EMA/151840/2021

European Medicines Agency decision

P/0142/2021

of 14 April 2021

on the agreement of a paediatric investigation plan and on the granting of a deferral for surufatinib (EMEA-002750-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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on the agreement of a paediatric investigation plan and on the granting of a deferral for surufatinib (EMEA-002750-PIP01-19) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 Hutchison MediPharma Ltd on 20 April 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 26 February 2021, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 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.

(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.

[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 surufatinib, capsule, hard, powder for oral suspension, oral 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 surufatinib, capsule, hard, powder for oral suspension, oral 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

This decision is addressed to Hutchison MediPharma Ltd, Building 4, 917 Halei Road, Zhangjiang Hi-Tech Park, 201203 - Pudong, Shanghai, China.

EMA/597938/2020
Amsterdam, 26 February 2021

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

EMEA-002750-PIP01-19

Scope of the application

Active substance(s):

Surufatinib

Condition(s):

Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms)

Treatment of malignant neoplasms of haematopoietic and lymphoid tissue

Pharmaceutical form(s):

Capsule, hard

Powder for oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Hutchison MediPharma Ltd

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Hutchison MediPharma Ltd submitted for agreement to the European Medicines Agency on 20 April 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 4 January 2021.

Supplementary information was provided by the applicant on 27 October 2020. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a waiver.

A meeting with the Paediatric Committee took place on 24 February 2021.

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, by a majority of 18 out of 25 votes:

   - 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.

   The divergent positions are appended to this opinion.

   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 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 appendices.

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

Not applicable.

2. Paediatric investigation plan

2.1. Condition:

Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms)

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from birth to less than 18 years of age with a paediatric solid tumour known or expected to have dysfunctional signalling pathways targeted by surufatinib.

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

From birth to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Capsule, hard

Powder for oral suspension

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of a 25mg capsule of size 3, to improve dosing accuracy in paediatric clinical studies. Additionally, feasibility study of smaller capsule size for 25mg capsule during further clinical development stages, to improve the dosing compliance in the paediatric population. **Study 2** Development of an oral suspension prepared from contents of 25 mg and 50 mg capsules.

Area	Number of measures	Description
Non-clinical studies	2	**Study 3** Dose range-finding juvenile toxicity study to establish the doses to be used in the definitive juvenile toxicity study. **Study 4** Definitive juvenile toxicity study to assess the potential effects of surufatinib on the growth and maturation of developing organ systems.
Clinical studies	2	**Study 5** Open-label, multiple dose, uncontrolled trial to evaluate pharmacokinetics, safety, activity, and acceptability/palatability of surufatinib in combination with gemcitabine in children from birth to less than 18 years of age with recurrent or refractory solid tumours known or expected to have dysfunctional signalling pathways targeted by surufatinib, including lymphoma. **Study 6** Open-label, randomised, active-controlled study to evaluate the efficacy and safety of surufatinib in combination with gemcitabine compared to standard of care in children from birth to less than 18 years of age with a paediatric solid tumour selected on the basis of the results of Study 5.
Extrapolation, modelling and simulation studies	1	**Study 7** Population-based modelling and simulation study to predict and characterise surufatinib pharmacokinetics (PK) in the paediatric population from birth to less than 18 years of age.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition:

Treatment of malignant neoplasms of haematopoietic and lymphoid tissue

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from birth to less than 18 years of age with lymphoma

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

From birth to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Capsule, hard

Powder for oral suspension

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Same as for the condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms). **Study 2** Same as for the condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms).
Non-clinical studies	2	**Study 3** Same as for the condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms). **Study 4** Same as for the condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms).
Clinical studies	2	**Study 5** Same as for the condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms). **Study 6** Same as for the condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms).
Extrapolation, modelling and simulation studies	1	**Study 7** Same as for the condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms).
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 January 2028
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Appendix

Divergent position statement

Divergent position statement dated 26 February 2021

Surufatinib (EMEA-002750-PIP01-19)

The undersigned members of the PDCO did not agree with the PDCO's positive opinion on the acceptance of a Paediatric Investigation Plan and a deferral for surufatinib (EMEA-002750-PIP01-19).

The reason for divergent opinion was the following:

Surufatinib is a multi-tyrosine kinase inhibitor which targets VEGFR-1, 2, 3, FGFR-1 and CSF-1R. The current inclusion criteria for paediatric studies however do not specify any minimum numbers for patients with tumours harbouring VEGFR-1, 2, 3, FGFR-1 or CSF-1R alterations. Therefore, there is a high risk that no such patients will be recruited as these alterations are present only in minority of rare paediatric tumours. If this happens and the paediatric data suggest concurrently insufficient efficacy, it might be due to the fact that inappropriate population was included in the study.

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Peter Sisovsky

Silvijus Abramavicius