28 June 2019
EMA/PDCO/297694/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes of the meeting on 27-29 May 2019

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

27 May 2019, 08:30- 19:00, room 2D

28 May 2019, 08:30- 19:00, room 2D

29 May 2019, 08:30- 16:00, room 2D

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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Table of contents

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 for 27-29 May meeting was adopted and published on the EMA website.

1.3. Adoption of the minutes

The minutes of 23-26 April 2019 meeting were adopted and will be published on the EMA website.

2. Opinions

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. Emricasan - EMEA-002457-PIP01-18

Novartis Europharm Limited; Non-alcoholic steatohepatitis (NASH) / Treatment of NASH with moderate to severe liver fibrosis (F2-F4) in patients aged 8 to less than 18 years old

Day 120 Opinion

Gastroenterology-Hepatology

Summary of Committee discussion:

The Applicant's response to the Day 90 issues was acceptable and a positive Opinion was adopted.

2.1.2. Tropifexor - EMEA-002471-PIP01-18

Novartis Europharm Limited; Non-alcoholic steatohepatitis / Treatment of NASH with moderate to severe liver fibrosis (F2/F3) in paediatric patients from 8 to less than 18 years of age

Day 120 Opinion

Gastroenterology-Hepatology

Summary of Committee discussion:

A positive Opinion was adopted on Day 120.

2.1.3. Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human βA-T87Q-globin gene - Orphan - EMEA-001665-PIP02-17

bluebird bio France; Sickle cell disease

Day 120 Opinion

Haematology-Hemostaseology

Summary of Committee discussion:

The PDCO re-discussed this procedure at Day 120 during the May 2019 plenary meeting. The PDCO adopted a positive Opinion at Day 120.

2.1.4. Allogeneic Epstein-Barr virus specific cytotoxic T lymphocytes - Orphan - EMEA-002025-PIP02-16 - WITHDRAWN

Atara Biotherapeutics, Inc.; Treatment of Epstein-Barr virus associated post-transplant lymphoproliferative disorder / Treatment of solid organ transplant (SOT) patients with Epstein-Barr virus associated post-transplant lymphoproliferative disease (EBV+ PTLD) who have failed prior therapy with rituximab, Treatment of allogeneic haematopoietic cell transplant (alloHCT) patients with Epstein-Barr virus associated post-transplant lymphoproliferative disease (EBV+ PTLD) who have failed prior therapy with rituximab

Day 120 Opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed this procedure at Day 120 during the May 2019 plenary meeting.

Taking the above into consideration, the PDCO adopted a positive Opinion at Day 120.

Post-meeting note: On 20 June 2019, the Applicant has withdrawn the application before the Decision.

2.1.5. (2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidine-2-carboxamide - EMEA-002310-PIP02-17

Achillion Pharmaceuticals, Inc.; Treatment of C3 glomerulopathy

Day 120 Opinion

Uro-nephrology

Summary of Committee discussion:

The PDCO adopted a positive Opinion. A deferral was granted.

2.1.6. Bisoprolol fumarate / ramipril - EMEA-002560-PIP01-19

Neopharmed Gentili S.p.A.; Adults: treatment essential hypertension, Adults: treatment heart failure

Day 60 Opinion

Cardiovascular Diseases

Summary of Committee discussion:

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 bisoprolol fumarate / ramipril for all subsets of the paediatric population (0 to less than 18 years of age) in the conditions of 'treatment of hypertension' and 'treatment of heart failure' on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2.1.7. Ezetimibe / rosuvastatin calcium - EMEA-002541-PIP01-18

Abbott Laboratories Limited; Elevated cholesterol

Day 60 Opinion

Cardiovascular Diseases

Summary of Committee discussion:

The PDCO adopted a full product-specific waiver for ezetimibe / rosuvastatin (calcium) for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'Treatment of elevated cholesterol', based on the grounds of lack of significant benefit over existing products.

2.1.8. Heparin (sodium) - EMEA-002557-PIP01-19

B. Braun Melsungen AG; Prevention of thromboembolic events

Day 60 Opinion

Cardiovascular Diseases

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the Applicant's request for a waiver. The PDCO

recommends granting a waiver for heparin (sodium) for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'Prevention of thromboembolic events'.

Idera Pharmaceuticals Inc.; Treatment of malignant melanoma

Day 60 Opinion

Oncology

Summary of Committee discussion:

The PDCO discussed this product specific waiver request for the condition of 'treatment of malignant melanoma'. So overall, the PDCO agreed to grant a waiver based on lack of significant therapeutic benefit, as clinical studies are not feasible.

2.1.10. Bemarituzumab - EMEA-002401-PIP01-18

Five Prime Therapeutics, Inc.; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms) overexpressing FGFR2b

Day 60 Opinion

Oncology

Summary of Committee discussion:

The PDCO discussed the requested waiver to the entire population for bemarituzumab (anti-FG (FR2b humanised IgG1 monoclonal antibody)) for the 'treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms) overexpressing FGFR2b', taking into account the data provided by the Applicant.
The PDCO therefore recommended granting a waiver for bemarituzumab for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of treatment of gastric and gastro-oesophageal junction cancer on the grounds that the disease does not occur in the paediatric population.
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.

2.1.11. Momelotinib - Orphan - EMEA-001656-PIP02-19

Sierra Oncology Inc.; Treatment of primary myelofibrosis

Day 60 Opinion

Oncology

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric

Committee, the PDCO agrees with the Applicant's request for a waiver. The PDCO recommends granting a waiver for momelotinib for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of primary myelofibrosis. 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.

