MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-100648-PIP01-22-M01

Scope of the Application

Active Substance(s)

TECOVIRIMAT MONOHYDRATE

Condition(s)

Treatment of orthopoxvirus disease (smallpox, monkeypox, cowpox, and vaccinia)

Pharmaceutical Form(s)

Capsule, hard; Powder for oral suspension

Route(s) of Administration

ORAL USE; GASTRIC USE

Name / Corporate name of the PIP applicant

SIGA Technologies, Inc.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, SIGA Technologies, Inc. submitted to the licensing authority on 18/08/2022 13:38 BST an application for a Modification

The procedure started on 31/08/2022 11:04 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

gov.uk/mhra

Final Decision Letter

MHRA-100648-PIP01-22-M01

Of 16/11/2022 08:42 GMT

On the adopted decision for TECOVIRIMAT MONOHYDRATE (MHRA-100648-PIP01-22-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for TECOVIRIMAT MONOHYDRATE, Capsule, hard; Powder for oral suspension , ORAL USE; GASTRIC USE .

This decision is addressed to SIGA Technologies, Inc., 4575 SW Research Way, Suite 110, Corvallis, UNITED STATES OF AMERICA, 97333

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of orthopoxvirus disease (smallpox, monkeypox, cowpox, and vaccinia)

2.2 Indication(s) targeted by the PIP:

Treatment of orthopoxvirus disease (smallpox, monkeypox, cowpox, and vaccinia)

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of powder for oral suspension.
Non-Clinical Studies	6	Study 2 (246-TX-007) Dose range-finding juvenile toxicity study to evaluate potential subchronic toxicity, and pharmacokinetics/ toxicokinetics of tecovirimat. Study 3 (2083-003-001-SN6) Dose range-finding juvenile toxicity study to evaluate the toxicity of tecovirimat, and to determine the reversibility of any toxic effects. Study 4 (MPI 1151-065) Repeat dosing pharmacokinetics of tecovirimat. Study 5 (FY10-087) Juvenile animal pharmacology study to evaluate pharmacokinetics and efficacy of tecovirimat after monkeypox virus (MPXV) challenge. Study 6 (AP-09-026G) Juvenile animal pharmacology study to determine the minimum effective dose of tecovirimat in treating symptomatic (lesional) disease in NHPs infected with MPXV. Study 7 (2083-003-001 SN9) Placental transfer and milk transfer study of tecovirimat.
Clinical Studies	2	Study 8 (SIGA-246-027) Open-label, two-part, crossover, single dose study to evaluate the pharmacokinetic (PK), dose proportionality, safety, tolerability, effect of refrigerated storage and taste of prototype powder for reconstitution liquid suspension formulations in healthy adult subjects

		compared to Tecovirimat SIGA 200 mg hard capsules. Study 9 (SIGA-246-029) Open-label, single oral dose, crossover pharmacokinetic study of tecovirimat capsules versus tecovirimat powder for reconstitution to liquid suspension dosed in fed state in healthy adult subjects.
Extrapolation, Modeling & Simulation Studies	1	Study 10 (Population PK Model for Paediatric Dose Determination) Modelling and simulation study to determine dosing of tecovirimat in paediatric patients from birth to less than 18 years of age.
Other Studies	0	Not applicable
Other Measures	0	Not applicable

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	30/11/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes