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5.01.059

Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Anti-infective Agents	**Original Policy Date:**	July 2, 2021
Subject:	Tembexa	**Page:**	1 of 4

Last Review Date: December 13, 2024

Tembexa

Description

Tembexa (brincidofovir)

Background
Tembexa (brincidofovir) is an antiviral drug against variola (smallpox) virus. Tembexa is a lipid conjugate of cidofovir, an acyclic nucleotide analog of deoxycytidine monophosphate. The lipid conjugate is designed to mimic a natural lipid, lysophosphatidylcholine, and thereby use endogenous lipid uptake pathways. Once inside cells, the lipid ester linkage of Tembexa is cleaved to liberate cidofovir, which is then phosphorylated to produce the active antiviral, cidofovir diphosphate. Based on biochemical and mechanism studies using recombinant vaccinia virus E9L DNA polymerase, cidofovir diphosphate selectively inhibits orthopoxvirus DNA polymerase-mediated viral DNA synthesis. Incorporation of cidofovir into the growing viral DNA chain results in reductions in the rate of viral DNA synthesis (1).

Regulatory Status
FDA-approved indications: Tembexa is an orthopoxvirus nucleotide analog DNA polymerase inhibitor and is indicated for the treatment of human smallpox disease in adult and pediatric patients, including neonates (1).

Limitations of Use:

- Tembexa is not indicated for the treatment of diseases other than human smallpox disease.
- The effectiveness of Tembexa for the 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.
- Tembexa efficacy may be reduced in immunocompromised patients based on studies in immune deficient animals.

Tembexa has a boxed warning regarding increased risk for mortality when used for longer duration. An increased risk of mortality was seen in Tembexa-treated subjects compared to placebo-treated subjects in a 24-week clinical trial when Tembexa was evaluated in another disease (1).

Hepatic laboratory testing should be performed in all patients before starting Tembexa and while receiving Tembexa, as clinically appropriate. Pregnancy testing should be performed before initiation of Tembexa in individuals of childbearing potential to inform risk (1).

Tembexa has warnings regarding the following: increased risk for mortality when used for longer duration; elevations in hepatic transaminases and bilirubin; diarrhea and other gastrointestinal adverse events; coadministration with related products; embryo-fetal toxicity; carcinogenicity; and male infertility (1).

Pregnancy testing should be performed in individuals of childbearing potential before initiation of Tembexa. Individuals of childbearing potential should be advised to avoid becoming pregnant and to use effective contraception during treatment with Tembexa and for at least 2 months after the last dose. Individuals of reproductive potential with partners of childbearing potential should be advised to use condoms during treatment with Tembexa and for at least 4 months after the last dose (1).

As in adults, the effectiveness of Tembexa in smallpox infected pediatric patients, including neonates, is based solely on efficacy studies in animal models of orthopoxvirus disease. The safety in adult and pediatric subjects treated with Tembexa were similar (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Tembexa may be considered **medically necessary** if the conditions indicated below are met.

Tembexa may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following:

Smallpox (variola virus)

AND ALL of the following:

1. Prescriber agrees to monitor AST, ALT, and bilirubin
2. Females of reproductive potential **only**: patient has had a negative pregnancy test
3. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Tembexa and for 2 months after the last dose
4. Males with female partners of reproductive potential **only**: patient will be advised to use condoms during treatment with Tembexa and for 4 months after the last dose

Prior – Approval *Renewal* Requirements

None

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Weight	Dosage Form	Quantity
Less than 48 kg	Oral suspension	1 bottle
48 kg and above	Oral suspension	1 bottle **OR**
	Tablet	4 tablets

Duration 30 days

Prior – Approval *Renewal* Limits

None

Rationale

Summary

Tembexa (brincidofovir) is an antiviral drug against variola (smallpox) virus. As in adults, the effectiveness of Tembexa in smallpox infected pediatric patients, including neonates, is based solely on efficacy studies in animal models of orthopoxvirus disease. Tembexa has a boxed warning regarding increased risk for mortality when used for longer duration. Tembexa has warnings regarding the following: increased risk for mortality when used for longer duration; elevations in hepatic transaminases and bilirubin; diarrhea and other gastrointestinal adverse events; coadministration with related products; embryo-fetal toxicity; carcinogenicity; and male infertility. The safety in adult and pediatric subjects treated with Tembexa were similar (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Tembexa while maintaining optimal therapeutic outcomes.

References

1. Tembexa [package Insert]. Durham, NC: Chimerix, Inc.; December 2021.

Policy History

Date	Action
July 2021	Addition to PA
September 2021	Annual review and reference update
July 2023	Revised requirement to monitor AST, ALT, and bilirubin. Revised background section. Changed policy number to 5.01.059
September 2023	Annual review
December 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.