2.1.12. Moxetumomab pasudotox - Orphan - EMEA-002525-PIP01-18

AstraZeneca AB; Treatment of hairy cellleukaemia

Day 60 Opinion

Oncology

Summary of Committee discussion:

The PDCO agreed on a positive Opinion at Day 60.

2.1.13. Bempedoic acid - EMEA-001872-PIP02-19

Esperion Therapeutics, Inc.; Treatment of mixed dyslipidaemia

Day 60 Opinion

Other / Cardiovascular Diseases

Summary of Committee discussion:

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 bempedoic acid for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'Treatment of mixed dyslipidaemia'.
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. The PDCO notes that the incidence of obesity and associated lipid disorders is increasing also in the paediatric population. Further alternative pharmacotherapeutic options may be required in the (near) future for those patients insufficiently responding to current therapies or in whom current therapies cannot be used. The PDCO will continue to observe the medical need in this therapeutic area and respond accordingly to changes in the medical need.

2.1.14. Ezetimibe / bempedoic acid - EMEA-002200-PIP02-19

Esperion Therapeutics, Inc.; Treatment of mixed dyslipidaemia

Day 60 Opinion

Other / Cardiovascular Diseases

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the Applicant's request for a waiver. The PDCO

recommends granting a waiver for ezetimibe / bempedoic acid for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'Treatment of mixed dyslipidaemia'.

2.1.15. Brimonidine tartrate - EMEA-002558-PIP01-19

Bausch Health Ireland Limited; Conjunctival hyperaemia due to minor eye irritation

Day 60 Opinion

Ophthalmology

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the Applicant's request for a waiver. The PDCO recommends granting a waiver for brimonidine tartrate for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'conjunctival hyperaemia'. The waiver was based on the grounds of lack of significant therapeutic benefit.
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.

2.1.16. Dexamethasone sodium phosphate / levofloxacin - EMEA-002375-PIP02-18

NTC srl; Acute otitis externa / Treatment of acute otitis externa

Day 60 Opinion

Oto-rhino-laryngology

Summary of Committee discussion:

The PDCO adopted a full product-specific waiver for dexamethasone (sodium phosphate) / levofloxacin for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'Treatment of acute otitis externa', based on the grounds of lack of significant benefit over existing products.

2.1.17. Bordetella pertussis antigen: pertactin / Bordetella pertussis antigen: Filamentous haemagglutinin / Bordetella pertussis antigen: Pertussis toxoid / Tetanus toxoid / Diphtheria toxoid - EMEA-002343-PIP01-18

Vakzine Projekt Management GmbH; ICD10: A36 (diphtheria), ICD10: A37 (whooping cough), ICD10: A35 (other tetanus) / Active booster immunization

Day 60 Opinion

Vaccines / Infectious Diseases

Summary of Committee discussion:

The PDCO adopted a full product-specific waiver for diphtheria toxoid / tetanus toxoid / pertussis toxoid / pertussis filamentous haemagglutinin / pertactin for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'Prevention of infectious diseases caused by Corynebacterium diphtheriae, Clostridium tetani and Bordetella pertussis', based on the grounds of lack of significant benefit over existing products.

2.1.18. Lonafarnib - Orphan - EMEA-002516-PIP01-18

Eiger BioPharmaceuticals Europe Limited; progeroid laminopathies, Hutchinson-Gilford progeria syndrome (HGPS)

Day 60 Opinion

Other

Summary of Committee discussion:

The PDCO noted the Applicant's answers to the Day 30 clarifications requests.

The PDCO therefore adopted a PIP for lonafarnib in the conditions of treatment of Hutchinson-Gilford Progeria syndrome (HGPS) and treatment of progeroid laminopathies.

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. Crizanlizumab - EMEA-C1-002141-PIP01-17-M01

Novartis Europharm Limited; Treatment of sickle cell disease

Day 30 letter

Haematology-Hemostaseology

Summary of Committee discussion:

The partial compliance check has been finalised with a confirmation of compliance of all those studies contained in the agreed paediatric investigation plan as set in the latest EMA Decision P/0060/2019 of 28/02/2019 that were subject of this procedure.

2.2.2. Filgotinib - EMEA-C1-001619-PIP04-17-M01

Gilead Sciences International Ltd.; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis, and juvenile idiopathic arthritis)

Day 30 letter

Immunology-Rheumatology-Transplantation

Summary of Committee discussion:

The PDCO discussed the completed study(ies) and considered that these are compliant with the latest Agency's Decision (P/0371/2018) of 06/12/2018.
The PDCO finalised this partially completed compliance procedure on 29/05/2019.

2.2.3. Lefamulin - EMEA-C1-002075-PIP01-16-M01

Nabriva Therapeutics AG; Treatment of community-acquired pneumonia

Day 30 letter

Infectious Diseases

Summary of Committee discussion:

The PDCO finalised this partially completed compliance procedure on 29 May 2019.

2.2.4. Peginterferon alfa-2a - EMEA-C-000298-PIP01-08-M06

Roche Registration GmbH; Treatment of chronic hepatitis B

Day 30 Opinion

Infectious Diseases

Summary of Committee discussion:

The PDCO took note of outcomes of preceding partial compliance check procedures: EMEA-C1-000298-PIP01-08.
The PDCO adopted on 29/05/2019 an Opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0143/2018) of 07/05/2018.

