August 10, 2022

Re: JYNNEOS Vaccine

Dear Healthcare Provider:

On August 9, 2022, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for: (i) the intradermal route of administration of JYNNEOS for the prevention of monkeypox disease in individuals 18 years of age and older determined to be at high risk for monkeypox infection; and (ii) subcutaneous administration of JYNNEOS for the prevention of monkeypox disease in individuals younger than 18 years of age determined to be at high risk for monkeypox infection.

To ensure the safe use of the vaccine please note the following:

1) JYNNEOS is supplied in vials that state "Single-dose: 0.5 mL" and the cartons state "Suspension for subcutaneous injection." Under this EUA, **each single dose vial may be used to obtain up to five 0.1 mL doses for intradermal administration** using five punctures of the vial stopper with an appropriate needle for administration; this is expected to vary depending on the needle and syringe combination that is used. Note that following initial puncture of a vial to withdraw the first dose, between withdrawal of the doses the vial can be held at +2°C to +8°C (+36°F to +46°F) for a total of up to 8 hours. After a total of 8 hours since first withdrawal the punctured vial must be discarded.

2) For adults 18 years and older determined to be at high risk for monkeypox infection, this EUA allows for two doses of JYNNEOS (each dose 0.1 mL) by intradermal injection four weeks apart. Those providers who do not routinely administer intradermal injections are encouraged to review the Centers for Disease Control and Prevention's (CDC) training video, which can be found here: https://www.cdc.gov/poxvirus/monkeypox/clinicians/index.html.

3) When administered intradermally, JYNNEOS is associated with a higher frequency of redness, induration, and itchiness at the injection site compared to subcutaneous administration. The redness may last several weeks. Appropriate supportive care measures should be provided per the local standard of care. Please consult the CDC website for additional information: https://www.cdc.gov/poxvirus/monkeypox/considerations-for-monkeypox-vaccination.html.

4) Under this EUA, individuals less than 18 years of age determined to be at high risk for monkeypox infection may receive two doses of JYNNEOS (0.5 mL each) by subcutaneous injection 4 weeks apart.

Additional Background

JYNNEOS is an FDA-licensed vaccine in the United States (U.S.) that is approved for prevention of monkeypox and smallpox disease in individuals 18 years of age and older who are determined to be at high risk for smallpox or monkeypox infection. It is a live virus vaccine produced from the strain Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN), an attenuated, non-replicating orthopoxvirus, that was originally developed for use in the event of a smallpox bioterrorist attack in certain populations (e.g., immunocompromised individuals). The virus in JYNNEOS is non-replicating, therefore, the vaccine is safe for use in significantly immunocompromised individuals who may not be indicated or recommended to

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receive certain other live attenuated vaccines. JYNNEOS is approved for use as a 2-dose (0.5 mL each) regimen administered by subcutaneous injection with the doses given 4 weeks apart.

There is currently a limited supply of JYNNEOS available globally and in the U.S. Data from a clinical trial conducted by the Division of Microbiology and Infectious Diseases at the National Institute of Allergy and Infectious Diseases supports the intradermal administration of the vaccine, under EUA, to individuals 18 years of age and older determined to be at high risk for monkeypox infection. Intradermal administration can provide up to five times as many doses as subcutaneous administration.

The available information provides evidence indicating that the immunogenicity of JYNNEOS administered by the subcutaneous and intradermal routes produced a similar immune response. The systemic side effect profile with the two routes of administration is also very similar. The local side effect profile using the route of intradermal administration is associated with less local pain, but more local redness and itching. These data, together with the data supporting the licensure of JYNNEOS, support a positive benefit-risk profile for JYNNEOS when administered intradermally to prevent monkeypox disease in individuals determined to be at high risk of monkeypox infection. In the current setting of a monkeypox outbreak that is continuing to spread, and in the context of a limited number of vaccine doses, the additional doses of vaccine that will be made available may also help to benefit public health by assisting in containment efforts.

In addition to the intradermal use, JYNNEOS administered by the subcutaneous route to individuals under 18 years of age determined to be at high risk for monkeypox infection is reasonable based on the available JYNNEOS safety and immunogenicity data in adults as well as the historical data with use of live vaccinia virus smallpox vaccine in pediatric populations.

Thank you for your continued work in support of public health.

Sincerely,

Peter W. Marks -S

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Peter Marks, MD, PhD

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