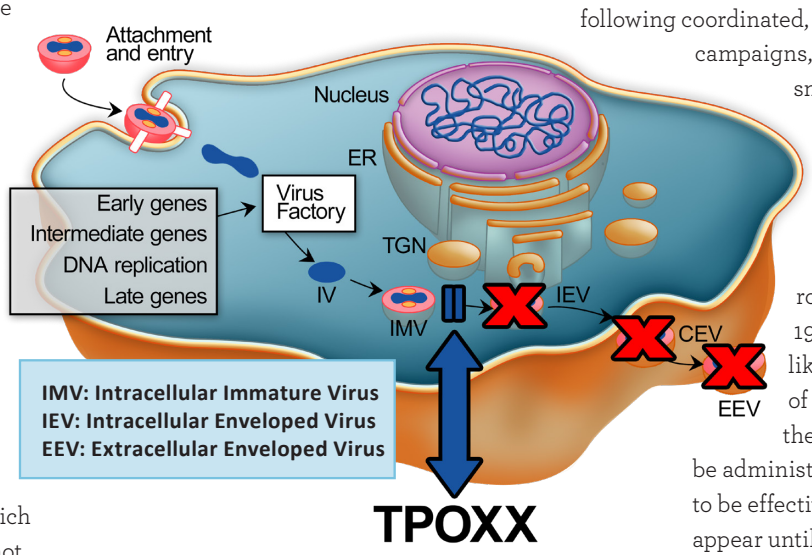
TPOXX® (tecovirimat) FACT SHEET

SIGA Technologies has developed TPOXX® (USAN tecovirimat, ST-246), the first drug approved by the U.S. Food and Drug Administration (FDA) that is specifically indicated for the treatment of smallpox disease in adults and pediatric patients weighing at least 13 kg. TPOXX is among the first novel small molecule therapies delivered to the Strategic National Stockpile (SNS) under Project BioShield, a U.S. government program designed to accelerate the research, development, purchase, and availability of effective medical countermeasures against biological, chemical, radiological, and nuclear (CBRN) agents. TPOXX's advanced development has been funded in partnership with the Biomedical Advanced Research and Development Authority (BARDA) of the U.S. Department of Health and Human Services. SIGA has supplied TPOXX for the treatment of smallpox to the SNS and has a contract with BARDA for the continuing replenishment of the stockpile as courses expire.

TPOXX inhibits systemic spread of variola virus (the virus that causes smallpox) by preventing the formation of a secondary viral envelope. In the absence of this envelope, viral particles remain inside the cell in which they are produced and cannot spread to and infect other cells.

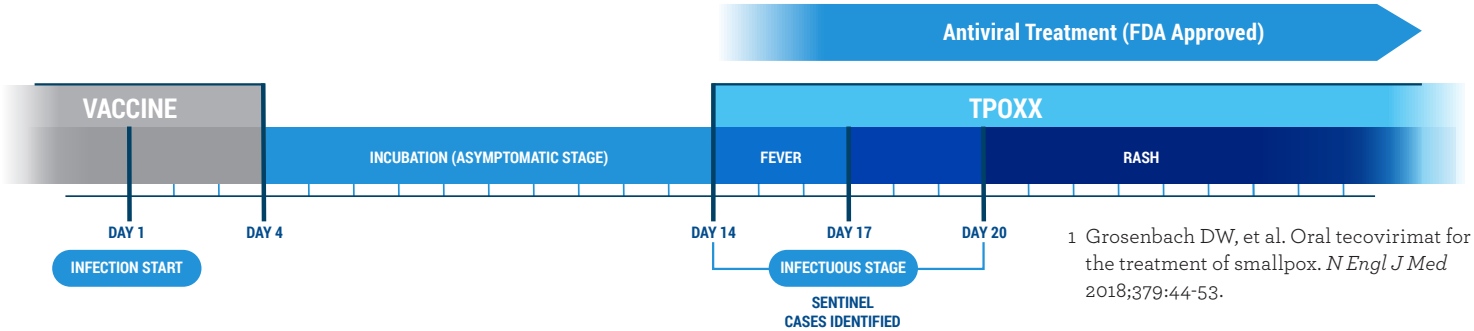
The minimum effective dose of TPOXX was demonstrated in lethal monkeypox/non-human primate (NHP) and rabbitpox/rabbit models and provided maximal survival benefit. Based on results from studies in immunocompromised animal models, the efficacy of TPOXX may be reduced in immunocompromised patients. A placebo-controlled human pharmacokinetic and safety study was performed in 449 adult volunteers, of which 359 received TPOXX. Human dosing at 600 mg twice daily for 14 days was selected for testing, and provided exposures in excess of animal exposures. While no pattern of concerning adverse events was observed, six subjects (2%) had their treatment discontinued due to adverse reactions. A dedicated drug-drug interaction study determined that drug interactions exist for co-administration of repaglinide and midazolam. Results of the animal studies and the pivotal human safety study were published in The New England Journal of Medicine in July 2018.[1]