2.2.5. Rituximab - EMEA-C-000308-PIP01-08-M04

Roche Registration GmbH;

Day 30 Opinion

Oncology

Summary of committee discussion:

The submitted study is compliant with the agreed PIP as set in the latest EMA Decision P/0064/2019 of 22/03/2019.
The PDCO took note of outcomes of preceding partial compliance check procedures: EMEA-C1-000308-PIP01-08-M01
The PDCO adopted on 29/05/2019 an Opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0064/2019) of 22/03/2019.

2.2.6. Efmoroctocog alfa - EMEA-C-001114-PIP01-10-M03

Swedish Orphan Biovitrum AB (publ); Treatment of hereditary Factor VIII deficiency

Day 30 Opinion

Haematology-Hemostaseology

Summary of Committee discussion:

The PDCO discussed the completed PIP studies and considered that these are compliant with the latest Agency's Decision (P/0149/2016) of 13 June 2016.
The PDCO took note of outcomes of preceding partial compliance check procedures: EMEA-C1-001114-PIP01-M02
The PDCO adopted on 29 May 2019 an Opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0149/2016) of 13 June 2016.

2.2.7. Ustekinumab - EMEA-C-000311-PIP01-08-M04

Janssen-Cilag International NV; Treatment of plaque psoriasis

Day 30 Opinion

Immunology-Rheumatology-Transplantation / Dermatology

Summary of Committee discussion:

The PDCO took note of outcomes of preceding partial compliance check procedures:
- EMEA-C1-000311-PIP-08
- EMEA-C3-000311-PIP-08-M02
The PDCO adopted on 29 May 2019 an Opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0003/2016) of 15 January 2016.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Baricitinib - EMEA-001220-PIP03-16-M01

Eli Lilly and Company Limited; Treatment of atopic dermatitis / Treatment of patients with moderate to severe 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 all 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/0291/2018 of 12 September 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.2. Terbinafine (hydrochloride) - EMEA-001259-PIP02-13-M02

Polichem, S.A.; Treatment of onychomycosis

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/0015/2017 of 31/01/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.3. Testosterone - EMEA-001529-PIP02-14-M02

Acerus Biopharma Inc.; Male hypogonadism / Treatment of male hypogonadism

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, 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/0132/2018 of 16 April 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.4. Human normal immunoglobulin for subcutaneous administration - EMEA-001853-PIP01-15-M02

Grifols Therapeutics LLC; Treatment for primary immunodeficiency

Day 60 Opinion

Immunology-Rheumatology-Transplantation

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 delay in PIP completion could be accepted.
The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0380/2017 of 19 December 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. Tocilizumab - EMEA-000309-PIP04-17-M02

Roche Registration GmbH; Cytokine release syndrome / Treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) in adults and paediatric patients 2 years of age and older

Day 60 Opinion

Immunology-Rheumatology-Transplantation

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/0181/2018 of 12/6/2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.6. Eravacycline - EMEA-001555-PIP01-13-M03

Tetraphase Pharmaceuticals, Inc.; Complicated intra-abdominal infection / Complicated intra-abdominal infections

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/0336/2016 of 02/12/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.7. Posaconazole - EMEA-000468-PIP02-12-M05

Merck Sharp & Dohme (Europe), Inc.; Prevention of invasive fungal infections, Treatment of invasive fungal infections / For treatment of invasive fungal infections in the following paediatric patients: -invasive aspergillosis in patients with disease that is refractory to amphotericin B or itraconazole or in patients who are intolerant of these medicinal products;, Treatment of Invasive Aspergillosis, -patients receiving remission-induction chemotherapy for acute myelogenous leukemia (AML) or myelodysplastic syndromes (MDS) expected to result in prolonged neutropenia and who are at high risk of developing invasive fungal infections; - haematopoietic stem cell transplant (HSCT) recipients who are undergoing high-dose immunosuppressive therapy for graft versus host disease and who are at high risk of developing invasive fungal infections.

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 many but not all 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/0041/2018 of 16 February 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. Tedizolid phospate - EMEA-001379-PIP01-12-M04

Merck Sharp & Dohme (Europe) Inc.; Treatment of acute bacterial skin and skin structure infections

Day 60 Opinion

Infectious Diseases

Summary of Committee discussion:

A positive Opinion was adopted on the majority of the modifications proposed by the Applicant.

2.3.9. Balovaptan - EMEA-001918-PIP01-15-M02

Roche Registration GmbH; ICD1O F84: Treatment of autism spectrum disorder / Treatment of core social and communication deficits in people with autism spectrum disorder aged 2 years or older

Day 60 Opinion

Neurology

Summary of Committee discussion:

The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0259/2018 of 15/8/2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.10. Eculizumab - Orphan - EMEA-000876-PIP03-14-M03

Alexion Europe SAS; Neuromyelitis optica spectrum disorders / Treatment of paediatric patients with relapsing neuromyelitis optica spectrum disorders

Day 60 Opinion

Neurology

Summary of Committee discussion:

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0364/2018 of 6 December 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.11. Galcanezumab - EMEA-001860-PIP03-16-M03

Eli Lilly and Company Limited; Prevention of migraine headaches

Day 60 Opinion

Neurology

Summary of Committee discussion:

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0111/2019 of 22/3/2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.12. Satralizumab - humanised anti-IL-6 receptor (IL-6R) monoclonal antibody - - Orphan - EMEA-001625-PIP01-14-M03

Roche Registration GmbH; Treatment of neuromyelitis optica

Day 60 Opinion

Neurology

Summary of Committee discussion:

Overall a positive Opinion on the requested modifications was adopted by the Committee.

