Tecovirimat

Tecovirimat is an inhibitor of the orthopoxvirus VP37 envelope wrapping protein.

Class: 8:18.92 • Antivirals, Miscellaneous (AHFS primary)

Brands: TPOXX®

Uses

Smallpox

Tecovirimat has the following uses:

Tecovirimat is indicated for the treatment of human smallpox disease in adults and pediatric patients weighing at least 3 kg.

Tecovirimat has the following limitations of use:

- The effectiveness of tecovirimat for treatment of smallpox disease has not been determined in humans because adequate and well-controlled field trials have not been feasible, and inducing smallpox disease in humans to study the drug's efficacy is not ethical.
- Tecovirimat efficacy may be reduced in immunocompromised patients based on studies demonstrating reduced efficacy in immunocompromised animal models.

Other Uses

- Use of tecovirimat for other orthopoxvirus infections including monkeypox is not approved by the FDA. However, the CDC holds a non-research expanded access Investigational New Drug (EA-INd) protocol that allows for the use of tecovirimat for primary or emergency treatment of non-varoiola orthopoxvirus infections, including monkeypox, in adults and children of all ages. For additional information, see the CDC website at https://www.cdc.gov/poxvirus/monkeypoxclinicians/Tecovirimat.html
- CDC states that tecovirimat may be considered for treatment of the following individuals infected with monkeypox: people with severe disease (e.g., hemorrhagic disease, confluent lesions, sepsis, encephalitis, or other conditions requiring hospitalization), people who are at high risk of severe disease including individuals with immunocompromising conditions (e.g., human immunodeficiency virus/acquired immune deficiency syndrome infection, leukemia, lymphoma, generalized malignancy, solid organ transplantation; therapy with alkylating agents, antimetabolites, radiation, tumor necrosis factor inhibitors, high-dose corticosteroids; being a recipient with hematopoietic stem cell transplant <24 months post-transplant or >24 months but with graft-versus-host disease or disease relapse, or having autoimmune disease with immunodeficiency as a clinical component), pediatric populations particularly patients younger than 8 years of age, people with a history or presence of atopic dermatitis, persons with other active exfoliative skin conditions (e.g., eczema, burns, impetigo, varicella zoster virus infection, herpes simplex virus infection, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier disease [keratosis follicularis]), pregnant or breastfeeding women, and people with one or more complications (e.g., secondary bacterial skin infection; gastroenteritis with severe nausea/vomiting, diarrhea, or dehydration; bronchopneumonia; concurrent disease or other comorbidities), and people with aberrant infections that include accidental implantation in eyes, mouth, or other anatomical areas where monkeypox virus infection might constitute a special hazard (e.g., the genitals or anus).

Dosage and Administration

General

Tecovirimat is available in the following dosage form(s) and strength(s):

Capsule: 200 mg (of anhydrous tecovirimat).

Injection: Single-use 30 mL vials containing 200 mg/20 mL of tecovirimat.

For patients who cannot swallow capsules, the capsules may be opened and the contents mixed with 30 mL of liquid (e.g., milk, chocolate milk) or soft food (e.g., applesauce, yogurt). The entire mixture should be administered within 30 minutes of preparation.

It is recommended that patients weighing 13 kg and above initiate oral treatment with tecovirimat capsules if possible. If patients are unable to take oral tecovirimat capsules (or the capsules opened and prepared in food), treatment may be initiated with tecovirimat injection. If IV treatment is necessary, conversion from IV to oral tecovirimat is recommended as soon as oral treatment can be tolerated. In patients receiving an IV infusion, the first dose of oral treatment should be given at the time of and in place of the next scheduled IV dosing. In patients receiving oral treatment who subsequently require IV treatment, the first dose of IV infusion should be given at the time of and in place of the next scheduled oral dosing.

Determine creatinine clearance in all patients before starting tecovirimat injection and monitor while receiving tecovirimat injection as clinically appropriate.

Dosage

It is essential that the manufacturer's labeling be consulted for more detailed information on dosage and administration of this drug. Dosage summary:

- Tecovirimat capsules should be taken within 30 minutes after a full meal of moderate or high fat.
- Tecovirimat injection is administered by IV infusion over 6 hours using an infusion pump; do not administer by IV bolus injection. Depending on the size of syringe available with the syringe pump system, two separate syringes may be needed for each 6 hour administration.
- Tecovirimat injection must be diluted prior to administration. The appropriate quantity of tecovirimat injection should be withdrawn into a syringe of suitable size and then diluted with 2 equal parts of either 0.9% sodium chloride injection or 5% dextrose injection; do not use prefilled infusion bags for product preparation and administration (see Table 1).

Table 1: Recommended Preparation Instructions for Tecovirimat Injection for IV Infusion in Pediatric Patients and Adults

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Volume of Tecovirimat Injection</th>
<th>Volume of Diluent</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 kg to less than 35 kg</td>
<td>0.6 mL/kg</td>
<td>1.2 mL/kg</td>
</tr>
<tr>
<td>35 kg to less than 120 kg</td>
<td>20 mL</td>
<td>40 mL</td>
</tr>
<tr>
<td>120 kg and above</td>
<td>30 mL</td>
<td>60 mL</td>
</tr>
</tbody>
</table>

- 10 mg/mL tecovirimat solution containing 40% hydroxypropyl betadex (8 g per vial) with water for injection
- Diluent is either 0.9% sodium chloride injection or 5% dextrose injection solution.

The diluted tecovirimat solution may be stored in the refrigerator (2–8°C) for up to 24 hours or at room temperature (15–25°C) for up to 4 hours.

