Indinavir (IDV, Crixivan)

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Formulations

Capsules: 100 mg, 200 mg, and 400 mg

For additional information, see Drugs@FDA.

Dosing Recommendations

Neonate and Infant Dose

- Not approved for use in neonates/infants
- Should not be administered to neonates because of the risks associated with hyperbilirubinemia (kernicterus)

Pediatric Dose

- Not approved for use in children
- A range of indinavir doses (234–500 mg/m^2 body surface area) boosted with low-dose ritonavir has been studied in children (see text below).

Adolescent and Adult Dose

- 800 mg indinavir plus 100 or 200 mg ritonavir every 12 hours
- The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV **does not recommend** the use of indinavir in adolescents.

Selected Adverse Events

- Nephrolithiasis
- Gastrointestinal intolerance, nausea
- Hepatitis
- Indirect hyperbilirubinemia
- Hyperlipidemia
- Hyperglycemia
- Fat maldistribution
- Possible increased bleeding episodes in patients with hemophilia

Special Instructions

- When indinavir is given in combination with ritonavir, meal restrictions are not necessary.
- Adequate hydration is required to minimize risk of nephrolithiasis (≥48 oz of fluid daily in adult patients).
- Indinavir capsules are sensitive to moisture; store at room temperature (59–86ºF) in original container with desiccant.

Metabolism/Elimination

- Cytochrome P450 3A4 (CYP3A4) inhibitor and substrate

Indinavir Dosing in Patients With Hepatic Impairment

- Dose should be decreased in patients with mild-to-moderate hepatic impairment (recommended dose for adults is 600 mg indinavir every 8 hours). No dosing information is available for children with any degree of hepatic impairment or for adults with severe hepatic impairment.

Drug Interactions

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

- *Metabolism:* Cytochrome P450 3A4 (CYP3A4) is the major enzyme responsible for metabolism. There is potential for multiple drug interactions with indinavir.
- Avoid other drugs that cause hyperbilirubinemia, such as atazanavir.
- Before administration, a patient's medication profile should be carefully reviewed for potential drug interactions with indinavir.

Major Toxicities

- *More common:* Nephrolithiasis/urolithiasis with indinavir crystal deposit is reported more frequently in children (29%) than in adults (12.4%).[1] Interstitial nephritis and urothelial inflammation has been commonly reported in adults.[2] Nausea, abdominal pain, headache, metallic taste, dizziness, asymptomatic hyperbilirubinemia (10%), lipid abnormalities, pruritus, and rash.
- *Less common (more severe):* Fat maldistribution.
- *Rare:* New-onset diabetes mellitus, hyperglycemia, ketoacidosis, exacerbation of preexisting diabetes mellitus, spontaneous bleeding in hemophiliacs, acute hemolytic anemia, and hepatitis (life-threatening in rare cases).

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

Indinavir has not been approved by the Food and Drug Administration for use in the pediatric population. Although indinavir was one of the first protease inhibitors to be studied in children, its use in pediatrics has never been common and is currently very rare.[3] Indinavir **is not recommended** by the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV for use in children and adolescents because of its unfavorable toxicity profile, limited efficacy data, and uncertain pharmacokinetics.

Efficacy and Pharmacokinetics

Both unboosted and ritonavir-boosted indinavir have been studied in children with HIV. In children, an unboosted indinavir dose of 500 to 600 mg/m^2 body surface area given every 8 hours results in peak blood concentrations and area under the curve that are slightly higher than those in adults, but trough concentrations are considerably lower. A significant proportion of children have trough indinavir concentrations less than the 0.1 mg/L value associated with virologic efficacy in adults.[4-7] Studies that investigated a range of indinavir/ritonavir doses in small groups of children have shown that indinavir 500 mg/m^2 body surface area plus ritonavir 100 mg/m^2 body surface area twice daily is probably too high,[8] that indinavir 234 to 250 mg/m^2 body surface area plus low-dose ritonavir twice

daily is too low,[9,10] and that indinavir 400 mg/m^2 body surface area plus ritonavir 100 to 125 mg/m^2 body surface area twice daily results in exposures approximating those seen with indinavir 800 mg plus ritonavir 100 mg twice daily in adults, albeit with considerable inter-individual variability and high rates of toxicity.[10-12]

References

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