TPOXX: Inhibits the viral envelope formation and spread of the virus

Hruby D.E., Byrd C.M. 2006. Less is More: Poxvirus Proteolysis. *Microbe*. 1(2):70-5.

Although naturally occurring smallpox was eradicated in 1980 following coordinated, decades-long global vaccination campaigns, there is growing concern that smallpox could be used as a bioweapon. A smallpox bioterror attack could be especially damaging because the majority of today's population is not immune to the virus, as routine vaccination ended in the 1970s. Vaccination alone would likely not be effective in the event of a smallpox bioterror attack due to the fact that vaccine would need to be administered within 3-5 days of infection to be effective as therapy, yet symptoms don't appear until 14 days after infection. As the first antiviral agent specifically indicated for the treatment of smallpox, TPOXX would play a critical role in responding to a smallpox bioterror attack.



1 Grosenbach DW, et al. Oral tecovirimat for the treatment of smallpox. *N Engl J Med* 2018;379:44-53.

ADDITIONAL TPOXX® INFORMATION

This summary does not include all the information needed to use TPOXX safely and effectively. See full prescribing information for TPOXX at: *https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208627s000lbl.pdf*

Dosage and Administration

TPOXX is supplied in capsules containing 200 mg of tecovirimat. TPOXX should be taken within 30 minutes after a full meal of moderate or high fat.

- Adult patients:
  - Up to 120 kg:
    600 mg of TPOXX twice daily for 14 days
  - 120 kg or more:
    600 mg of TPOXX three times daily for 14 days
- Pediatrics patients weighing 13 kg or more:
  - 13 kg to less than 25 kg:
    200 mg of TPOXX twice daily for 14 days
  - 25 kg to less than 40 kg:
    400 mg of TPOXX twice daily for 14 days
  - 40 kg or more:
    600 mg of TPOXX twice daily for 14 days

Contraindications:

None

Warnings and Precautions

Hypoglycemia: Co-administration with repaglinide may cause hypoglycemia. Monitor blood glucose and monitor for hypoglycemic symptoms during co-administration.

Adverse Reactions

Common adverse reactions in healthy adult subjects (≥ 2%) were headache, nausea, abdominal pain (which includes abdominal pain upper or lower, abdominal distension, abdominal discomfort, epigastric pain), and vomiting. These are not all of the possible side effects of TPOXX.

Drug Interactions

The full prescribing information should be consulted prior to and during treatment for potential drug interactions.

Active Ingredient

Tecovirimat

Inactive Ingredients

Colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl methyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and sodium lauryl sulfate. The capsule shell is made of gelatin, FD&C blue #1, FD&C red #3, FD&C yellow #6, and titanium dioxide.

Other Approvals

Oral tecovirimat was approved by the European Medicines Agency (EMA) in 2022. See full prescribing information: https://www.ema.europa.eu/documents/product-information/tecovirimat-siga-epar productinformation_ en.pdf

In 2021 Health Canada also authorized the use of oral TPOXX. The patient medication information can be found at: https://pdf.hres.ca/dpd_pm/00063782.PDF

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