World Health Organization

WHO Target Product Profiles for Monkeypox Therapeutics

DRAFT

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Purpose of the document

The target audience are all those working to evaluate repurposed therapeutic agents for Monkeypox or to develop new therapeutic agents for Monkeypox. The document is also aimed at those developing Monkeypox therapeutic agents that have not yet reached the clinical testing phase. This document is relevant to those groups who wish to obtain WHO policy recommendations for use and WHO prequalification for their products.

All the requirements contained in WHO guidelines for WHO policy recommendation and prequalification will also apply. The criteria below lay out some of the considerations that will be relevant in WHO's case-by-case assessments of Monkeypox therapeutic agents in the future. Therefore, should a therapeutic agent's profile be sufficiently superior to the critical characteristics under one or more categories, this may outweigh failure to meet another specific critical characteristic. Therapeutic agents which fail to meet multiple critical characteristics are unlikely to achieve favourable outcomes from WHO's processes. Likewise, preferred characteristics should not be considered as the maximum desirable characteristics; therapeutic agents that exceed these characteristics may find advantages in WHO's processes.

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I. Background

Monkeypox is a viral zoonosis (a virus transmitted to humans from animals) with symptoms similar to those seen in the past in smallpox patients, although it is clinically less severe. With the eradication of smallpox in 1980 and subsequent cessation of smallpox vaccination, monkeypox has emerged as the most important orthopoxvirus for public health. Monkeypox primarily occurs in central and west Africa, often in proximity to tropical rainforests, and has been increasingly appearing in urban areas. Animal hosts include a range of rodents and non-human primates In May 2022, multiple cases of monkeypox were identified in several non-endemic countries. Studies are currently underway to further understand the epidemiology, sources of infection, and transmission patterns[1].

This document describes the preferred and minimally acceptable profiles for therapeutic agents. This Target Product Profile (TPP) was developed through a consultation process with key stakeholders in human and animal health, scientific, funding and manufacturing communities. It is intended to guide and prioritize the evaluation of repurposed therapeutic agents for Monkeypox or the development of new therapeutic agents. As new scientific evidence is generated, this TPP may require further review and revision.

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[1] https://www.who.int/news-room/fact-sheets/detail/monkeypox

II. Target Product Profiles

TPP for Monkeypox cases

	Preferred	Critical or Minimal
Indication for use[2]	Treatment of confirmed asymptomatic, pre-symptomatic and symptomatic monkeypox cases, at any stage of infection.	For the treatment of probable/suspected symptomatic monkeypox cases (using the WHO Monkeypox case definition). Test and treat strategy.
Target population	Individuals of any age including at higher risk.[3]	Individuals > 6 years of age.
Safety/tolerability	No adverse events that require biological or clinical monitoring.[4]	A safety profile where the risk/benefit shows an overall acceptable use of the drug.[5]
Efficacy	Rapid resolution of lesions to reduce virus transmission and reduction in clinical complication (e.g., pain), progression of disease, admission tohospital and mortality. High barrier to resistance. Prevention of symptomatic disease amongst pre-symptomatic or asymptomatic cases to prevent transmission.	Rapid resolution of lesions to reduce virus transmission.

[2] Working group suggested to create a separate TPP for post exp prophylaxis for determining its own indication andspecificities for use.
[3] There is insufficient data available, therefore the current suggestion is to consider treatment of monkeypox among vulnerable populations who are at higher risk of hospitalization and severe disease outcome depending upon different co-morbidities and factors that influence the course of disease and antiviral effectiveness. For example, people who are immunosuppressed, children < 6 years, pregnant women, lactating mothers, malnourished, PLHIV, TB etc.
[4] There should be no embryo-fetal developmental toxicity in pre-clinical studies as the drug would be available to pregnantwomen
[5] Current information suggests the risk/benefit may differ between clades.

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TPP for Monkeypox cases

	Preferred	Critical or Minimal
Treatment regimen	Once per day or per week dosing. Treatment duration should be as short as possible, e.g., no more than 7 days.	Twice per day dosing.
Route of administration	Oral and parenteral Topical for specific use, e.g., ophthalmic or facial lesions, can be considered as additional treatment modality.	Oral or parenteral.
Product Stability and Storage	Shelf life of at least 36 months. Room temperature shipping and storage in climatic Zone IV. Heat stability demonstrated to 40 °C short term.	Shelf life of at least 12 months. Storage and shipping at -20°C, 2-8°C or room temperature.
Interactions	No DDI (including with ART as PLHIV are a target population). Suitable for combination therapy.	No significant DDI with products commonly used including antiretroviral treatment.
Formulation	Tablets/capsules, paediatric suspension with acceptable taste, injectables. Topical for local treatment of lesions.	Tablets/capsules, injectables, and IV for severe cases.

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TPP for Monkeypox cases

	Preferred	Critical or Minimal
Accessibility	Capability to rapidly scale-up production at cost/dose that allows broad use, including in LMIC.	Capability to rapidly scale-up production atcost/dose that allows broad use, including in LMIC.
Registration and Prequalification	Manufacturers are recommended to interact with the WHO Prequalification ofmedicines team well ahead of submission to NRAs for licensure or marketing authorization. https://extranet.who.int/prequal/information/manufacturers	

The above prioritization decisions are preliminary and may change as further information is provided to WHO

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