2.3.13. Afatinib - EMEA-001596-PIP02-17-M01

Boehringer Ingelheim International GmbH; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms), Treatment of malignant neoplasms of the central nervous system

Day 60 Opinion

Oncology

Summary of Committee discussion:

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0320/2018 of 12 September 2018)
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.14. Durvalumab - EMEA-002028-PIP01-16-M01

AstraZeneca AB; Treatment of malignant neoplasms of haematopoietic and lymphoid tissue, Treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lyphoid tissue) / Treatment of paediatric patients from birth to less than 18 years old with a paediatric haematological malignancy, Treatment of paediatric patients from birth to less than 18 years old with a paediatric solid tumour

Day 60 Opinion

Oncology

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/0082/2018 of 16 March 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. Tremelimumab - EMEA-002029-PIP01-16-M01

AstraZeneca AB; Treatment of malignant neoplasms of haematopoietic and lymphoid tissue, Treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lyphoid tissue) / Treatment of paediatric patients from birth to less than 18 years old with a paediatric haematological

malignancy, Treatment of paediatric patients from birth to less than 18 years old with a paediatric solid tumour

Day 60 Opinion

Oncology

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/0081/2018 of 16 March 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.16. Venetoclax - Orphan - EMEA-002018-PIP02-16-M02

AbbVie Ltd; Treatment of haematopoietic and lymphoid malignant neoplasms, Treatment of solid tumour malignant neoplasms / Treatment of a specific paediatric hematopoietic and lymphoid malignant neoplasm or of a solid malignant neoplasm as agreed by PDCO, in patients from 1 month to 18 years of age

Day 60 Opinion

Oncology / Haematology-Hemostaseology

Summary of Committee discussion:

Overall a positive Opinion on the requested modifications was adopted by the Committee.

2.3.17. Concentrate of proteolytic enzyme enriched in bromelain - Orphan - EMEA-000142-PIP02-09-M08

MediWound Germany GmbH; Treatment of burns of external body surfaces / Removal of eschar in deep partial and/or full thickness burns

Day 60 Opinion

Other

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 some but not all 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/0112/2018 of 11 April 2018).

2.3.18. Lanadelumab - Orphan - EMEA-001864-PIP01-15-M04

Shire Pharmaceuticals Ireland Limited (an indirect wholly owned subsidiary of Shire plc"); Hereditary angioedema / Treatment of hereditary angioedema

Day 60 Opinion

Other

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/0055/2018 of 9 March 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.19. Fentanyl hydrochloride - EMEA-001509-PIP01-13-M02

Incline Therapeutics Europe Ltd.; Treatment of acute pain

Day 60 Opinion

Pain

Summary of Committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, including the responses to the questions raised during the Day 30 discussion, the PDCO acknowledged the product-specific waiver on the grounds that this medicinal product does not represent a significant therapeutic benefit over existing treatments, namely with regards to the specific device in this product. It should be noted that the PDCO still considers the active substance to be of significant therapeutic benefit and that the route of administration with another device/presentation may still be of benefit to the paediatric population.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0335/2016 of 2 December 2016).

2.3.20. Ivacaftor / tezacaftor - Orphan - EMEA-001640-PIP01-14-M05

Vertex Pharmaceuticals (Europe) Ltd.; Cystic fibrosis / Treatment of cystic fibrosis

Day 60 Opinion

Pneumology - Allergology

Summary of Committee discussion:

The PDCO re-discussed the proposed changes, taking into account the supplementary information by the Applicant. The PDCO considered that the proposed changes could be accepted.
The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0069/2018 of 16 March 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.21. Esketamine (hydrochloride) - EMEA-001428-PIP03-15-M01

Janssen-Cilag International NV; Major depressive disorder (MDD)

Day 60 Opinion

Psychiatry

Summary of Committee discussion:

Therefore, 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.
A favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0020/2017 of 31 January 2017) was adopted.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.22. Pneumococcal Polysaccharide Serotype 33F – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 23F – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 22F – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 19F – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 19A – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 18C – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 14 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 9V – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 7F – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 6B – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 6A – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 5 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 4 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 3 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 1 – Diphtheria CRM197 Conjugate - EMEA-002215-PIP01-17-M02

Merck Sharp & Dohme (Europe), Inc.; Prevention of disease caused by Streptococcus pneumoniae / Active immunisation for the prevention of invasive disease, pneumonia and acute otitis media caused by Streptococcus pneumoniae in infants, children and adolescents from 6 weeks to less than 18 years of age

Day 60 Opinion

Vaccines

Summary of Committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, and the response provided to the issue raised at Day 30, 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/0347/2018 of 16/11/2018)
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.23. Recombinant Influenza Hemagglutinin-strain B (Yamagata lineage) / Recombinant Influenza Hemagglutinin-strain B (Victoria lineage) / Recombinant Influenza Hemagglutinin-strain A (H3N2 subtype) / Recombinant Influenza Hemagglutinin-strain A (H1N1 subtype) - EMEA-002418-PIP01-18-M01

Sanofi Pasteur; Prevention of influenza infection

Day 30 Opinion

Vaccines

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/0088/2019 of 23/03/2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.4. Opinions on Re-examinations

No items

2.5. Opinions on Review of Granted Waiver

No items

2.6. Finalisation and adoption of Opinions

No items

2.7. Partial Compliance Checks completed by EMA

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

2.7.1. Mirikizumab - EME-C1-002208-PIP01-17

Eli Lilly and Company; Treatment of psoriasis

Day 1 letter

Dermatology / Gastroenterology-Hepatology

Summary of Committee discussion:

The compliance was confirmed with no need for discussion by the PDCO.

2.7.2. Isatuximab - EMEA-C1-002205-PIP01-17-M01

Sanofi-Aventis Recherche & Développement; Treatment of malignant neoplasms of the haematopoietic and lymphoid tissue

Day 1 letter

Oncology

Summary of Committee discussion:

The submitted study is hereby confirmed to be compliant as set out in the EMA's Decision

(P/0193/2019) of 13 May 2019.

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. EMEA-002329-PIP01-18

Treatment of dermatitis and eczema

Day 90 discussion

Dermatology

3.1.2. EMEA-002350-PIP01-18

Treatment of psoriasis / Treatment of moderate to severe plaque psoriasis in paediatric patients 6 years of age and older

Day 90 discussion

Dermatology

Treatment of atopic dermatitis / Treatment of patients with moderate-to-severe atopic dermatitis

Day 90 discussion

Dermatology

3.1.4. Oxalobacter formigenes Strain HC-1 - Orphan - EMEA-000370-PIP02-18

OxThera AB; ICD10-E72.53 (Hyperoxaluria) / Treatment of primary hyperoxaluria

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Uro-nephrology

3.1.5. Humanized anti-CD19, Fc engineered, monoclonal antibody - Orphan - EMEA-002414-PIP01-18

Xencor, Inc.; Immunoglobulin G4-related disease / Treatment of adults, adolescents and children (> 23 months of age) with immunoglobulin G4-related disease

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.6. Vedolizumab - EMEA-000645-PIP03-18

ICD-9-CM 279.51 / ICD-10-CM D89.810 - Other disorders involving the immune

mechanism, not elsewhere classified: acute graft-versus-host disease

Day 90 discussion

Immunology-Rheumatology-Transplantation / Gastroenterology-Hepatology

3.1.7. Bulevirtide - Orphan - EMEA-002399-PIP01-18

MYR GmbH; Chronic hepatitis D infection

Day 90 discussion

Infectious Diseases

3.1.8. Recombinant adeno-associated viral vector serotype 2 carrying the gene for the human aromatic L-amino acid decarboxylase protein - Orphan - EMEA-002435-PIP01-18

PTC Therapeutic International imited; Aromatic L-amino acid decarboxylase (AADC) deficiency / Treatment of aromatic L-amino acid decarboxylase (AADC) deficiency

Day 90 discussion

Neurology

3.1.9. EMEA-002446-PIP01-18

Ichthyosis associated with Sjögren-Larsson syndrome (SLS) / Treatment of ichthyosis associated with Sjögren-Larsson syndrome (SLS)

Day 90 discussion

Other / Endocrinology-Gynaecology-Fertility-Metabolism / Dermatology

3.1.10. EMEA-002327-PIP02-19

Treatment and prevention of oral mucositis

Day 60 discussion

Dermatology

3.1.11. Tezepelumab - EMEA-002579-PIP01-18

Atopic dermatitis

Day 60 discussion

Dermatology

3.1.12. EMEA-002552-PIP01-19

Treatment of non-alcoholic steatohepatitis (NASH)

Day 60 discussion

Gastroenterology-Hepatology

3.1.13. Hematopoietic stem cells modified with a lentiviral vector encoding for the human Beta 2 Integrin/CD18 gene - Orphan - EMEA-002562-PIP01-19

Rocket Pharmaceuticals, Inc.; Severe leukocyte adhesion deficiency type I (LAD-I)

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.14. Obinutuzumab - Orphan - EMEA-001207-PIP02-19

Roche Registration GmbH; Systemic lupus erythemathosus

Day 60 discussion

Immunology-Rheumatology-Transplantation

Loxo Oncology, Inc.; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms). / Treatment of paediatric patients from ≥6 months to <18 years of age with RET-altered, locally advanced or metastatic, solid tumours or primary central nervous system (CNS) tumours.

Day 60 discussion

Oncology

3.1.16. Belantamab mafodotin - Orphan - EMEA-002468-PIP03-19

GlaxoSmithKline Trading Services; Treatment of mature B-cell neoplasms / Treatment for adult patients with BCMA-expressing mature B-cell neoplasms

Day 60 discussion

Oncology

3.1.17. Carfilzomib - Orphan - EMEA-001806-PIP04-19

Amgen Europe BV; Treatment of acute lymphoblastic leukemia (ALL) / Treatment of pediatric patients aged 1 year or older and young adult patients up to 21 years of age with bone marrow relapse of T-cell ALL treated with at least 1 prior therapy or B-cell ALL treated with at least 2 prior therapies, with or without extramedullary disease

Day 60 discussion

Oncology / Haematology-Hemostaseology

3.1.18. Atropine sulphate - EMEA-002538-PIP01-18

Treatment of myopia

Day 60 discussion

Ophthalmology

3.1.19. Selonsertib - EMEA-001868-PIP04-18

Chronic kidney disease / Treatment of patients with progressive chronic kidney disease (CKD) resulting from congenital anomalies of the kidney and urinary track (CAKUT) aged 3 to less than 18 years

Day 60 discussion

Uro-nephrology

3.1.20. Remimazolam - EMEA-001880-PIP02-19

Sedation during medical procedures / General anaesthesia and post-operative sedation up to 24h, Sedation in the intensive care unit (ICU), Sedation for short procedures

Day 30 discussion

Anaesthesiology

3.1.21. EMEA-002568-PIP01-19

Psoriasis / Treatment of moderate to severe chronic plaque-type psoriasis who are candidates for systemic therapy

