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

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and grant a waiver

MHRA-101445-PIP01-24

Scope of the Application

Active Substance(s)

CANNABIDIOL

Condition(s)

Treatment of fragile X syndrome

Pharmaceutical Form(s)

Gel

Route(s) of Administration

TRANSDERMAL USE

Name / Corporate name of the PIP applicant

Harmony Biosciences Management Inc.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Harmony Biosciences Management Inc. submitted to the licensing authority on 03/07/2024 13:38 BST an application for a Paediatric Investigation Plan

The procedure started on 03/09/2024 08:34 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 agree a paediatric investigation plan and grant a deferral and grant a waiver

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.

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Final Decision Letter

MHRA-101445-PIP01-24

Of 23/10/2024 18:56 BST

On the adopted decision for CANNABIDIOL (MHRA-101445-PIP01-24) 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 a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for CANNABIDIOL, Gel , TRANSDERMAL USE .

This decision is addressed to Harmony Biosciences Management Inc., 630 W. Germantown Pike, Suite 215, Plymouth Meeting, Plymouth Meeting, PA, UNITED STATES OF AMERICA, 19462

ANNEX I

1. Waiver

1.1 Condition:

Treatment of fragile X syndrome The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 3 years of age Pharmaceutical form(s): Gel Route(s) of administration: TRANSDERMAL USE Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of fragile X syndrome

2.2 Indication(s) targeted by the PIP:

Treatment of fragile X syndrome

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

The paediatric population from 3 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Gel

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	1	Study 1 (ZYN2-NC-34) Definitive juvenile toxicity study to evaluate safety of cannabidiol administered as transdermal gel in children from 3 years of age.
Clinical Studies	5	Study 2 (ZYN2-CL-009) Open-label, multi-centre study to assess safety and efficacy of cannabidiol administered as a transdermal gel for the treatment of children and adolescents from 6 years to less than 18 years of age with fragile X syndrome. Study 3 (ZYN2-CL-016) Randomised, double-blind, placebo-controlled, multi-centre study to assess the efficacy and safety of cannabidiol administered as a transdermal gel for treatment of children and adolescent patients from 3 years to less than 18 years of age with fragile X syndrome. Study 4 (ZYN2-CL-017) Open-label extension study to assess the long-term safety and tolerability of cannabidiol administered as a transdermal gel to children, adolescents from 3 years to less than 18 years of age (and adults) with fragile X syndrome. Study 5 (ZYN2-CL-033) Randomised, double-blind, placebo-controlled, multi-centre, study to evaluate

		efficacy and safety of cannabidiol administered as a transdermal gel to children and adolescents from 3 years to less than 18 years of age (and adults) with fragile X syndrome. Study 6 Randomised, double-blind, placebo-controlled, multi-centre, study to evaluate efficacy and safety of cannabidiol administered as a transdermal gel to children and adolescents from 3 years to less than 18 years of age (and adults) with fragile X syndrome.
Extrapolation, Modeling & Simulation Studies	1	Study 7 (ZYN2-CL-015) Modelling and simulation population PK analysis to evaluate the use of the product in fragile X syndrome in children from 3 years 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:	Yes
Date of completion of the paediatric investigation plan:	31/01/2030
Deferral of one or more studies contained in the paediatric investigation plan:	Yes