EMA/443829/2024

European Medicines Agency decision

P/0353/2024

of 25 October 2024

on the acceptance of a modification of an agreed paediatric investigation plan for dupilumab (Dupixent), (EMEA-001501-PIP07-20-M02) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0153/2021 issued on 16 April 2021, and the decision P/0297/2023 issued on 11 August 2023,

Having regard to the application submitted by Sanofi Winthrop Industrie on 30 May 2024 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 6 September 2024, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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 acceptance of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for dupilumab (Dupixent), solution for injection in pre-filled syringe, subcutaneous use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0169/2014 issued on 8 July 2014, including subsequent modifications thereof.

Article 3

This decision is addressed to Sanofi Winthrop Industrie, 82 avenue Raspail, 94250 – Gentilly, France.

EMA/PDCO/273618/2024 Corr[1,2]
Amsterdam, 6 September 2024

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-001501-PIP07-20-M02

Scope of the application

Active substance(s):

Dupilumab

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of chronic spontaneous urticaria

Pharmaceutical form(s):

Solution for injection in pre-filled syringe

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Sanofi Winthrop Industrie

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Sanofi Winthrop Industrie submitted to the European Medicines Agency on 30 May 2024 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0153/2021 issued on 16 April 2021, and the decision P/0297/2023 issued on 11 August 2023.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

[1] 18 September 2024
[2] 19 September 2024

The procedure started on 8 July 2024.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion.

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

2. The measures and timelines of the 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 annexes 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 chronic spontaneous urticaria

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- solution for injection in pre-filled syringe, subcutaneous use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of chronic spontaneous urticaria

2.1.1. Indication(s) targeted by the PIP

Treatment of chronic spontaneous urticaria (CSU) in patients aged 2 years and older whose disease is not adequately controlled with H1 antihistamine and an anti-IgE antibody treatment

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

From 2 years to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Solution for injection in pre-filled syringe

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable.
Non-clinical studies	Not applicable.
Clinical studies	**Study 1 (EFC16461)** (CUPID) Study A and Study B Double-blind, randomised, placebo-controlled parallel-group trial to evaluate safety and efficacy of dupilumab in paediatric patients from 6 years to less than 18 years of age (and in adults) with chronic spontaneous urticaria (CSU) who remain symptomatic despite the use of H1-antihistamine (Study A) and in adolescents from 12 years to less than 18 years of age (and in adults) with CSU who remain symptomatic despite the use of or H1-antihistamine and an anti-IgE antibody treatment (Study B)

	Study 2 Open-label, single-arm trial to evaluate pharmacokinetics, safety and activity of dupilumab in children from 2 years to less than 12 years of age with chronic spontaneous urticaria (CSU) who remain symptomatic despite the use of H1-antihistamine **Study 4 (EFC16461 CUPID Study C)** Added during procedure EMEA-001501-PIP07-20-M02 Double-blind, randomised, placebo-controlled trial to evaluate safety and efficacy of dupilumab in paediatric patients from 6 years to less than 18 years of age (and in adults) with chronic spontaneous urticaria (CSU) who remain symptomatic despite the use of H1-antihistamine
Modelling and simulation studies	**Study 3** Deleted during procedure EMEA-001501-PIP07-20-M01
Other studies	Not applicable.
Extrapolation plan	Added during procedure EMEA-001501-PIP07-20-M01 Dupilumab PK and response data in paediatric patients from 2 to less than 12 years from Study 2 and Studies 1 and 4 (EFC16461, CUPID) and supportive exposure-response data from adult / adolescent patients with CSU from Studies 1 and 4 (EFC16461, CUPID Studies A, B, and C) are a part of the extrapolation plan of efficacy from adults/ adolescents to the paediatric population from 2 years to less than 12 years of age with chronic spontaneous urticaria.

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 July 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of atopic dermatitis

Authorised indication(s):

- *Adults and adolescents*

Dupixent is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy.

- *Children 6 months to 11 years of age*

  Dupixent is indicated for the treatment of severe atopic dermatitis in children 6 months to 11 years old who are candidates for systemic therapy.

  - Invented name(s): Dupixent
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure

2. Treatment of asthma

Authorised indication(s):

- *Adults and adolescents*

  Dupixent is indicated in adults and adolescents 12 years and older as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised FeNO (see section 5.1), who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment.

- *Children 6 to 11 years of age*

  Dupixent is indicated in children 6 to 11 years old as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised fraction of exhaled nitric oxide (FeNO) who are inadequately controlled with medium to high dose inhaled corticosteroids (ICS) plus another medicinal product for maintenance treatment.

  - Invented name(s): Dupixent
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure

3. Treatment of chronic rhinosinusitis with nasal polyposis (CRSwNP)

Authorised indication(s):

- Dupixent is indicated as an add-on therapy with intranasal corticosteroids for the treatment of adults with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control.
  - Invented name(s): Dupixent
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure

4. Treatment of prurigo nodularis

- Dupixent is indicated for the treatment of adults with moderate-to-severe prurigo nodularis (PN) who are candidates for systemic therapy.
  - Invented name(s): Dupixent
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure

5. Treatment of eosinophilic esophagitis

- Dupixent is indicated for the treatment of eosinophilic esophagitis in adults and adolescents 12 years and older, weighing at least 40 kg, who are inadequately controlled by, are intolerant to, or who are not candidates for conventional medicinal therapy.
  - Invented name(s): Dupixent
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure

6. Treatment of chronic obstructive pulmonary disease (COPD)

Dupixent is indicated in adults as add-on maintenance treatment for uncontrolled chronic obstructive pulmonary disease (COPD) characterised by raised blood eosinophils on a combination of an inhaled corticosteroid (ICS), a long-acting beta2-agonist (LABA), and a long-acting muscarinic antagonist (LAMA), or on a combination of a LABA and a LAMA if ICS is not appropriate.

  - Invented name(s): Dupixent
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure