EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Emergency Task Force

Possible use of the vaccine Jynneos against infection by monkeypox virus

Since May 2022, outbreaks of monkeypox have been reported in several non-endemic countries including throughout Europe and in North America without known epidemiological links to endemic areas[1,2]. The disease is caused by monkeypox virus which is an orthopoxvirus closely related to smallpox virus.

Activities to contain the spread of the infection have so far focused on isolation and treatment of cases and contact tracing. The European Health Emergency preparedness and Response Authority (HERA) and EU Member States (MSs) have initiated purchase agreements of medical countermeasures.

Currently only one vaccine, Imvanex (Bavarian Nordic A/S), is authorised by EMA for prevention of smallpox in adults in the EU under exceptional circumstances due to the impossibility to generate efficacy data as smallpox virus is no longer circulating. Imvanex is a non-replicating live attenuated third-generation vaccine based on the Modified Vaccinia Ankara – Bavarian Nordic vector (MVA-BN), to be used as a standalone 2-dose regimen via subcutaneous administration.

The vaccine is authorised in adults against infection and disease caused by both smallpox and monkeypox virus in the USA (Jynneos) and Canada (Imvamune) as well as other related orthopoxviruses (Canada only). There are minor differences in terms of manufacturing process and quality specifications between the various marketing authorisations in the different regions, which are due to differences in the datasets but which do not affect the final quality of the vaccine.

Since the EU authorised vaccine Imvanex is not immediately available, in order to allow rapid containment of the outbreaks, EU MSs agreed to the purchasing of close to 110.000 doses of the US made vaccine Jynneos by HERA. Their delivery is foreseen to start to MSs with highest number of cases in the coming days.

The EMA Emergency Task Force together with the CHMP Biologics Working Party and the European Directorate for the Quality of Medicines & HealthCare (EDQM) have evaluated the specificities of the FDA-approved Jynneos, in case it is used as a replacement of Imvanex.

Efficacy and safety considerations

[1] https://www.ecdc.europa.eu/en/monkeypox
[2] https://www.who.int/news-room/fact-sheets/detail/monkeypox

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The use of the vaccine in either indication (monkeypox or smallpox) is based on immunogenicity data generated both in humans and animals and on protection in animals challenged with the virus.

Clinical data show that the vaccine is able to induce similar immunogenicity against vaccinia virus strains (both in terms of geometric mean titres of neutralising antibodies and seroconversions) as compared to previous generation vaccines (ACAM2000)at selected time points after vaccination[3]. Jynneos is shown to boost pre-existing immunity induced by previous generation smallpox primary vaccination.

Non-clinical data are available from several animal models, including primates, indicating similar humoral and cell mediated immune responses and protection against lethal challenge with vaccinia and monkeypox virus as compared to previous generation smallpox vaccines that were used to eradicate smallpox.

In addition, previous generation vaccines against smallpox are estimated to have an effectiveness against monkeypox disease of approximately 85%, based on observational data from Zaire collected during monkeypox outbreaks in the '80s in individuals previously vaccinated against smallpox vs. unvaccinated individuals[4,5].

Jynneos is therefore expected to provide protection against monkeypox disease in line with the approved indication in the US and Canada. A regulatory review to extend the indication of Imvanex in the EU, is planned to start shortly and will assess all available data.

Jynneos can be used in subjects living with HIV[6]. Data are limited in immunosuppressive conditions[7] but this should not prevent vaccination especially when at risk of exposure.

Jynneos is well tolerated in subjects ≥18 years of age. The most common side effects are injection site reactions (pain, redness, swelling, hardening and itching), followed by muscle pain, headache and fatigue. They tend to be mild or moderate in severity and clear within a few days.

Jynneos is not contraindicated in pregnancy. The limited clinical data on use in pregnancy and the animal studies on fertility and developmental toxicity did not identify any specific reason for concern.

Safety and efficacy of Jynneos is currently not established in children, but data with similar vaccines including the MVA-based vaccines used in the vaccination campaigns in the 70's for smallpox are reassuring[8]. If Jynneos is used in the paediatric population, the adult regimen should be considered and data collected to confirm a positive benefit/risk profile.

Despite the lack of clinical data on the level of protection conferred in the context of post-exposure prophylaxis (PEP) against monkeypox, vaccination of cases' contacts is being considered based on estimates of vaccine effectiveness calculated with previous generation smallpox vaccines[9] and based on clinical experience with other viral diseases. In PEP use, the time of vaccination should be as close as possible to the potential date of exposure. To maximise the benefit of vaccination against further spread of the virus in a PEP context, Jynneos should be used according to robust contact tracing and

[3] two weeks after the second dose of Jynneos or 4 weeks after the single dose of ACAM2000, and 2 weeks after a single dose of Jynneos and ACAM2000 - https://www.nejm.org/doi/full/10.1056/NEJMoa1817307

[4] https://www.nature.com/articles/d41586-022-01587-1#ref-CR1

[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2491159/pdf/bullwho00069-0046.pdf

[6] https://www.sciencedirect.com/science/article/pii/S0264410X20300852?via%3Dihub

[7] Safety and Immunogenicity of Modified Vaccinia Ankara in Hematopoietic Stem Cell Transplant Recipients: A Randomized, Controlled Trial | The Journal of Infectious Diseases | Oxford Academic (oup.com)

[8] https://pubmed.ncbi.nlm.nih.gov/4426258/

[9] https://academic.oup.com/jid/article/188/7/973/820489?login=true

ring vaccination strategy, based on experience in similar contexts such as during recent Ebola outbreaks.

Among the vaccines that are currently authorised globally against orthopoxvirus, Imvanex and its FDA-authorised equivalent, Jynneos, are considered the most suitable vaccines against monkeypox based on the substantially safer profile compared to older generation smallpox vaccines.

Quality and manufacturing considerations

Jynneos is manufactured at the Danish Bavarian Nordic site, which is currently not authorised for EU production. The manufacturing process and specification differences between Jynneos and Imvanex were evaluated to support the proposed use of Jynneos in Europe as a temporary measure. Differences are deemed to be minor and do not raise any concern regarding immunisation with Jynneos.

Jynneos has a shelf life of 3 years at -20°C and an in-use shelf life after thawing of 12 hours, if stored at 2°C–8°C[10].

At the same temperature of -20°C, Imvanex has an authorised shelf life of 2 years and an in-use shelf life up to 2 months after thawing, if stored at 2°C–8°C in the dark[11].

Differences in shelf life, including in-use shelf life after thawing, between the US and the EU marketing authorisations are due to different datasets submitted to the two Agencies. These aspects will be further evaluated by the CHMP in upcoming submissions for which complementary quality data are expected.

For the time being, the Marketing Authorisation Holder has provided bridging data to confirm that based on preliminary assessment a 3 years shelf life could also apply to Imvanex when stored at -20°C.

However regarding the in-use shelf-life, available information is not sufficient at this time to confirm that the potency specification for Jynneos would be maintained if the EU in-use shelf-life recommendations, i.e. 2 months storage at 2-8°C post-thawing (after 2 years at -20C), were to be implemented after 3 years storage at -20°C.

It is acceptable to use Jynneos under the stated EU storage conditions for Imvanex as a temporary measure until the EU and US data sets are aligned.

[10] https://www.fda.gov/media/131078/download

[11] https://www.ema.europa.eu/en/documents/product-information/imvanex-epar-product-information_en.pdf