aged >8 Months)

- 120 mg/m^2 of body surface area every 12 hours
- Dose range: 90–150 mg/m^2 of body surface area every 12 hours. Do not exceed maximum adult dose; see table below.
- In treatment-naive children aged 3 years to 21 years, 240 mg/m^2 of body surface area once daily (oral solution or capsules) has resulted in viral suppression.

Pediatric Dose of Videx EC or Generic Capsules (Aged 6–**18 Years and Weighing ≥20 kg)**

Body Weight	Dose
20 kg to <25 kg	200 mg once daily
25 kg to <60 kg	250 mg once daily
≥60 kg	400 mg once daily

Selected Adverse Events

- Peripheral neuropathy
- Diarrhea, abdominal pain, nausea, vomiting
- Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported (the risk is increased when didanosine is used in combination with stavudine).
- Pancreatitis (less common in children than in adults, more common when didanosine is used in combination with tenofovir disoproxil fumarate or stavudine)
- Non-cirrhotic portal hypertension
- Retinal changes, optic neuritis
- Insulin resistance/diabetes mellitus

Special Instructions

- Administer didanosine on an empty stomach (30 minutes before or 2 hours after a meal). To improve adherence, some practitioners administer didanosine without regard to timing of meals (see text below).
- Didanosine powder for oral solution contains antacids that may interfere with the absorption of other medications, including protease inhibitors (PIs). See individual PI for instructions on timing of administration.
- Shake didanosine oral solution well before use. Keep refrigerated; solution is stable for 30 days.

Adolescent and Adult Dose

Body Weight	Dose
<60 kg	250 mg once daily
≥60 kg	400 mg once daily

Pediatric and Adolescent Dose of Didanosine when Combined with Tenofovir Disoproxil Fumarate

- This combination should be avoided because of enhanced didanosine toxicity, reports of immunologic nonresponse, high rates of early virologic failure, and rapid selection of resistance mutations (see the Adult and Adolescent Guidelines).

Metabolism/Elimination

- Renal excretion 50%
- Decrease dosage in patients with impaired renal function. Consult manufacturer's prescribing information for adjustment of dosage in accordance with creatinine clearance.

Drug Interactions

Additional information about drug interactions is available in the Adult and Adolescent Guidelines and the HIV Drug Interaction Checker.

- *Absorption:* Antacids in didanosine oral solution can decrease the absorption of a number of medications if given at the same time. Avoid giving other medications concurrently with didanosine oral solution.
- *Mechanism unknown:* Didanosine serum concentrations are increased when didanosine is co-administered with tenofovir disoproxil fumarate (TDF). This combination should be avoided.
- *Renal elimination:* Drugs that decrease renal function can decrease didanosine clearance.
- *Overlapping toxicities:* The combination of stavudine with didanosine may result in enhanced toxicity. This combination should be avoided (see the Major Toxicities section below).

Major Toxicities

- *More common:* Diarrhea, abdominal pain, nausea, vomiting
- *Less common (more severe):* Peripheral neuropathy, electrolyte abnormalities, and hyperuricemia. Lactic acidosis and hepatomegaly with steatosis, including fatal cases, have been reported, and are more common when didanosine is used in combination with stavudine. Pancreatitis (less common in children than in adults, more common when didanosine is used in combination with TDF or stavudine) can occur. Increased liver enzymes, retinal depigmentation, and optic neuritis have been reported. Decreases in CD4 T lymphocyte counts have been reported when didanosine is used in combination with TDF.
- *Rare:* Non-cirrhotic portal hypertension, presenting clinically with hematemesis, esophageal varices, ascites, and splenomegaly, and associated with increased transaminases, increased alkaline phosphatase, and thrombocytopenia, has been associated with long-term didanosine use.[1]
- *Possible risk of cancer after in-utero exposure*: In a study of 15,163 children without HIV infection who were exposed to at least one nucleoside reverse transcriptase inhibitor (NRTI) *in utero*, 21 cancers were identified. Didanosine accounted for only 10% of prescriptions but was associated with one-third of identified cancers, and, in multivariate analysis, didanosine was

associated with a 5.5-fold (95% CI, 2.1–14.4) increased risk of cancer with first-trimester exposure.[2] Pregnant adolescents or sexually active female adolescents on didanosine should be cautioned about this risk.

Resistance

The International AIDS Society–USA maintains a list of updated resistance mutations and the Stanford University HIV Drug Resistance Database offers a discussion of each mutation.

Pediatric Use

Approval

Although didanosine is a Food and Drug Administration (FDA)-approved NRTI for use in children as part of antiretroviral therapy, it **is not recommended** for in children due to its significant toxicity and the availability of safer agents.

Dosing

Standard Dose in Children Aged >8 Months

The standard dose of didanosine oral solution in children aged >8 months is 120 mg/m^2 of body surface area twice daily.[3,4] Doses higher than 180 mg/m^2 of body surface area twice daily are associated with increased toxicity.[5]

Special Considerations for Children Aged 2 Weeks to <8 Months

For infants aged 2 weeks to 8 months, the FDA recommends 100 mg/m^2 of body surface area per dose twice daily. However, because pharmacokinetic (PK) differences in younger infants (aged 2 weeks–3 months) compared with older children raise concerns for increased toxicity in this younger age group, the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV recommends a dose of 50 mg/m^2 of body surface area twice daily for infants aged 2 weeks to 3 months, with an increase to 100 mg/m^2 of body surface area per dose twice daily at 3 months, and finally increasing to 120 mg/m^2 of body surface area per dose twice daily at age 8 months (as discussed above).

Frequency of Administration (Once Daily or Twice Daily)

In those aged >3 years, a once-daily dosing regimen may be preferable to promote adherence, and multiple studies support the favorable PKs and efficacy of once-daily dosing of 240 mg/m^2 of body surface area.[6]

Food Restrictions

Although the prescribing information recommends taking didanosine on an empty stomach, this is impractical for infants who must be fed frequently, and it may decrease medication adherence by increasing regimen complexity. A comparison showed that systemic exposure measured by area under the curve was similar whether didanosine oral solution was given to children with or without food; absorption of didanosine administered with food was slower and elimination more prolonged.[7]

To improve adherence, some practitioners administer didanosine without regard to timing of meals. Studies in adults suggest that didanosine can be given without regard to food.[8,9] A European study dosed didanosine oral solution as part of a four-drug regimen either 1 hour before or 1 hour after meals, but allowed the extended-release formulation to be given without food restriction. The study showed good virologic outcome with up to 96 weeks of follow-up.[10]

References

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