EMA/33676/2021

European Medicines Agency decision

P/0019/2021

of 29 January 2021

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for dexmedetomidine (hydrochloride) (EMEA-002758-PIP01-19) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by BioXcel Therapeutics, Inc. on 27 January 2020 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 December 2020, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for dexmedetomidine (hydrochloride), sublingual tablet, sublingual use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for dexmedetomidine (hydrochloride), sublingual tablet, sublingual use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for dexmedetomidine (hydrochloride), sublingual tablet, sublingual use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to BioXcel Therapeutics, Inc., 555 Long Wharf Drive, 12th Floor, 06511 - New Haven, United States.

EMA/PDCO/505272/2020
Amsterdam, 11 December 2020

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-002758-PIP01-19

Scope of the application

Active substance(s):

Dexmedetomidine (hydrochloride)

Condition(s):

Treatment of schizophrenia

Treatment of bipolar disorder

Pharmaceutical form(s):

Sublingual tablet

Route(s) of administration:

Sublingual use

Name/corporate name of the PIP applicant:

BioXcel Therapeutics, Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, BioXcel Therapeutics, Inc. submitted for agreement to the European Medicines Agency on 27 January 2020 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 2 March 2020.

Supplementary information was provided by the applicant on 12 August 2020. The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adult populations.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annex and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of schizophrenia

The waiver applies to:

- the paediatric population from birth to less than 13 years of age,
- sublingual tablet, sublingual use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

1.2. Condition:

Treatment of bipolar disorder

The waiver applies to:

- the paediatric population from birth to less than 10 years of age,
- sublingual tablet, sublingual use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of schizophrenia

2.1.1. Indication(s) targeted by the PIP

Rapid control of agitation in patients with schizophrenia

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 13 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Sublingual tablet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of a lower strength sublingual formulation for

		dexmedetomidine appropriate for the paediatric population.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 2 (BXCL501-PEDIATRIC)** Randomised, double-blind, placebo-controlled study evaluating the efficacy, safety and tolerability of dexmedetomidine in adolescents from 13 to less than 18 years of age with acute agitation associated with schizophrenia, and in children and adolescents from 10 to less than 18 years of age with acute agitation associated with bipolar disorder.
Extrapolation, modelling and simulation studies	1	**Study 3** Population pharmacokinetic and pharmacodynamic (PK/PD) analysis of sublingually administered dexmedetomidine in adults to determine paediatric dosing.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition:

Treatment of bipolar disorder

2.2.1. Indication(s) targeted by the PIP

Rapid control of agitation in patients with bipolar disorder

2.2.2. Subset(s) of the paediatric population concerned by the paediatric development

From 10 to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Sublingual tablet

2.2.4. Measures

Area	**Number of measures**	**Description**
Quality-related studies	1	**Study 1** *Same as study 1 for condition: Treatment of schizophrenia.*
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 2 (BXCL501-PEDIATRIC)**

		Same as study 2 for condition: Treatment of schizophrenia.
Extrapolation, modelling and simulation studies	1	**Study 3** *Same as study 3 for condition: Treatment of schizophrenia.*
Other studies	0	Not applicable.
Other measures	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By August 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes