18 July 2017
EMA/PDCO/396495/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes for the meeting on 20-23 June 2017

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

20 June 2017, 14:00 - 19:00, room 3A

21 June 2017, 08:30 - 19:00, room 3A

22 June 2017, 08:30 - 19:00, room 3A

23 June 2017, 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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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 was adopted with amendments.

1.3. Adoption of the minutes

The minutes of the May 2017 PDCO plenary meeting were adopted with amendments 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. Methacholine Chloride - EMEA-002120-PIP01-17

MWK Healthcare Ltd; Diagnosis of asthma

Day 60 opinion

Diagnostic

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee at Day 60, the PDCO recommends granting a waiver on its own motion for methacholine chloride for all subsets of the paediatric population (0 to 18 years of age) in the condition of Diagnosis of asthma on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as the needs are already covered.

2.1.2. tocilizumab - EMEA-000309-PIP04-17

Roche Registration Limited; Treatment of SSc (ICD 10-M34)/scleroderma and associated disorders (MedDRA). / Treatment of juvenile Systemic Sclerosis (jSSc) in children 5 years of age and older.

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The applicant has responded satisfactorily to the outstanding issue raised on D30 and a positive opinion on this PIP was adopted on D60.

2.1.3. Fc- and CDR-modified humanised monoclonal antibody against C5 - Orphan - EMEA-002077-PIP01-16

Alexion Europe SAS; Treatment of Paroxysmal Nocturnal Haemoglobinuria

Day 120 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO adopted a positive opinion.

2.1.4. Daunorubicin (liposomal combination) / Cytarabine (liposomal combination) - Orphan - EMEA-001858-PIP02-16

Jazz Pharmaceuticals Ireland Limited; Acute myeloid leukemia

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed on 22/06/2017 the application 1 (a liposomal combination of cytarabine and daunorubicin) taking into account the further clarification provided by the applicant after the D90 discussion.
All the pending issues were considered solved.
In conclusion, the PDCO recommended granting a paediatric investigation plan for liposomal combination of cytarabine and daunorubicin, a waiver and a deferral.

2.1.5. Venetoclax - Orphan - EMEA-002018-PIP02-16

AbbVie Ltd; Treatment of haematopoietic and lymphoid malignant neoplasms, Treatment of solid tumour malignant neoplasms / As monotherapy, or in combination with chemotherapy, for the treatment of relapsed or refractory NHL patients < 18 years of age, who have progressed following autologous stem cell transplantation or who are ineligible for transplantation, As monotherapy or in combination for the treatment of patients with relapsed or refractory neuroblastoma < 18 years of age, As monotherapy, or in combination with chemotherapy, for the treatment of relapsed or refractory ALL in the third line setting in patients < 18 years of age, As monotherapy, or in combination with chemotherapy, for the treatment of relapsed or refractory AML in patients < 18 years of age

Day 120 opinion

Oncology / Haematology-Hemostaseology

Summary of committee discussion:

At their June 2017 meeting, taking into account the further information received from the applicant the PDCO adopted a positive opinion for venetoclax for the conditions treatment of malignant neoplasms of the haematopoietic and lymphoid tissue and treatment of solid malignant tumours (identical measures).

2.1.6. Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1) - EMEA-002068-PIP01-16

Seqirus UK Limited; Prevention of influenza

Day 120 opinion

Vaccines

Summary of committee discussion:

Since thus all the issues raised at Day 90 were satisfactorily resolved, PDCO granted a positive opinion on the paediatric plan proposed by the applicant for this cell-based quadrivalent inactivated influenza vaccine.

2.1.7. 5,7-Dihydroxy-2-[3-hydroxy-4-methoxy-2-(2-methyl-2-propenyl)phenyl]-6,8-bis(2-methyl-2-propenyl)-4H-chromen-4-one - EMEA-002148-PIP01-17

Ilkos Therapeutic Inc; Treatment of venous and mixed (venous/arterial) leg ulcers

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 5, 7-dihydroxy-2-[3-hydroxy-4-

methoxy-2-(2-methyl-2-propenyl) phenyl]-6, 8-bis (2-methyl-2-propenyl)-4H-chromen-4-one for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of venous and mixed (venous/arterial) leg ulcers.

