27 April 2018
EMA/PDCO/263134/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes of the meeting on 24-27 April 2018

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

24 April 2018, 14:00- 19:00, room 3A

25 April 2018, 08:30- 19:00, room 3A

26 April 2018, 08:30- 19:00, room 3A

27 April 2018, 08:30- 13:00, room 3A

Disclaimers

Some of the information contained in this set of minutes is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the PDCO Committee meeting reports (after the PDCO Opinion is adopted), and on the Opinions and decisions on paediatric investigation plans webpage (after the EMA Decision is issued).

Of note, this set of minutes is a working document primarily designed for PDCO members and the work the Committee undertakes.

Further information with relevant explanatory notes can be found at the end of this document.

Note on access to documents

Some documents mentioned in the minutes cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

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1. Introductions

1.1. Welcome and declarations of interest of members, alternates and experts

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 23 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

The agenda was adopted.

1.3. Adoption of the minutes

The minutes of the March 2018 PDCO were adopted and will be published on the EMA website.

2. Opinions

Disclosure of some information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

2.1. Opinions on Products

2.1.1. Lasmiditan - EMEA-002166-PIP01-17

Eli Lilly and Company Limited; Migraine with and without aura

Day 120 opinion

Neurology

Summary of committee discussion:

The PDCO at their April 2018 meeting discussed the replies provided by the applicant on the comments raised in the opinion. The PDCO agreed a positive opinion with a waiver and a deferral for lasmiditan in the treatment of migraine headaches.

2.1.2. Setmelanotide - Orphan - EMEA-002209-PIP01-17

Rhythm Pharmaceuticals, Inc; Treatment of appetite and general nutrition disorders / Treatment of obesity and/or hyperphagia associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway

Day 120 opinion

Nutrition

Summary of committee discussion:

During its plenary on 27 April 2018, the PDCO discussed the responses from the applicant to the outstanding issue for setmelanotide, a selective agonist of the melanocortin 4 receptor (MC4R), for children with obesity and/or hyperphagia associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway. The PDCO adopted a positive opinion on the PIP.

2.1.3. Daratumumab - Orphan - EMEA-002152-PIP01-17

Janssen-Cilag international N.V.; Lymphoid malignancies except mature B-cell neoplasms / Daratumumab in combination with standard chemotherapy is indicated for the treatment of paediatric patients from birth to 18 years with T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO adopted a positive opinion on the PIP.

2.1.4. Isatuximab - Orphan - EMEA-002205-PIP01-17

Sanofi-Aventis Recherche & Développement; Treatment of malignant neoplasms of the haematopoietic and lymphoid tissue / Treatment of relapsed, refractory acute lymphoblastic leukemia in combination with standard treatment in paediatric patients with no more than one prior salvage therapy, Treatment of relapsed, refractory acute myeloblastic leukemia in combination with standard treatment in paediatric patients with no more than one prior salvage therapy

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the application for isatuximab taking also into account the clarifications provided by the applicant after the D90 discussion and the comments received on the draft Opinion.
All pending issues were considered solved.
In conclusion the PDCO recommended granting a paediatric investigation plan for the entire paediatric population from 28 days to less than 18 years of age for and a deferral in the condition 'Treatment of malignant neoplasms of the haematopoietic and lymphoid tissue'.

2.1.5. Trandolapril / verapamil - EMEA-002276-PIP01-17

Abbott Laboratories; Hypertension in adults

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO re-discussed and endorsed its views expressed on day 30.
Based on the assessment of this application, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for verapamil / trandolapril for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of "treatment of hypertension" on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

2.1.6. Andecaliximab - EMEA-002304-PIP01-17

Gilead Sciences International Ltd; Treatment of gastric and gastroesophageal junction adenocarcinoma

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the requested for a waiver for all subsets of the paediatric population for andecaliximab for the treatment of gastric adenocarcinoma taking into account the clarification provided by the applicant after D30.
In conclusion, the PDCO recommends granting a waiver for andecaliximab for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of 'treatment of gastric and gastroesophageal junction adenocarcinoma'. The condition 'treatment of gastric and gastroesophageal junction adenocarcinoma' was included in the opinion as considered more appropriate to ensure that the condition completely cover the planned adult indication considering the 'heterogeneity' of the classification of gastric/ gastroesophageal junction carcinomas and oesophageal carcinomas.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.7. Somapacitan - EMEA-001469-PIP02-17

Novo Nordisk /S; Growth hormone deficiency, Short stature (ICD10 code: R6252)
Treatment of paediatric patients with short stature born small for gestational age (SGA) with insufficient catch-up growth by age 2 to 4 years

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

During its plenary on 27 April 2018, the PDCO discussed the PIP application for somapacitan, a long acting human growth hormone, for the treatment of paediatric patients with short stature born small for gestational age (SGA) with insufficient catch-up growth by age 2 to 4 years (EMEA-001469-PIP02-17). Since the previous day 30 discussion in March 2018, the applicant has provided additional information/clarification.
The PDCO adopted an Opinion on the refusal of a PIP and agreed on a full waiver on own motion for somapacitan for the treatment of short stature in children on the following grounds:
From birth to 4 years of age
The waiver in this age subset should be based on the lack of significant therapeutic benefit (catch-up growth may still occur until 4 years of age; prior growth hormone treatment may lead to the unnecessary overtreatment of children).
From 4 to less than 18 years of age
The waiver in this age subset should be based on safety grounds.

2.1.8. Split influenza virus, inactivated containing antigens equivalent to the B-like strain / Split influenza virus, inactivated containing antigens equivalent to the

A/H3N2-like strain / Split influenza virus, inactivated containing antigens equivalent to the A/H1N1-like strain - EMEA-002353-PIP01-18

Sanofi Pasteur; Prevention of influenza infection

Day 30 opinion

Vaccines

Summary of committee discussion:

The applicant proposes a full product-specific waiver for the prevention of influenza infection based on the lack of significant benefit.
PDCO concluded that the product, does not provide a significant benefit over existing standard-dose quadrivalent influenza vaccine due to its reduced strain coverage, and thus PDCO recommends granting a waiver for 'split influenza virus, inactivated containing antigens equivalent to the A/H1N1-like strain / split influenza virus, inactivated containing antigens equivalent to the A/H3N2-like strain / split influenza virus, inactivated containing antigens equivalent to the B-like strain' for all subsets of the paediatric population (0 to 18 years of age) in the condition of prevention of influenza infection. The opinion was adopted at Day 30.

2.2. Opinions on Compliance Check

The following compliance checks have been put up for discussion and the members of the PDCO have been invited to comment on issues of possible non-compliance

2.2.1. Cobicistat / Darunavir - EMEA-C2-001280-PIP01-12-M01

Janssen-Cilag International NV; Treatment of HIV-1 infection

Day 30 letter

Infectious Diseases

Summary of committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed.
The PDCO finalised on the 27 April 2018 this partial compliance procedure and considered that Study contained in the agreed paediatric investigation plan and completed until this date is not compliant with the latest Agency's Decision.

2.2.2. Ozanimod - EMEA-C3-001710-PIP02-14-M02

Celgene Europe Limited; Treatment of Multiple Sclerosis

Day 30 letter

Neurology

Summary of committee discussion:

The PDCO finalised on 25 April 2018 this partial compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that

were to be completed until this date.

2.2.3. Eltrombopag (eltrombopag olamine) / Eltrombopag - EMEA-C1-000170-PIP03-13-M03

Novartis Europharm Limited; Treatment of aplastic anaemia

Day 1 letter

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO finalised on 27 April 2018 this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be completed until this date.

2.2.4. Fc- and CDR-modified humanised monoclonal antibody against C5 - EMEA-C2-002077-PIP01-16-M01

Alexion Europe SAS; Treatment of Paroxysmal Nocturnal Haemoglobinuria

Day 30 letter

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO finalised on 27 April 2018 this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be completed by this date.

2.2.5. Angiotensin II - EMEA-C1-001912-PIP02-16-M01

La Jolla Pharmaceutical II B.V.; Treatment of hypotension associated with distributive or vasodilatory shock

Day 30 letter

Cardiovascular Diseases

Summary of committee discussion:

PDCO confirmed that the study is compliant with the PIP requirements.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Apixaban - EMEA-000183-PIP01-08-M06

Bristol-Myers Squibb / Pfizer EEIG; Prevention of arterial thromboembolism, Prevention of venous thromboembolism / Prevention of venous thromboembolism VTE) in paediatric

subjects (1 to < 18 years old) with a newly diagnosed acute lymphoblastic leukemia (ALL) or lymphoma (T or B cell), a functioning central venous access device (CVAD) and receiving asparaginase during chemotherapy induction., Prevention of TE in paediatric patients (birth to below 18 years old) with cardiac disease

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0196/2017 of 14/07/17).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.2. Apixaban - EMEA-000183-PIP02-12-M02

Bristol-Myers Squibb / Pfizer EEIG; Treatment of venous thromboembolism

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0235/2013 of 24/09/2013).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.3. Betrixaban - EMEA-001834-PIP02-16-M01

Portola Pharma UK Limited; Prevention of venous thromboembolism

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0352/2016 of 2/12/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO

Opinion.

2.3.4. Apremilast - EMEA-000715-PIP03-11-M05

Celgene Europe Limited; Psoriasis in children

Day 60 opinion

Dermatology

Summary of committee discussion:

The applicant's responses to the D30 issues were considered acceptable.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0145/2017 of 7 June 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. Dupilumab - EMEA-001501-PIP01-13-M05

Regeneron Pharmaceuticals, Inc; atopic dermatitis

Day 60 opinion

Dermatology

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0069/2017 of 3 April 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.6. Empagliflozin - EMEA-000828-PIP04-16-M01

Boehringer Ingelheim International GmbH; Treatment of type 1 diabetes mellitus

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan and in line with the day 30 conclusions, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP

as set in the Agency's latest decision (P/0162/2017 of 30/06/2017).

2.3.7. Baricitinib - EMEA-001220-PIP01-11-M03

Eli Lilly and Company Limited; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis) / Treatment of juvenile idiopathic arthritis, Treatment of JIA-associated uveitis

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

Between Day 30 and Day 60 the applicant had provided satisfactory responses to most of the PDCO's requests and only a few remaining issues required discussions at Day 60.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0026/2018 of 30/01/2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. Emapalumab - Orphan - EMEA-002031-PIP01-16-M01

Novimmune B.V; Treatment of Haemophagocytic Lymphohistiocytosis

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO re-discussed this procedure at Day 60 during the April 2018 plenary.
The Committee assessed the answers the applicant provided after the Day 30 discussion and found them acceptable.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0358/2017 of 1 December 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.9. Ceftaroline fosamil - EMEA-000769-PIP01-09-M08

Pfizer Limited; Treatment of cSSTI (complicated skin and soft tissue infections) / Treatment of CAP (community-aquired pneumonia)

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO re-discussed and endorsed its views expressed on day 30.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0013/2018 of 30 January 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.10. Ceftazidime / avibactam - EMEA-001313-PIP01-12-M07

Pfizer Limited; Treatment of bacterial infections / For the treatment of complicated urinary tract infections, For the treatment hospital acquired pneumonia, For the treatment of complicated intra-abdominal infections, For the treatment of infections due to aerobic Gram-negative organism

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

All remaining issues were satisfactorily addressed between Day 30 and Day 60.
Moreover, it was agreed that the wording of the condition should be amended from "Treatment of Gram-negative bacterial infections" to "Treatment of infections due to aerobic Gram-negative organisms" in line with the adult indication. The wording of the PIP indication has also been updated
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan; the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0314/2017 of 31 October 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.11. Dasabuvir sodium monohydrate - EMEA-001439-PIP01-13-M02

Abbvie Ltd; Treatment of chronic hepatitis C / Treatment of children and adolescents from >= 3 years to less than 18 years of age with chronic HCV infection with compensated cirrhosis or without compensated cirrhosis in combination with ombitasvir, paritaprevir and ritonavir

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The applicant provided clarification on 9 April 2018.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be

accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0066/2017 of 17 March 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.12. Lamivudine (3TC) / Dolutegravir (DTG) - EMEA-001940-PIP01-16-M01

ViiV Healthcare UK Limited; Treatment of human immunodeficiency virus (HIV-1) infection

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO discussed at their April 2018 meeting the responses received from the applicant to the points raised at D30.
The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0074/2017 of 17/3/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.13. Ritonavir / paritaprevir / ombitasvir - EMEA-001440-PIP01-13-M02

Abbvie Ltd; Chronic Hepatitis C (HCV) infection / Treatment of children and adolescents from >= 3 years to < 18 years of age with chronic HCV infection with compensated cirrhosis or without compensated cirrhosis in combination with other medicinal products

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The applicant provided the requested clarification regarding the current status of the PIP study on 9 April 2018.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0067/2017 of 17 March 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.14. Sofosbuvir - EMEA-001276-PIP01-12-M02

Gilead Sciences International Ltd.; Treatment of chronic Hepatitis C in adolescents and children 3 years of age and older

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0178/2014 of 7 July 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. Tenofovir Alafenamide / Emtricitabine - EMEA-001577-PIP02-14-M03

Gilead Sciences International Ltd.; Treatment of human immunodeficiency virus (HIV-1) infection

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

Following the Day 30 discussion, additional justifications were provided by the applicant on 12 April 2018.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that some of the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0024/2017 of 31 January 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.16. Velpatasvir / Sofosbuvir - EMEA-001646-PIP01-14-M02

Gilead Sciences International Ltd.; Treatment of chronic Hepatitis C in adolescents and children 3 years of age and older

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0190/2017 of 03 July 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.17. Fenfluramine hydrochloride - Orphan - EMEA-001990-PIP01-16-M01

Zogenix International Ltd; Dravet syndrome / The adjunctive treatment of seizures in paediatric patients at least 1 year of age with Dravet syndrome

Day 60 opinion

Neurology

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision. The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.18. Spheroids of human autologous matrix-associated chondrocytes - EMEA-001264-PIP01-12-M02

CO.DON AG; Treatment of symptomatic articular cartilage defects of the femoral condyle and the patella of the knee (International Cartilage Repair Society [ICRS] grade III or IV) with defect sizes up to 10 cm2

Day 60 opinion

Other

Summary of committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0253/2012 of 30/11/2012).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.19. Formoterol fumarate dihydrate / Beclometasone dipropionate - EMEA-000548-PIP01-09-M08

Chiesi Farmaceutici S.p.A.; COPD, Asthma / Maintenance therapy of asthma where use of a combination product (inhaled corticosteroid and long-acting beta2-agonist) is appropriate: - patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting beta2-agonist or - patients already adequately controlled on both inhaled corticosteroids and long-acting beta2-agonists

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

The PDCO re-discussed and endorsed its views expressed on day 30.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0320/2017 of 31 October 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.20. Peanut flour - EMEA-001734-PIP01-14-M02

Aimmune Therapeutics Inc; Peanut Allergy / Peanut oral immunotherapy for the reduction in clinical reactivity to accidental exposure in peanut children and adults

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

The PDCO discussed the information submitted by the applicant after Day 30.
The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0275/2016 of 7 October 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.21. Lurasidone hydrochloride - EMEA-001230-PIP01-11-M04

AZIENDE CHIMICHE RIUNITE ANGELINI FRANCESCO - A.C.R.A.F. S.p.A.; Schizophrenia

Day 60 opinion

Psychiatry

Summary of committee discussion:

The PDCO re-discussed the application. The scientific conclusion of the PDCO at Day 30 was reviewed and endorsed.
PDCO adopted a positive opinion modifying the PIP accordingly. The new modified opinion supersedes the previous PDCO opinion.

2.3.22. Etelcalcetide - EMEA-001554-PIP01-13-M02

Amgen Europe B.V.; Hyperparathyroid disorders / Hyperparathyroidism Secondary

Day 60 opinion

Uro-nephrology

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed

paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0074/2016 of 18 March 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.23. Lubiprostone - EMEA-000245-PIP01-08-M05

Sucampo AG; chronic idiopathic constipation

Day 30 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The PDCO discussed this procedure on D30.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0353/2017 of 1 December 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.24. Pibrentasvir / Glecaprevir - EMEA-001832-PIP01-15-M01

AbbVie Ltd; Treatment of Chronic Hepatitis C

Day 30 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO discussed this modification on 25 April 2018.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO thus considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0152/2016 of 14 June 2016).

2.4. Opinions on Re-examinations

None

2.5. Opinions on Review of Granted Waivers

2.5.1. Delafloxacin - EMEA-001080-PIP01-10

A.Menarini - IndustrieFarmaceutiche Riunite - s.r.l.; Treatment of local infections of skin and subcutaneous tissuesDay 30 adoption

Infectious Diseases

Summary of committee discussion:

The paediatric validation of the initial MAA for this medicinal product revealed that the applied for oral formulation, i.e. tablet, is not covered by the current EMA decision on a full waiver (covering only the intravenous formulation, i.e. powder for solution for infusion, and capsules as oral formulation).

To not unnecessarily delay the MAA by awaiting a new waiver application by the applicant for the applied for pharmaceutical form “tablet”, it was agreed with the applicant to review the granted waiver according to Article 14(2) of Reg 1901/2006 (as amended), which states that the Paediatric Committee may, at any time, adopt an opinion advocating the review of a granted waiver.

The PDCO discussed and agreed to adopt an opinion on the review of a granted product specific waiver to cover the pharmaceutical form “tablet”, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

2.6. Finalisation and adoption of opinions

2.7. Partial Compliance Checks completed by EMA

For the following partial compliance checks, no need to refer them to PDCO Committee for discussion was identified by the PME coordinator and PDCO Rapporteur. The PDCO has been informed in writing.

None

3. Discussion of applications

Disclosure of some information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.1. Discussions on Products D90-D60-D30

3.1.1. Bimekizumab - EMEA-002189-PIP01-17

Treatment of psoriasis / Treatment of moderate to severe chronic plaque psoriasis in children from the age of 6 years and older

Day 90 discussion

Dermatology

3.1.2. EMEA-002216-PIP01-17

Treatment of Atopic Dermatitis

Day 90 discussion

Dermatology

3.1.3. Dasiglucagon - Orphan - EMEA-002233-PIP01-17

Zealand Pharma A/S; Treatment of hypoglycaemia

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.4. Ustekinumab - EMEA-000311-PIP05-17

Treatment of Ulcerative Colitis

Day 90 discussion

Gastroenterology-Hepatology

3.1.5. Itacitinib - Orphan - EMEA-002178-PIP01-17

Incyte Biosciences UK Ltd.; Treatment of acute Graft versus Host Disease (D89.810, ICD-10-CM) / Treatment of steroid naïve paediatric population with acute graft versus host disease after allogeneic hematopoietic stem cell transplantation

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.6. Recombinant IgG degrading enzyme of Streptococcus pyogenes - Orphan - EMEA-002183-PIP01-17

Hansa Medical AB; Patients with chronic kidney disease in need of kidney transplantation / Prevention of graft rejection following solid organ transplantation

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.7. The whole range of unmanipulated autologous mononuclear cells derived from human umbilical cord blood (Hau-UCB-mnc) - Orphan - EMEA-001799-PIP02-17

BrainRepair UG (haftungsbeschränkt); Periventriculaleukomalacia (PVL) ICD-10-CM P91.2

Day 90 discussion

Neonatology - Paediatric Intensive Care

3.1.8. EMEA-002184-PIP01-17

Treatment of obstructive sleep apnoea, Treatment of narcolepsy, Treatment of excessive daytime sleepiness in narcolepsy patients

Day 90 discussion

Neurology

3.1.9. Palbociclib - EMEA-002146-PIP01-17

Treatment of refractory or recurrent Ewing sarcoma

Day 90 discussion

Oncology

3.1.10. Purified Rabies virus - EMEA-002234-PIP01-17

Prevention of rabies disease, treatment of exposure to rabies virus

Day 90 discussion

Vaccines

3.1.11. Mavacamten - EMEA-002231-PIP01-17

Treatment of Hypertrophic Cardiomyopathy / Treatment of obstructive Hypertrophic Cardiomyopathy

Day 60 discussion

Cardiovascular Diseases

3.1.12. Brincidofovir - Orphan - EMEA-001904-PIP03-18

Chimerix UK Limited; Treatment of smallpox

Day 60 discussion

Infectious Diseases

3.1.13. Ibalizumab - EMEA-002311-PIP01-17

Treatment of human immunodeficiency virus (HIV-1) infection / Ibalizumab, a CD4 domain 2-directed HIV-1 inhibitor, in combination with other antiretroviral(s), is indicated for the treatment of children and adolescents (aged 6 to less than 18 years) infected with

HIV-1 resistant to at least 1 agent in 3 different classes.

Day 60 discussion

Infectious Diseases

3.1.14. Pretomanid - Orphan - EMEA-002115-PIP01-17

Global Alliance for TB Drug Development; Treatment of multi-drug-resistant tuberculosis

Day 60 discussion

Infectious Diseases

3.1.15. Rezafungin acetate - EMEA-002319-PIP01-17

Treatment of invasive candidiasis

Day 60 discussion

Infectious Diseases

3.1.16. Tedizolid phosphate - EMEA-001379-PIP03-17

Treatment of Gram-positive bacterial pneumonia

Day 60 discussion

Infectious Diseases

3.1.17. Brigatinib - EMEA-002296-PIP01-17

Inflammatory Myofibroblastic Tumors (IMT), Non-small cell lung cancer (NSCLC), Anaplastic large cell lymphoma (ALCL) / Treatment of anaplastic lymphoma kinase (ALK) positive advanced non-small cell lung cancer (NSCLC)., Treatment of paediatric patients ≥2 years of age with ALK+ unresectable or recurrent IMT., Treatment in combination with standard chemotherapy in paediatric patients ≥2 years of age with newly diagnosed ALK+ ALCL at high risk for recurrence.

Day 60 discussion

Oncology

3.1.18. Palovarotene - EMEA-001662-PIP03-17

Treatment of Multiple Osteochondromas (MO)

Day 60 discussion

Other

3.1.19. Meloxicam / Bupivacaine - EMEA-002246-PIP01-17

Acute Post-Operative Pain

Day 60 discussion

Pain / Anaesthesiology

3.1.20. EMEA-002297-PIP02-18

Treatment of Microvascular Coronary Artery Disease

Day 30 discussion

Cardiovascular Diseases

3.1.21. Allogeneic bone-marrow derived adherent, ex-vivo expanded multipotent adult progenitor cells product - EMEA-002317-PIP01-17

Acute ischaemic stroke

Day 30 discussion

Cardiovascular Diseases

3.1.22. Dapagliflozin - EMEA-000694-PIP03-17

I50 Heart Failure

Day 30 discussion

Cardiovascular Diseases

3.1.23. Moxonidine - EMEA-002275-PIP01-17

Treatment of Hypertension

Day 30 discussion

Cardiovascular Diseases

3.1.24. Trandolapril - EMEA-002274-PIP01-17

Mild or moderate hypertension

Day 30 discussion

Cardiovascular Diseases

3.1.25. Patidegib - EMEA-002322-PIP01-17

Treatment of basal cell carcinoma (BCC)

Day 30 discussion

Dermatology / Oncology

3.1.26. Evinacumab - EMEA-002298-PIP01-17

Treatment of elevated cholesterol / Treatment of homozygous familial hypercholesterolemia (HoFH)

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.27. Ianalumab - EMEA-002338-PIP01-18

Treatment of autoimmune hepatitis in patients aged 12 years to <18 years in whom steroids and/or azathioprine are contraindicated, are not tolerated, or do not provide an adequate response

Day 30 discussion

Gastroenterology-Hepatology

3.1.28. Abatacept - EMEA-000118-PIP04-17

Treatment of childhood-onset of Sjögren's Syndrome

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.29. Liposomal ciclosporin A (L-CsA) - Orphan - EMEA-002344-PIP01-18

Breath Therapeutics GmbH; Treatment of Bronchiolitis obliterans Syndrome (BOS)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.30. Upadacitinib Hemihydrate - EMEA-001741-PIP05-17

Treatment of Vasculitides

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.31. EMEA-002240-PIP02-17

Treatment of Urinary Tract Infections

Day 30 discussion

Infectious Diseases

3.1.32. Reltecimod - Orphan - EMEA-002325-PIP01-18

Atox Bio Ltd.; Treatment for necrotizing soft tissue infections

Day 30 discussion

Infectious Diseases

3.1.33. EMEA-001970-PIP02-17

Treatment of Clostridium difficile infection / indicated to reduce recurrence of Clostridium difficile infection (CDI) in paediatric patients who have received antibacterial drug treatment for recurrent CDI.

Day 30 discussion

Infectious Diseases

3.1.34. Isoflurane - EMEA-002320-PIP01-17

Sedation

Day 30 discussion

Neonatology - Paediatric Intensive Care

3.1.35. Fostamatinib - EMEA-001196-PIP02-17

Treatment of immune thrombocytopenia (idiopathic thrombocytopenic purpura)

Day 30 discussion

Other

3.1.36. Bupivacaine - EMEA-000877-PIP03-17

Postsurgical analgesia

Day 30 discussion

Pain

3.1.37. Nitrous oxide - EMEA-002340-PIP01-18

Anesthesia, analgesia / sedation / In analgesia / sedation in all conditions in which pain relief / sedation with rapid onset and rapid fall in effect is required (short-term surgical interventions, traumatology, burns, dentistry, otorhinolaryngology, childbirth)., Under anesthesia, in combination with other anesthetics administered by inhalation or intravenously.

Day 30 discussion

Pain / Anaesthesiology

3.1.38. Calcifediol - EMEA-002093-PIP02-17

Treatment of secondary hyperparathyroidism (SHPT) in non-dialysis chronic kidney disease (ND-CKD) patients with low serum 25-hydroxyvitamin D levels

Day 30 discussion

Uro-nephrology

3.1.39. Bilastine - EMEA-000347-PIP03-18

Treatment of allergic rhinoconjunctivitis, Treatment of urticaria

Day 30 discussion

Dermatology / Pneumology - Allergology / Oto-rhino-laryngology

3.2. Discussions on Compliance Check

The following compliance checks have been put up for discussion and the members of the PDCO have been invited to comment on issues of possible non-compliance

3.2.1. Osilodrostat - EMEA-C1-000315-PIP02-15-M01

Novartis Europharm Limited; Treatment of adrenal cortical hyperfunctions

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.2.2. Birch pollen extract (Betula verrucosa) - EMEA-C1-001879-PIP01-15-M01

ALK Abelló A/S; Treatment of allergic rhinitis / rhino-conjunctivitis

Day 30 discussion

Pneumology - Allergology

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Bempedoic acid - EMEA-001872-PIP01-15-M01

Esperion Therapeutics, Inc.; Treatment of elevated cholesterol / Treatment of heterozygous and homozygous familial hypercholesterolemia

Day 30 discussion

Cardiovascular Diseases

3.3.2. Regadenoson - EMEA-000410-PIP01-08-M03

GE Healthcare AS; Diagnostic evaluation of myocardial perfusion disturbances

Day 30 discussion

Cardiovascular Diseases

3.3.3. Ticagrelor - EMEA-000480-PIP01-08-M11

AstraZeneca AB; thromboembolic events (children), acute coronary syndrome, history of myocardial infarction / reduction in occurrence of vaso-occlusive crises in paediatric patients with sickle cell disease

Day 30 discussion

Cardiovascular Diseases / Haematology-Hemostaseology

3.3.4. Brodalumab - EMEA-001089-PIP02-13-M01

LEO Pharma A/S; Treatment of psoriasis

Day 30 discussion

Dermatology

3.3.5. Ligelizumab - EMEA-001811-PIP02-15-M02

Novartis Europharm Ltd.; Treatment of chronic spontaneous urticaria

Day 30 discussion

Dermatology

3.3.6. 2-hydroxypropyl-ß-cyclodextrin (HP-ß-CD) - Orphan - EMEA-001866-PIP01-15-M02

Mallinckrodt Pharmaceuticals Ireland Ltd; Treatment of progressive neurological manifestations in children and adolescent patients with Niemann-Pick disease, type C

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.7. Empagliflozin - EMEA-000828-PIP01-09-M07

Boehringer Ingelheim International GmbH; Treatment of type 2 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.8. Glycerol phenylbutyrate - Orphan - EMEA-000297-PIP02-12-M02

Horizon Pharma Ireland Limited; E72.2 Urea cycle disorders / indicated for use as adjunctive therapy for chronic management of patients with urea cycle disorders (UCDs) including deficiencies of carbamoyl phosphate-synthase-I (CPS), ornithine carbamoyltransferase (OTC), argininosuccinate synthetase (ASS), argininosuccinate lyase (ASL), arginase I (ARG) and ornithine translocase deficiency hyperornithinaemia-hyperammonaemia homocitrullinuria syndrome (HHH) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone.

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.9. Linagliptin - EMEA-000498-PIP01-08-M08

Boehringer Ingelheim International GmbH; Treatment of type 2 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.10. EMEA-001356-PIP02-12-M02

Alfasigma S.p.A.; any clinical procedures requiring a clean bowel e.g. bowel endoscopy or radiology

Day 30 discussion

Gastroenterology-Hepatology

3.3.11. Vonicog alfa - Orphan - EMEA-001164-PIP01-11-M02

Baxalta Innovations GmbH; Von Willebrand Disease / Treatment and control of haemorrhage (spontaneous and surgical) and prevention of bleeding in surgery in paediatric patients (age of < 18 years) diagnosed with VWD when desmopressin (DDAVP) treatment alone is ineffective or not indicated

Day 30 discussion

Haematology-Hemostaseology

3.3.12. Eculizumab - Orphan - EMEA-000876-PIP05-15-M03

Alexion Europe SAS; Treatment of Refractory Generalized Myasthenia Gravis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.13. Expanded donor-derived allogenic T cells transduced with the retroviral vector expressing the transgenes for inducible caspase9 and the truncated CD19 selectable marker - Orphan - EMEA-001869-PIP01-15-M01

Bellicum Pharma Ltd; Adjunctive treatment in haematopoietic stem cell transplantation

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.14. Rimiducid - Orphan - EMEA-001870-PIP01-15-M01

Bellicum Pharma Ltd.; Treatment of graft versus host disease

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.15. Tofacitinib - EMEA-000576-PIP01-09-M09

Pfizer Limited; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis) / Juvenile idiopathic arthritis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.16. Arimoclomol citrate - Orphan - EMEA-001748-PIP01-15-M01

Orphazyme A/S; Treatment of Niemann-Pick Disease, Type C

Day 30 discussion

Neurology

3.3.17. Domagrozumab - Orphan - EMEA-001763-PIP01-15-M02

Pfizer Ltd; Duchenne Muscular Dystrophy

Day 30 discussion

Neurology

3.3.18. Pitolisant - Orphan - EMEA-001176-PIP01-11-M03

BIOPROJET PHARMA; Narcolepsy with or without cataplexy

Day 30 discussion

Neurology

3.3.19. Tasimelteon - Orphan - EMEA-001531-PIP01-13-M04

Vanda Pharmaceuticals; ICD-10 G47.24 Circadian rhythm sleep disorder, free-running type (Non-24) / Non24-Hour Sleep-Wake Disorder (Non-24) in the totally blind

Day 30 discussion

Neurology

3.3.20. Cobimetinib - EMEA-001425-PIP01-13-M03

Roche Registration Limited; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue) with Ras, Raf or MEK pathway activation / Treatment of children with a paediatric solid malignant tumour with known or expected Ras, Raf or MEK pathway activation, at first relapse or refractory to initial treatment.

Day 30 discussion

Oncology

3.3.21. Larotrectinib - Orphan - EMEA-001971-PIP02-16-M01

Bayer AG; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haemtopoietic and lymphoid tissue neoplasms). / Treatment of paediatric patients from birth to less than 18 years of age with advanced solid tumours harbouring an NTRK fusion.

Day 30 discussion

Oncology

3.3.22. Sirolimus - Orphan - EMEA-001416-PIP01-12-M02

Santen Incorporated; Treatment of non-infectious uveitis affecting the posterior segment of the eye

Day 30 discussion

Ophthalmology

3.3.23. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with lentiviral vector that encodes for the human ARSA cDNA sequence - Orphan - EMEA-001765-PIP02-15-M02

GlaxoSMithKline Trading Services Limited; For the treatment of Metachromatic leukodystrophy (MLD)

Day 30 discussion

Other

3.3.24. Calcium chloride / Aprotinin / Fibrinogen / Thrombin - EMEA-001079-PIP01-10-M04

Kedrion S.p.A.; Treatment and prevention of haemorrhage resulting from a surgical procedure

Day 30 discussion

Other

3.3.25. Mexiletine hydrochloride - Orphan - EMEA-002012-PIP01-16-M01

Lupin (Europe) Ltd.; Symptomatic treatment of myotonic disorders

Day 30 discussion

Other

3.3.26. Gabapentin - EMEA-001310-PIP01-12-M03

PHARM Srl; Treatment of chronic pain in paediatric patients aged from 3 months to less than 18 years

Day 30 discussion

Pain

3.3.27. Tezepelumab - EMEA-001613-PIP01-14-M01

AstraZeneca AB; Treatment of asthma / Tezepelumab is indicated as add-on maintenance treatment of patients with severe asthma aged 5 years and older.

Day 30 discussion

Pneumology - Allergology

3.3.28. Potassium hydrogen carbonate / Potassium citrate monohydrate - EMEA-001535-PIP01-13-M01

Advicenne; Cystinuria (ICD 10: E72.0)

Day 30 discussion

Uro-nephrology

3.3.29. Sucroferric oxyhydroxide - EMEA-001061-PIP01-10-M03

Vifor Fresenius Medical Care Renal Pharma France; Hyperphosphataemia / Control of serum phosphorus levels in paediatric and adolescent subjects with chronic kidney

disease (CKD)

Day 30 discussion

Uro-nephrology

3.3.30. Influenza virus surface antigens (haemagglutinin and neuraminidase) of the following strains: A/<Official Strain>(H1N1), A/<Official Strain>(H3N2), B/<Official Strain>Yamagata lineage, B/<Official Strain>Victoria lineage based on annual recommendations by WHO, CHMP (EU) and other regional or local authorities - EMEA-001782-PIP01-15-M03

Abbott Biologicals B.V.; Prophylaxis of influenza; especially in those who run an increased risk of associated complications

Day 30 discussion

Vaccines

3.3.31. Recombinant Varicella Zoster Virus (VZV) glycoprotein E antigen - EMEA-001426-PIP01-13-M02

GlaxoSmithKline Biologicals SA; Prevention of VZV reactivation / Prevention of herpes zoster in immunocompromised subjects aged 1 to 17 years

Day 30 discussion

Vaccines

4. Nominations

Disclosure of information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

4.1. List of letters of intent received for submission of applications with start of procedure 26 June 2018 for Nomination of Rapporteur and Peer reviewer

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.2. Nomination of Rapporteur for requests of confirmation on the applicability of the EMA decision on class waiver.

