EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Emergency Task Force

Possible use of the medicinal product TPOXX for the treatment of monkeypox

On July 23rd, 2022, the World Health Organisation (WHO) declared the monkeypox outbreak a Public Health Emergency of International Concern (PHEIC)[1]. The disease is caused by the monkeypox virus which is an orthopoxvirus closely related to smallpox virus.

Currently, Tecovirimat (SIGA Technologies Netherlands B.V.) is the only medicinal product authorised in the EU for the treatment of orthopoxvirus caused disease including smallpox, monkeypox, and cowpox in adults and children with body weight at least 13 kilograms[2]. Tecovirimat is a synthetic small antiviral molecule which inhibits the activity of a protein called VP37 that is found on the surface of orthopoxviruses. By interacting with this protein, the medicine prevents the viruses from reproducing normally and slowing down the spread of infection[3,4]. It is given orally as capsules for 14 days, and the dose depends on bodyweight. Tecovirimat is likely to be more beneficial if started earlier in the course of the infection.

The medicinal product is approved in the EU under exceptional circumstances, Tecovirimat is also authorised in USA and Canada under the trade name TPOXX for treatment of smallpox. In the USA, the Center of Disease Control (CDC) holds a protocol to allow access and use of TPOXX for treatment of non-variola[5] infections including monkeypox in adults and children; in Canada, a licensed healthcare professional may request this drug based on clinical judgement[6].

Since the EU authorised medicinal product Tecovirimat SIGA is not immediately available and in order to allow disease treatment, the European Health Emergency preparedness and Response Authority (HERA) purchased TPOXX, through rescEU, to cover the request of assistance by EU Member States and UCPM Participating States or under a Joint Procurement Agreement.

The EMA Emergency Task Force (ETF) together with the Rapporteur team and the CHMP Quality Working Party (QWP) have evaluated the specificities of the approved TPOXX, in case it is used as a replacement of Tecovirimat SIGA.

[1] WHO Director-General declares the ongoing monkeypox outbreak a Public Health Emergency of International Concern
[2] Tecovirimat SIGA, tecovirimat monohydrate (europa.eu)
[3] Oral Tecovirimat for the Treatment of Smallpox | NEJM
[4] An Orally Bioavailable Antipoxvirus Compound (ST-246) Inhibits Extracellular Virus Formation and Protects Mice from Lethal Orthopoxvirus Challenge | Journal of Virology (asm.org)
[5] Clinical Use of Tecovirimat (Tpoxx) for Treatment of Monkeypox Under an Investigational New Drug Protocol — United States, May–August 2022 | MMWR (cdc.gov)
[6] Monkeypox: For health professionals - Canada.ca

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Quality and manufacturing considerations

There are minor differences in terms of manufacturing process and specifications between the EU approved product and TPOXX, which do not negatively affect the final quality of the medicinal product.

TPOXX (the US authorised product) is manufactured and packaged at the same site as Tecovirimat SIGA.

The manufacturing process and specifications for TPOXX and Tecovirimat SIGA were evaluated to support the proposed use of TPOXX in Europe as a temporary measure. Any differences are deemed to be minor and do not raise any concern regarding the use of TPOXX; specifically, these relate to dissolution, assay and related substances specifications. Nevertheless, the MAH has provided data to show that the batches to be supplied to the EU comply with the EU specifications.

TPOXX has a shelf-life of 7 years when stored in the original bottle below 25 °C, while Tecovirimat SIGA has a shelf-life of 5 years when stored in the original bottle below 25 °C. Differences in shelf-life between the US and EU marketing authorisations are due to different datasets submitted to the two Agencies. The Marketing Authorisation Holder has provided data to demonstrate that TPOXX would comply with the EU shelf-life specification until the end of its 7-year shelf-life.

Therefore, it is acceptable to use TPOXX under the stated EU storage conditions for Tecovirimat SIGA as a temporary measure until EU authorised medicinal product Tecovirimat SIGA is available.