<Date>

Tecovirimat SIGA ▼ (tecovirimat monohydrate): restriction of indication due to lack of efficacy shown in randomised clinical trials in patients with mpox

Dear Healthcare professional,

SIGA Technologies Netherlands B.V. in agreement with the European Medicines Agency and the <National Competent Authority> would like to inform you of the following:

Summary

- New patients should not initiate Tecovirimat SIGA for the treatment of mpox.
- This restriction is based on data from recently completed clinical trials, showing that Tecovirimat SIGA lacked efficacy in generally immunocompetent patients with active mpox lesions under the settings studied.
- This restriction of indication is not based on safety concerns.
- There are no other medicines authorised in the EU for treating mpox infections. Patients who already have started treatment with Tecovirimat SIGA can complete their treatment course.
- Physicians should contact patients currently on treatment with Tecovirimat SIGA for mpox to discuss options for clinical management.
- Tecovirimat SIGA remains authorised for the treatment of smallpox and cowpox, and to treat complications due to replication of vaccinia virus following vaccination against smallpox, in adults and children with a body weight of at least 13 kg.

Background information

In January 2022, a marketing authorisation under exceptional circumstances was granted for Tecovirimat SIGA for the treatment of the following viral infections in adults and children with a body weight of at least 13 kg: smallpox, mpox, and cowpox. Tecovirimat SIGA is also indicated to treat complications due to replication of vaccinia virus following vaccination against smallpox in adults and children with body weight at least 13 kg. Treatment is to be initiated as soon as possible after diagnosis.

At the time of authorisation, comprehensive data on the efficacy and safety of Tecovirimat SIGA could not be provided under normal conditions of use, due to the absence or rare circulation of these orthopoxviruses in humans[1]. Efficacy was evaluated using data from animal studies with extrapolation to humans while safety was evaluated based on data from animal and healthy volunteer studies. In the animal studies, the efficacy of Tecovirimat SIGA was demonstrated if treatment was initiated within four days after exposure to monkeypox or rabbitpox virus, while later treatment initiation in non-human primates (6 days after intravenous monkeypox viral challenge) resulted in a reduction of the survival rate compared to animals treated earlier (83% at 4 days, 50% at 6 days, 0% without treatment). Tecovirimat SIGA was therefore granted a marketing authorisation under exceptional circumstances with the obligation for the marketing authorisation holder (MAH) to provide additional data post-approval. The MAH is required to submit annual reports on any new data relevant for the

[1] Tecovirimat SIGA, public assessment report of the initial marketing authorisation

safety and efficacy of Tecovirimat SIGA in its authorised indications, together with an annual reassessment of its overall benefit-risk balance.

Following an EU-wide review of all available data, including available results from four randomised, placebo-controlled, double-blind trials (i.e. PALM007[2], STOMP[3], UNITY[4] and PLATINUM-UK[5]) evaluating the safety and efficacy of tecovirimat for the treatment of mpox in humans, EMA has concluded that under the conditions studied, tecovirimat did not reduce the time to lesion resolution compared with placebo. The randomised controlled trials had a similar design based on the World Health Organization (WHO) core protocol. Of the four clinical trials, three were undertaken in the context of outbreaks related to Clade II mpox infections (STOMP, UNITY, PLATINUM-UK) while the fourth (PALM007), was conducted in the context of Clade I mpox in the Democratic Republic of Congo. In these trials, patients were treated late in the course of disease progression, usually between 6 and 9 days following the appearance of lesions. The trials failed to show any efficacy in patients diagnosed with mpox based on established skin or mucosal lesions. While tecovirimat treated patients did not achieve a faster time to lesion resolution versus placebo in these trials, it is plausible that the patients were not treated early enough in their disease course for tecovirimat to be effective.

No new safety concerns have been identified within the context of the EU-wide review and therefore the safety profile of the medicine remains unchanged.

In view of the above clinical data, the benefit-risk balance of Tecovirimat SIGA for the treatment of patients with mpox is no longer considered favourable.

Due to the lack of clinical data evaluating the efficacy of tecovirimat in the other indications, the in vitro and animal data presented at the time of authorisation are still considered relevant for the use of tecovirimat in treating these viruses in humans. Furthermore, the expected context of use and disease courses of smallpox, cowpox, and vaccina virus are each different compared to mpox. Therefore, the restriction is limited to the use of Tecovirimat SIGA in mpox.

Consequently, the indication (included in section 4.1 of the SmPC) is being restricted, and it will appear as follows:

Tecovirimat SIGA is indicated for the treatment of the following viral infections in adults and children with body weight at least 13 kg:

- *Smallpox*
- *Cowpox*

Tecovirimat SIGA is also indicated to treat complications due to replication of vaccinia virus following vaccination against smallpox in adults and children with body weight at least 13 kg (see sections 4.4 and 5.1).

Tecovirimat SIGA should be used in accordance with official recommendations.

[2] PALM007 Writing Group. Tecovirimat for Clade I MPXV Infection in the Democratic Republic of Congo. N Engl J Med. 2025 Apr 17;392(15):1484-1496.
[3] Zucker J, Fischer WA 2nd, Zheng L, McCarthy C, Saha PT, Javan AC, et al; STOMP/A5418 Investigators. Tecovirimat for the Treatment of Mpox. N Engl J Med. 2026 Feb 26;394(9):884-895.
[4] https://mpx-response.eu/large-trial-unity-from-the-european-programm-mpx-response-confirms-the-lack-of-efficacy-for-treating-mpox/
[5] https://www.isrctn.com/ISRCTN17461766

Call for reporting

Healthcare professionals should continue to report suspected adverse drug reactions (ADRs) associated with the use of Tecovirimat SIGA to National Competent Authorities in accordance with the national spontaneous reporting system.

This product is subject to additional monitoring as it contains a new active substance that was not contained in any authorised medicine in the EU on 1 January 2011 and is authorised under exceptional circumstances.

Company contact point

If you require any further information, please contact SIGA Technologies via email at siga.safety@soterius.com or phone at +30 213 0908872.

Communication Plan for Direct Healthcare Professional Communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Tecovirimat SIGA (tecovirimat monohydrate) 200 mg hard capsules
Marketing authorisation holder(s)	SIGA Technologies Netherlands B.V.
Concern and purpose of the communication	Tecovirimat SIGA (tecovirimat monohydrate): restriction of indication due to lack of efficacy shown in randomised clinical trials in patients with mpox
DHPC recipients	Infectious disease specialists involved in the prescription, supervision, and monitoring of mpox patients in the EU. The target group should be further defined at national level, in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	Austria, Belgium, Cyprus, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, and Sweden.

Timetable	Date
DHPC and communication plan (in English) agreed by CHMP	26/03/2026
Submission of translated DHPCs to the national competent authorities for review	31/03/2026
Agreement of translations by national competent authorities	21/04/2026
Dissemination of DHPC	11/05/2026