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.3. Nominations for other activities

None

5. Scientific Advice Working Party (SAWP) and Paediatric Committee (PDCO) Interaction

Disclosure of information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

6. Discussion on the applicability of class waivers

Disclosure of some information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

6.1. Discussions on the applicability of class waiver for products+

6.1.1. Inhibitor of ADAMTS-5 – EMEA-03-2018

LES LABORATOIRES SERVIER; All classes of medicinal products for treatment of primary and secondary osteoarthrosis/ Disease-modifying drug in treatment of mild to moderate osteoarthritis of the knee and hip to reduce the degradation of cartilage

Summary of committee discussion:

The applicability of the class waiver as referred to in the Agency's Decision CW/0001/2015 to the planned therapeutic indication was confirmed.

Other potential paediatric interests of this medicine suggested by PDCO: severe or old inflammatory arthritis, post septic arthritis, post slipped upper femoral epiphesis and Perthes (any avascular necrosis that may predispose to osteoarthrosis), potentially in some skeletal dysplasias, single destroyed joints in juvenile idiopathic arthritis where other joints have responded to treatment.

6.1.2. Poly(oxy-1,2-ethanediyl), alpha-hydro-.omega.-hydroxy-,15,15'-diester with N-acetyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminylL-.alpha.-aspartyl-L-tryptophylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinylL-threonyl-2-[2-(2-aminoethoxy)ethoxy]acetyl-N6-carboxy-L-lysinamide cyclic (2.fwdarw.12)-(disulfide); where two identical synthetic peptide domains are covalently linked to the ends of the polyethylene glycol chain - EMEA-04-2018

Apellis Pharmaceuticals Inc; All classes of medicinal products for treatment of age-related macular degeneration and diabetic macular oedema/ Treatment of geographic atrophy secondary to age related macular degeneration

Summary of committee discussion:

The applicability of the class waiver as referred to in the Agency's Decision CW/0001/2015 to the planned therapeutic indication was confirmed.

Other potential paediatric interests of this medicine suggested by PDCO: Stargardt disease.

7. Discussion on the inclusion of an indication within a condition in an agreed PIP / waiver

7.1. Discussion on the possibility to include an indication within a condition in an agreed PIP / waiver

None

8. Annual reports on deferrals

Note: The annual reports on deferrals to be noted by the members of the PDCO are flagged in the Annex B.

9. Organisational, regulatory and methodological matters

9.1. Mandate and organisation of the PDCO

None

9.2. Coordination with EMA Scientific Committees or CMDh-v

9.2.1. Committee for Medicinal Products for Human Use (CHMP)

Summary of committee discussion:

The list of procedures with paediatric indications to be evaluated by the CHMP, starting in March 2018, was presented to the PDCO members.

The members were also informed about 1 medicinal product, Ivemendt for which the CHMP adopted a positive opinion recommending a paediatric indication during their meeting in March 2018.

9.2.2. Committee for Medicinal Products for Human Use (CHMP)

CHMP/PDCO joint session

PDCO Member: Martina Riegl

Summary of committee discussion:

The Committees discussed a PIP modification request for a product for schizophrenia in the context of the requirements set by the current schizophrenia guideline.

9.3. Coordination with EMA Working Parties / Working Groups / Drafting Groups

9.3.1. Non-clinical Working Group: D30 Products identified

PDCO member: Karen van Malderen

Summary of committee discussion:

The chair of the Non-clinical Working Group identified the products which will require Non-clinical Working Group evaluation and discussion.

9.3.2. Formulation Working Group

PDCO member: Brian Aylward

Summary of committee discussion:

The chair of the Formulation Working Group identified the products which will require Formulation Working Group evaluation and discussion.

9.4. Cooperation within the EU regulatory network

9.4.1. European Network of Paediatric Research (Enpr) - European Medicines Agency (EMA)

Summary of committee discussion:

Not discussed this month

9.4.2. Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)

Request for PDCO advice (EMEA-000018-PIP01-07-M13)

PDCO member: Sabine Scherer

Summary of committee discussion:

Responses on a question by question basis are not possible, as this would require assessment of all available data, which is beyond PDCO's remit. The PDCO discussion therefore focused on general approach.

PDCO agreed that their considerations can be quoted in RMS assessment report.

9.5. Cooperation with International Regulators

None

9.6. Contacts of the PDCO with external parties and interaction with the Interested Parties to the Committee

None

9.7. PDCO work plan

None

9.8. Planning and reporting

9.8.1. Business Pipeline Report - Forecast for 2018 - Update Q1/2018

Summary of committee discussion:

The document was tabled for information.

10. Any other business

10.1.1. Training needs for PDCO members and alternates

Summary of committee discussion:

A discussion was held on the training needs for PDCO members and alternates.

10.1.2. Preparedness of the system and capacity increase - POSTPONED

Scope: Update on the recent discussions/activities in relation to Brexit

10.1.3. Update on the EMA relocation

Summary of committee discussion:

The PDCO noted the update. There is a tracking tool on the relocation published on EMA website:
http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500244941

The temporary building, the Spark building is available as of 1 January 2019. The EMA is scheduled to be fully operational in temporary premises as of 30 March 2019.

10.1.4. Collaborative papers of PDCO with Rome Foundation on Irritable Bowel Syndrome and Functional Constipation in children – POSTPONED TO MAY

PDCO member: Johannes Taminiau

10.1.5. Haemophilia registries workshop

Summary of committee discussion:

The EMA secretariat presented to the PDCO a plan for dealing with potential modifications of the PIPs and for new PIPs for recombinant factor VIII products related to the ongoing revision of the Guideline on the clinical investigation of recombinant and human plasma-derived factor VIII products. The agenda of the Haemophilia registry workshop organised for the 8th of June was presented.

10.1.6. Workshop on EMA stakeholder interaction on the development of medicinal products for chronic non-infectious liver diseases (PBC, PSC and NASH)

Summary of committee discussion:

The plans for a workshop in non-infectious liver diseases in adults and children in Q4 2018 were presented to the committee for information.

10.1.7. EC/EMA action plan to further improve the implementation of the Paediatric Regulation

Scope: Next steps for development of action plan

Summary of committee discussion:

The next steps towards the development of an action plan to further improve the implementation of the Paediatric Regulation were presented to the Committee.

10.1.8. Involvement of young people into PDCO activities

Summary of committee discussion:

The PDCO agreed to systematically include to the PIP discussion whether or not input from young/people and/or patients is required by adding this question to the presentation slide template.

