WHO Target Product Profile (TPP) Therapeutics for Monkeypox cases

Preamble

The Director-General of WHO decided that the global monkeypox outbreak represents a public health emergency of international concern. [Source: WHO Director-General's press statement] and it was agreed that WHO would develop the Monkeypox target product profiles for therapeutics to provide guidance on WHO's preferences (please see table below).

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.

Acknowledgement

WHO gratefully acknowledges the members of the WHO TPP Therapeutics Monkeypox Working Group, led by the chair Dr. Marco Cavaleri, for developing the draft TPP as a starting point for this document.

Introduction

This document is intended to serve as guidance for scientists, regulators, and funding agencies, and for industry groups. It is relevant to those groups who wish to obtain WHO policy recommendations for use and WHO prequalification for their products and meet the public health need related to future Monkeypox outbreaks.

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 COVID-19 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.

A generic description of WHO's Medicines Prequalification process can be found at the end of this document.

Criteria	**Preferred**	**Critical or Minimal**
Indication for use[1]	Treatment of confirmed asymptomatic, pre-symptomatic and symptomatic monkeypox cases.	For the treatment of probable/suspected symptomatic monkeypox cases (using the WHO Monkeypox case definition). Test and treat strategy.

[1] Working group suggested to create a separate TPP for post exp prophylaxis for determining its own indication and specificities for use.

Criteria	Preferred	Critical or Minimal
Target population	Individuals of any age including at higher risk[2]	Individuals > 6 years of age
Safety/tolerability	No adverse events that require monitoring[3]	A safety profile where the risk/benefit shows an overall acceptable use of the drug. [4]
Efficacy	Rapid resolution of lesions to reduce virus transmission and reduction in clinical complication (e.g., pain), progression of disease, admission to hospital 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 .
Treatment regimen	Once per day or per week dosing. Treatment duration should be as short as possible.	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 6 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).	No significant DDI with products commonly used.

[2] 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.

[3] There should be no embryo-fetal developmental toxicity in pre-clinical studies as the drug would be available to pregnant women

[4] Current information suggests the risk/benefit may differ between clades.

Criteria	Preferred	Critical or Minimal
	Suitable for combination therapy.	
Formulation	Tablets/capsules, paediatric suspension with acceptable taste, injectables Topical for local treatment of lesions.	Tablets/capsules, injectables.
Accessibility	Capability to rapidly scale-up production at cost/dose that allows broad use, including in LMIC.	Capability to rapidly scale-up production at cost/dose that allows broad use, including in LMIC.
Registration and Prequalification	Manufacturers are recommended to interact with the WHO Prequalification of medicines 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

WHO Medicines Prequalification

WHO medicines prequalification ensures good availability, quality, safety and efficacy of medicines for everyone. Its mission is to work in close cooperation with national regulatory agencies and partner organizations to make quality priority medicines available for those who urgently need them. This is achieved through assessment and inspection activities, building national capacity for manufacture, regulation and monitoring of medicines, and working with regulators to register those medicines quickly.

The WHO Medicines Prequalification Guidance is available here: https://extranet.who.int/pqweb/medicines/who-medicines-prequalification-guidance

WHO prequalification requirements for finished pharmaceutical products and active pharmaceutical ingredients are based on international, pharmaceutical norms and standards. WHO prequalification assessors and inspectors therefore welcome the opportunity to provide technical and scientific advice to manufacturers: https://extranet.who.int/pqweb/medicines/technical-advice

Guidance document to manufacturers: https://extranet.who.int/pqweb/sites/default/files/documents/103%20Advice%20manufacturers_Oct2016.pdf

Information for regulatory agencies: https://extranet.who.int/pqweb/medicines/information/regulatory-agencies

Information for Quality Control Laboratories: https://extranet.who.int/pqweb/medicines/information/quality-control-laboratories

Information for Procurement Agencies: https://extranet.who.int/pqweb/medicines/information/medicines-purchasing-organizations