Pediatric Patients

Smallpox

Oral: Patients weighing 13 kg to less than 25 kg: 200 mg taken every 12 hours orally for 14 days.

Patients weighing 25 kg to less than 40 kg: 400 mg (two 200-mg capsules) taken every 12 hours orally for 14 days.

Patients weighing 40 kg to less than 120 kg: 600 mg (three 200-mg capsules) taken every 12 hours orally for 14 days.

Patients weighing 120 kg or more: 800 mg (three 200-mg capsules) taken every 8 hours orally for 14 days.

IV: Patients weighing 3 kg to less than 35 kg: 6 mg/kg every 12 hours by IV infusion over 6 hours for up to 14 days.

Patients weighing 35 kg to less than 120 kg: 6 mg/kg every 12 hours by IV infusion over 6 hours for up to 14 days.

Patients weighing 120 kg or more: 8 mg/kg every 12 hours by IV infusion over 6 hours for up to 14 days.

Pediatric Patients weighing at least 13 kg should be switched to tecovirimat capsules to complete the 14 day treatment course as soon as oral therapy can be tolerated.

Adults

Smallpox

Oral: Patients weighing 13 kg to less than 25 kg: 200 mg taken every 12 hours orally for 14 days.

Patients weighing 25 kg to less than 120 kg: 600 mg taken every 12 hours orally for 14 days.

Patients weighing 120 kg or more: 800 mg taken every 8 hours orally for 14 days.

IV: Patients weighing 3 kg to less than 35 kg: 6 mg/kg every 12 hours by IV infusion over 6 hours for up to 14 days.

Patients weighing 35 kg to less than 120 kg: 6 mg/kg every 12 hours by IV infusion over 6 hours for up to 14 days.

Patients weighing 120 kg or more: 8 mg/kg every 12 hours by IV infusion over 6 hours for up to 14 days.

Pediatric Patients weighing at least 13 kg should be switched to tecovirimat capsules to complete the 14 day treatment course as soon as oral therapy can be tolerated.

Cautions

Contraindications

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**Mechanism of Action**

Tecovirimat is an antiviral agent active against variola (smallpox) virus. Tecovirimat targets and inhibits the activity of the orthopoxvirus VP37 protein (encoded by and highly conserved in all members of the orthopoxvirus genus) and blocks its interaction with cellular RAB9 GTPase and TIP47, which prevents the formation of egress-competent enveloped virions necessary for cell-to-cell and long-range dissemination of virus.

**Spectrum**

In cell culture assays, the effective concentrations of tecovirimat resulting in a 50% reduction in virus-induced cytotoxic effect (EC50) were 0.016-0.067 µM, 0.014-0.039 µM, 0.015 µM, and 0.009 µM for variola, monkeypox, rabbitpox, and vaccinia viruses, respectively. Ranges given for variola and monkeypox viruses are reflective of results from multiple strains assayed.

**Resistance**

There are no known instances of naturally occurring tecovirimat-resistant orthopoxviruses, although tecovirimat resistance may develop under drug selection. Tecovirimat has a relatively low resistance barrier, and certain amino acid substitutions in the target VP37
protein can confer large reductions in tecovirimat antiviral activity. The possibility of resistance to tecovirimat should be considered in patients who either fail to respond to therapy or who develop recrudescence of disease after an initial period of responsiveness.

- **Cross Resistance:** Cross-resistance between tecovirimat and brincidofovir is not expected based on their distinct mechanisms of action. Where tested, orthopoxvirus isolates resistant to cidofovir (the active metabolite of brincidofovir) have not been resistant to tecovirimat. Likewise, orthopoxvirus isolates resistant to tecovirimat retain their sensitivity to cidofovir.

### Advice to Patients

- Advise the patient to read the FDA-approved patient labeling (Patient Information).
- Inform patients that the efficacy of tecovirimat is based solely on efficacy studies demonstrating a survival benefit in animals and that the effectiveness of tecovirimat has not been tested in humans with smallpox disease.
- Advise patients to take tecovirimat capsules as directed within 30 minutes of eating a full meal of moderate or high fat with 6-8 oz. of water. Inform patients to take tecovirimat for the entire duration without missing or skipping a dose. Inform patients who cannot swallow capsules to refer to the manufacturer's Instructions for Use to mix the contents of the capsule with soft food or liquid.
- Inform patients that tecovirimat may interact with other drugs. Advise patients to report to their healthcare provider the use of other prescription drugs. Co-administration of tecovirimat with repaglinide may cause hypoglycemia.
- Advise patients that if a dose of oral tecovirimat is missed, to take the missed dose as soon as possible, up to 8 hours prior to the next dose. If less than 8 hours remain before the next scheduled dose, do not take the missed dose and resume dosing with the next scheduled dose.
- Inform patients with smallpox not to breastfeed their infant because of the risk of passing variola virus to the breastfed infant.

### Preparations

Excipients in commercially available drug preparations may have clinically important effects in some individuals; consult specific product labeling for details.

Tecovirimat is stored in the US Strategic National Stockpile (SNS) and is not commercially available in the US. The SNS ensures that certain drugs and medical supplies are readily available to prevent or treat specific diseases, including during public health emergencies, and is managed by the US Department of Health and Human Services (HHS) Office of the Assistant Secretary for Preparedness and Response (ASPR). To request a drug from the SNS, state health departments can contact the US Centers for Disease Control and Prevention (CDC) Emergency Operations Center at 770-488-7100 or the HHS Secretary's Operations Center at 202-619-7800.

**Tecovirimat**

**Oral**

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**Injection, for IV infusion**

| 200mg/20 mL |

† Use is not currently included in the labeling approved by the US Food and Drug Administration.

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