Day 30 discussion

Dermatology

3.1.22. Botulinum toxin type A - EMEA-002521-PIP01-18

Muscle-induced wrinkles

Day 30 discussion

Dermatology

3.1.23. Hydrogen peroxide - EMEA-001884-PIP03-18

Treatment of common warts (verrucae vulgaris) / Topical treatment to remove common warts (verrucae vulgaris)

Day 30 discussion

Dermatology

3.1.24. Recombinant humanized anti-blood dendritic cell antigen 2 (BDCA2) monoclonal antibody - EMEA-002555-PIP01-19

Cutaneous lupus erythematosus

Day 30 discussion

Dermatology

3.1.25. EMEA-002577-PIP01-19

Prostate-specific membrane antigen (PSMA)-expressing metastatic prostate cancer

Day 30 discussion

Diagnostic / Oncology

3.1.26. Human chorionic gonadotrophin - EMEA-002547-PIP01-19

Infertility / Assisted reproductive technology (ART) program such as in vitro fertilisation, anovulatory or oligo-ovulatory women

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.27. Mifepristone - EMEA-001437-PIP02-19

Endometriosis

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.28. Norethisterone acetate / estradiol / relugolix - EMEA-002428-PIP02-18

Endometriosis / treatment of symptoms associated with endometriosis

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.29. Cilofexor - EMEA-002554-PIP01-19

Treatment of primary sclerosing cholangitis (PSC), (DB96.2)

Day 30 discussion

Gastroenterology-Hepatology

3.1.30. Dupilumab - EMEA-001501-PIP04-19

Treatment of eosinophilic esophagitis

Day 30 discussion

Gastroenterology-Hepatology

3.1.31. CD34+enriched cells from patients with Fanconi anemia subtype A (FA-A) transduced ex vivo with lentiviral vector carrying the FANCA gene - Orphan - EMEA-002578-PIP01-19

Rocket Pharmaceuticals, Inc.; Treatment of Fanconi anemia subtype A

Day 30 discussion

Haematology-Hemostaseology

3.1.32. Probenecid / sulopenem etzadroxil - EMEA-002602-PIP01-19

Urinary tract infections, abdominal and gastrointestinal infections / uncomplicated urinary tract infections, complicated intra-abdominal infections, complicated urinary tract infections

Day 30 discussion

Infectious Diseases

3.1.33. Sulopenem - EMEA-002478-PIP01-18

Urinary tract infections, abdominal and gastrointestinal infections / uncomplicated urinary tract infections, complicated intra-abdominal infections, complicated urinary tract infections

Day 30 discussion

Infectious Diseases

3.1.34. Istradefylline - EMEA-002540-PIP01-18

Parkinson's disease

Day 30 discussion

Neurology

3.1.35. EMEA-002575-PIP01-19

Treatment of lung carcinoma (small cell and non-small cell carcinoma)

Day 30 discussion

Oncology

3.1.36. EMEA-002573-PIP01-19

Treatment of lung carcinoma (small cell and non-small cell carcinoma)

Day 30 discussion

Oncology

3.1.37. Orphan - EMEA-002499-PIP02-19

MorphoSys AG; Diffuse large B-cell lymphoma

Day 30 discussion

Oncology

3.1.38. Pracinostat - Orphan - EMEA-002567-PIP01-19

Helsinn Birex Pharmaceuticals limited; Acute myeloid leukemia / ICD10 code C92.0

Day 30 discussion

Oncology

3.1.39. Ciclosporin - EMEA-002491-PIP02-19

Treatment of dry eye disease

Day 30 discussion

Ophthalmology

3.1.40. EMEA-002559-PIP01-19

Haemolytic disease of the foetus and newborn (HDFN)

Day 30 discussion

Other

3.1.41. Budesonide - Orphan - EMEA-002500-PIP01-18

Calliditas Therapeutics AB; Primary IgA nephropathy

Day 30 discussion

Uro-nephrology

3.2. Discussions on Compliance Check

No items

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Apixaban - EMEA-000183-PIP01-08-M07

Bristol-Myers Squibb / Pfizer EEIG; Prevention of arterial thromboembolism, Prevention of venous thromboembolism / Prevention of TE in paediatric patients with cardiac disease, Prevention of venous thromboembolism (VTE) in paediatric subjects 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.

Day 30 discussion

Cardiovascular Diseases

3.3.2. Fluciclovine (^{18}F) - Orphan - EMEA-001644-PIP02-14-M01

Blue Earth Diagnostics Ireland Ltd; Diagnosis of amino acid metabolism in solid malignant tumours / diagnosis of primary and recurrent brain tumours

Day 30 discussion

Diagnostic / Oncology

3.3.3. Saxagliptin - EMEA-000200-PIP01-08-M08

AstraZeneca AB; E11 Type 2 Diabetes / Treatment of Type 2 Diabetes

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

Bristol-Myers Squibb Pharma EEIG; Prevention of rejection of transplanted kidney / In combination with corticosteroids and a mycophenolic acid (MPA), is indicated for prophylaxis of graft rejection in paediatric patients at least 12 years of age and with a stable renal transplant for at least 6 months, who convert to a CNI-free maintenance immunosuppressive regimen.

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.5. Ixekizumab - EMEA-001050-PIP02-18-M01

Eli Lilly Nederland B.V.; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis) / Children with juvenile idiopathic arthritis subtypes of enthesitis-related arthritis (including JoAS) and juvenile psoriatic arthritis.

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.6. Recombinant human monoclonal antibody to GM-CSF - EMEA-001882-PIP02-16-M01

GlaxoSmithKline Trading Services Limited; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis) / Treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 1 year of age and older, Treatment of active polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years of age and older

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.7. Delamanid - Orphan - EMEA-001113-PIP01-10-M06

Otsuka Pharmaceutical Development & Commercialisation Europe GmbH; Treatment of multi drug resistant tuberculosis

Day 30 discussion

Infectious Diseases

3.3.8. Eslicarbazepine acetate - EMEA-000696-PIP02-10-M06

BIAL - Portela & Ca, SA; Treatment of epilepsy with partial onset seizures / Treatment of

epilepsy with partial onset seizures with eslicarbazepine acetate (ESL) as adjunctive therapy /Treatment of epilepsy with partial onset seizures with eslicarbazepine acetate (ESL) as monotherapy

Day 30 discussion

Neurology

3.3.9. Eteplirsen - Orphan - EMEA-001722-PIP01-14-M02

Sarepta Therapeutics Ireland Limited; Duchenne muscular dystrophy

Day 30 discussion

Neurology

3.3.10. Lasmiditan - EMEA-002166-PIP01-17-M02

Eli Lilly and Company Limited; Migraine with and without aura

Day 30 discussion

Neurology

3.3.11. Recombinant human tripeptidyl peptidase 1 (rhTPP1) - Orphan - EMEA-001362-PIP01-12-M04

BioMarin International Limited; neuronal ceroid lipofuscinosis type 2 (CLN2) disease / Treatment of neuronal ceroid lipofuscinosis type 2 (NCL2)

Day 30 discussion

Neurology

3.3.12. Bosutinib - EMEA-000727-PIP01-09-M03

Pfizer Europe MA EEIG; Treatment of chronic myeloid leukemia (CML) / Treatment of chronic, accelerated or blast phase CML with resistance or intolerance to prior tyrosine kinase inhibitor (TKI) therapy, Treatment of newly-diagnosed chronic phase Ph+ CML

Day 30 discussion

Oncology

3.3.13. Daunorubicin (liposomal formulation) / cytarabine (liposomal formulation) - Orphan - EMEA-001858-PIP02-16-M03

Jazz Pharmaceuticals Ireland Limited; Acute myeloid leukaemia / Treatment of acute myeloid leukaemia

Day 30 discussion

Oncology

3.3.14. Ixazomib - Orphan - EMEA-001410-PIP02-17-M02

Takeda Pharm A/S; Treatment of lymphoid malignancies (excluding multiple myeloma) / Treatment of multiple myeloma (MM) / Treatment of adult patients with newly diagnosed multiple myeloma (NDMM) / Treatment of paediatric patients diagnosed with relapsed precursor B-ALL (Acute lymphoblastic leukemia) or T-ALL

Day 30 discussion

Oncology

3.3.15. Selumetinib - Orphan - EMEA-001585-PIP01-13-M03

AstraZeneca AB; Treatment of thyroid cancer, Treatment of neurofibromatosis Type 1 (NF1)/ Selumetinib in combination with adjuvant radioactive iodine therapy is indicated for the treatment of adolescents newly diagnosed with differentiatd thyroid cancer who are at high risk of primary treatment failure, Selumetinib is indicated for the treatment of inoperable NF1 related plexiform neurofibroma in children and adolescents

Day 30 discussion

Oncology

3.3.16. Palonosetron / fosnetupitant - EMEA-001198-PIP03-17-M02

Helsinn Birex Pharmaceuticals Limited; Prevention of chemotherapy-induced nausea and vomiting

Day 30 discussion

Other

3.3.17. Octenidine (dihydrochloride) - EMEA-001514-PIP01-13-M01

Cassella-med GmbH & Co. KG; Treatment of upper respiratory tract infections / Treatment of sore-throat due to infectious pharyngitis

Day 30 discussion

Oto-rhino-laryngology

3.3.18. Reslizumab - EMEA-001202-PIP02-13-M03

Teva Pharmaceuticals Europe; Treatment of asthma / Add-on treatment to reduce exacerbations, relieve symptoms and improve lung function in paediatric patients from 6 to less than 18 years of age with inadequately controlled severe asthma who have a blood eosinophil count greater than equal to 300 micro liter

Day 30 discussion

Pneumology - Allergology

3.3.19. Tezepelumab - EMEA-001613-PIP01-14-M03

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

3.3.20. Mirabegron - EMEA-000597-PIP02-10-M07

Astellas Pharma Europe B.V.; Treatment of idiopathic overactive bladder / Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in patients with overactive bladder syndrome

Day 30 discussion

Uro-nephrology

4. Nominations

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 2019 for Nomination of Rapporteur and Peer reviewer

Summary of Committee discussion:

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

Summary of Committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers

4.3. Nominations for other activities

No items

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

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

5.1. New Scientific Advice

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

5.2. Ongoing Scientific Advice

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

5.3. Final Scientific Advice (Reports and Scientific Advice letters)

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

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. Anti-vascular endothelial growth factor/ angiopoietin-2 nanobody - EMEA-06-2019

Boehringer Ingelheim International GmbH; All classes of medicinal products for treatment of age-related macular degeneration and diabetic macular oedema/anti-vascular endothelial growth factor/ angiopoietin-2 nanobody indicated for treatment of patients with wet age-related macular degeneration and diabetic macular edema

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: retinopathy of prematurity.

6.1.2. Enzalutamide - Xtandi - EMEA-07-2019

Astellas Pharma Europe B.V.; The classes of androgen receptor modulator / oestrogen receptor modulator / growth and sex hormone as well as their releasing or inhibiting factors, and of sex hormone-metabolism modulator medicinal products for treatment of breast malignant neoplasms, prostate malignant neoplasms and neuroendocrine malignant neoplasms / Treatment of adult men with metastatic hormone-sensitive prostate cancer in combination with androgen deprivation therapy

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: none identified at this stage.

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

7.1.1. Fragment crystallisable (Fc)- and complementarity-determining regions (CDR)-modified humanised monoclonal antibody against C5 - EMEA-001943-PIP01-16-M01

Alexion Pharma GmbH; Treatment of atypical haemolytic uremic Syndrome

Proposed indication: Treatment of patients with complement-mediated thrombotic microangiopathy (TMA)

Summary of Committee discussion:

The Applicant requested confirmation that the planned indication in adults "treatment of patients with complement-mediated thrombotic microangiopathy (TMA)" would be covered by the wording of the condition of the agreed PIP, namely "treatment of atypical haemolytic uremic syndrome (aHUS)". The PDCO agreed that the classification surrounding this disorder is challenging and has been evolving. However, the Committee mentioned that complement-mediated TMA might not only be seen in patients with aHUS but also as a result of conditions other than aHUS. Therefore, the Committee tended to disagree with the Applicant's position. The Applicant may provide further justification to corroborate their position that complement-mediated TMA would be completely covered by aHUS, in which case the PDCO would re-discuss the issue at its next meeting.

Alternatively, a request for modification of the agreed PIP for aHUS could be considered, in order to add the condition of complement-mediated TMA. In this case it would need to be discussed if any additional measures would need to be added to the PIP.

8. Annual reports on deferrals

The members of the PDCO took note of the products listed in the Annex B.

9. Organisational, regulatory and methodological matters

9.1. Mandate and organisation of the PDCO

9.1.1. Update on PDCO member(s)/alternate(s) mandate status

No items

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 PDCO members were informed about the final CHMP Opinions on medicinal products

with recommended paediatric indications adopted in April 2019. These included Dovato (dolutegravir / lamivudine), Esperoct (turoctocog alfa pegol) and Xromi (hydroxycarbamide).

The list of procedures with paediatric indications to be evaluated by the CHMP, starting in April 2019, was presented to the PDCO members.

9.2.2. Concept paper on the need for revision of the guideline on the investigation of medicinal products in the term and preterm neonate

Summary of Committee discussion:

The concept paper was adopted by the Committee.

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 (NCWG) evaluation and discussion.

9.3.2. Formulation Working Group

PDCO member: Brian Aylward

Summary of Committee discussion:

The Chair of the Formulation Working Group (FWG) identified the products which will require Formulation Working Group evaluation and discussion.

9.4. Cooperation within the EU regulatory network

No items

9.5. Cooperation with International Regulators

No items

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

9.6.1. 4th Accelerate Paediatric Strategy forum on acute myeloid leukaemia (AML)

Summary of Committee discussion:

The main topics and outcomes of the 4th Accelerate Paediatric Strategy forum on acute myeloid leukaemia were presented to the Committee.

9.7. PDCO work plan

No items

9.8. Planning and reporting

No items

10. Any other business

No items

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of Committee discussion:

The group discussed paediatric indications currently under assessment at CHMP and related to PIP procedures.

11.1.2. Neonatology

Summary of Committee discussion:

The Neonatology Breakout session discussed the next steps in the Guideline revision process.

11.1.3. Inventory

Summary of Committee discussion:

The inventory group breakout session continued discussion on how to best assess unmet needs for some of the procedures discussed during the plenary meeting and reflect the discussion in the minutes.

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 23-26 April 2019 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	When chairing the meeting: To be replaced for discussions, final deliberations and voting When not chairing the meeting: No participation in final deliberations and voting	Recombinant human monoclonal antibody to GM-CSF (GSK3196165) - EMEA-001882-PIP02-16-M01 GlaxoSmithKline Trading Services Limited Belantamab mafodotin - Orphan - EMEA-002468-PIP03-19 GlaxoSmithKline Trading Services;
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Georgios Savva	Member	Cyprus	No interests declared	
Tereza Bazantova	Member	Czech Republic	No interests declared	
Petra Dominikova	Alternate	Czech Republic	No interests declared	
Kirstine Moll Harboe	Member	Denmark	No interests declared	
Irja Lutsar	Member	Estonia	No interests declared	
Jana Lass	Alternate	Estonia	No interests declared	
Ann Marie Totterman	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	
Yuansheng Sun	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	
Dina Apele-Freimane	Member	Latvia	No restrictions applicable to this meeting	
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	
Maria Jesus Fernández Cortizo (via TC)	Alternate	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	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No interests declared	
Jorrit Gerritsen	Alternate	Healthcare Professionals' Representative	No interests declared	
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Catherine Cornu	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Doina Plesca	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Günter Karl-Heinz Auerswald	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Paola Baiardi	Alternate	Patients' Organisation Representative	No restrictions applicable to this meeting	
Michal Odermarsky	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Roel Bolt	Expert - in person*	Netherlands	No interests declared	
María Estela Moreno Martín	Expert - in person*	Spain	No interests declared	

For CMDh: Ad hoc experts* and a representative from the European Commission attended the meeting
Meeting run with support from relevant EMA staff
* Experts were only evaluated against the agenda topics or activities they participated in

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/