It was further suggested to add this question into the summary report template to raise awareness among applicants and to encourage them to seek input from young people/patients before submitting a PIP application.

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

The group discussed general topics on paediatric oncology PIPs.

11.1.2. Neonatology

Summary of committee discussion:

The neonatology group was updated on discussions at the INC (International Neonatal Consortium) 2018 Annual International Neonatal Scientific Workshop by members who attended the meeting. The group also discussed an ongoing PIP with relevance for neonates.

11.1.3. Inventory

Summary of committee discussion:

The inventory group met on the margins of the plenary meeting to continue working on a methodology for the assessment of unmet needs.

12. List of participants

List of participants including any restrictions with respect to involvement of members/alternates/ experts following evaluation of declared interests for the 24 – 27 April 2018 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Dirk Mentzer	Chair	Germany	No interests declared	
Karl-Heinz Huemer	Member	Austria	No interests declared	
Koenraad Norga	Member (Vice-Chair)	Belgium	No participation in discussion, final deliberations and voting on:	3.3.24 EMEA-001765-PIP02-15-M02
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Adriana Andrić	Member	Croatia	No interests declared	
Georgios Savva	Member	Cyprus	No interests declared	
Peter Szitanyi	Alternate	Czech Republic	No interests declared	
Kirstine Moll Harboe	Member	Denmark	No interests declared	
Mona Ring Gatke	Alternate	Denmark	No interests declared	
Ann Marie Kaukonen	Member	Finland	No interests declared	
Sylvie Benchetrit	Member	France	No interests declared	
Dominique Ploin	Alternate	France	No interests declared	
Sabine Scherer	Member	Germany	No interests declared	
Immanuel Barth	Alternate	Germany	No interests declared	
Eleni Katsomiti	Member	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
Sara Galluzzo	Member	Italy	No interests declared	
Alessandro Jenkner	Alternate	Italy	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Dina Apele-Freimane	Member	Latvia	No restrictions applicable to this meeting	
Sigita Burokiene	Member	Lithuania	No interests declared	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No interests declared	
Herbert Lenicker	Alternate	Malta	No interests declared	
Maaike van Dartel	Member	Netherlands	No interests declared	
Siri Wang	Member	Norway	No interests declared	
Anette Solli Karlsen	Alternate	Norway	No interests declared	
Marek Migdal	Member	Poland	No interests declared	
Helena Fonseca	Member	Portugal	No interests declared	
Hugo Tavares	Alternate	Portugal	No interests declared	
Dana Gabriela Marin	Member (CHMP alternate)	Romania	No interests declared	
Peter Sisovsky	Member	Slovakia	No interests declared	
Stefan Grosek	Member	Slovenia	No interests declared	
Fernando de Andrés Trelles	Member	Spain	No interests declared	
Ninna Gullberg	Member	Sweden	No interests declared	
Eva Agurell	Alternate	Sweden	No interests declared	
Angeliki Siapkara	Member	United Kingdom	No interests declared	
Martina Riegl	Alternate	United Kingdom	No interests declared	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No interests declared	
Riccardo Riccardi	Alternate	Healthcare Professionals' Representative	No participation in final deliberations and voting on:	3.3.21 EMEA-001425-PIP01-13-M03

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Michal Odermarsky	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Valentina Mantua	Expert - via telephone*	Italy	No restrictions applicable to this meeting	
David Khan	Expert - via telephone*	Sweden	No interests declared	
Catriona Elisabeth Baker	Expert - in person*	United Kingdom	No interests declared	
Christine Gispen-de Wied	Expert - via telephone*	Netherlands	No interests declared	
Hans-Karl Heim	Expert - via telephone*	Germany	No interests declared	
Karoline Buhre	Expert - via telephone*	Germany	No restrictions applicable to this meeting	
Juliana Min	Expert - in person*	United Kingdom	No interests declared	
Shiva Ramroop	Expert - in person*	United Kingdom	No interests declared	
Representative from the European Commission participated in the meeting				
Meeting run with support from relevant EMA staff				

* Experts were only evaluated against the product(s) they have been invited to talk about.

13. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

Paediatric investigation plan (PIP) (section 2.1 Opinion on PIPs and section 3.1 Discussions on PIPs)
A paediatric investigation plan (PIP) is a development plan aimed at ensuring that the necessary data are obtained through studies in children, when it is safe to do so, to support the authorisation of a medicine for children. Pharmaceutical companies submit proposals for PIPs to the European Medicines Agency's Paediatric Committee (PDCO). This Committee is responsible for agreeing or refusing the plan.

Compliance checks (section 2.2 Opinions on Compliance check, section 3.2 Discussions on Compliance check)
A compliance check may be necessary before any application for marketing authorisation (even for an adult indication) can be considered valid, if there was no deferral for at least one of the studies agreed in the PIP, or after the due date of initiation or completion of a study/measure. The same applies to some regulatory applications for authorised products, as described above.

Modification of an Agreed Paediatric Investigation Plan (section 2.3 Opinions on Modification of an agreed PIP, section 3.3 Discussions on Modification of an agreed PIP)
The development plan for a medicine can be modified at a later stage as knowledge increases. Modifications can also be made if the applicant encounters such difficulties with the implementation of a PIP, which render it unworkable or no longer appropriate.
In some cases, studies can be deferred until after the studies in adults have been conducted. This ensures that research in children is done only when it is safe and ethical to do so. Even when studies are deferred, the PIP will include details of the paediatric studies and their timelines.

Class waiver (section 6 Discussion on the applicability of class waiver)
As some diseases do not affect children (for example Parkinson's disease), the development of medicines for these diseases should not be performed in children. In these cases, a PIP is not required and it will be waived**.** For more information on the classes of diseases subject to waivers, see class waivers.

Annual reports on deferrals (section 8)
If the medicinal product is approved in the EU, annual reports on the deferred measures in the PIP must be submitted to the Agency.

More detailed information on the above terms can be found on the EMA website:
www.ema.europa.eu/