2.1.8. macitentan - Orphan - EMEA-001032-PIP02-17

Actelion Registration Ltd.; Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

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 macitentan for all subsets of the paediatric population (0 to less than 18 years of age) in the condition of Chronic Thromboembolic Pulmonary Hypertension (CTEPH).
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.

2.1.9. Empagliflozin - EMEA-000828-PIP05-17

Boehringer Ingelheim International GmbH; Prevention of cardiovascular events in patients with chronic heart failure

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism / Cardiovascular Diseases

Summary of committee discussion:

Based on the assessment of this application and discussion on the applicant’s responses the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for empagliflozin for all subsets of the paediatric population (0 to 18 years of age) in the condition of Prevention of cardiovascular events in patients with chronic heart failure.

2.1.10. H-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-Lys-Leu-Ser-Ser-Ile-Glu-Ser-Asp-Val-OH (YGRKKRRQRRRKLSSIESDV) - EMEA-002108-PIP01-16

NoNO Inc.; Acute Ischemic Stroke (AIS) in adult subjects with a large intracranial arterial occlusion, a small ischemic core, and good collaterals.

Day 60 opinion

Neurology

Summary of committee discussion:

The PDCO has re-discussed the application including the additional information received since Day 30 and concluded that the applicant’s position is well justified and agreeable. 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 H-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-Lys-Leu-Ser-Ser-Ile-Glu-Ser-Asp-Val-OH (YGRKKRRQRRRKLSSIESDV) for all subsets of the paediatric population (0 to 18 years of age) in the condition Treatment of acute ischaemic stroke.
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. Recombinant humanized anti-alpha-synuclein IgG1 monoclonal antibody - EMEA-002137-PIP01-17

Roche Registration Limited; treatment of Parkinson's disease (in adults)

Day 60 opinion

Neurology

Summary of committee discussion:

The committee's view expressed on day 30 was re-discussed and endorsed.
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 Recombinant humanized anti-alpha-synuclein IgG1 monoclonal antibody for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of Parkinson's disease on the grounds, that the medicinal product is likely to be ineffective in all of the paediatric population.

2.1.12. OSIMERTINIB MESYLATE - EMEA-002125-PIP01-17

AstraZeneca AB; Treatment of lung carcinoma (small cell and non-small cell carcinoma)

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO's views expressed at D30 were confirmed. The PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for osimertinib (as mesylate for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of lung carcinoma (small cell and non-small cell carcinoma) based on the ground that the disease or condition for which the specific medicinal product is intended 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.

2.1.13. Pexastimogene devacirepvec - Orphan - EMEA-002124-PIP01-17

Transgene S.A.; Treatment of hepatocellular carcinoma. (MedDra PT: 10073071)

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO confirmed all points and tentative conclusions taken during the Day 30 discussion.

Committee agreed with granting a waiver for Pexastimogene devacirepvec for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of hepatocellular carcinoma on the grounds that the product could be unsafe 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.

2.1.14. daxibotulinumtoxinA - EMEA-002149-PIP01-17

Revance Therapeutics Inc; Treatment for temporary improvement in the appearance of moderate to severe glabellar lines with corrugator and/or procerus muscle activity in adults.

Day 60 opinion

Other

Summary of committee discussion:

A positive opinion was adopted on D60.
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 daxibotulinumtoxinA for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of glabellar lines.

2.1.15. Diclofenac sodium - EMEA-002132-PIP01-17

Dimethaid (UK) Limited; Symptomatic relief of pain associated with osteoarthritis, Symptomatic relief of mild to moderate pain and inflammation / Indicated for the symptomatic relief of pain associated with osteoarthritis in superficial joints, including the knee., For the local symptomatic relief of mild to moderate pain and inflammation following acute blunt trauma of small and medium-sized joints and periarticular structures, such as trauma of the tendons, ligaments, muscles and joints e.g. due to sprains and strains.

Day 60 opinion

Pain

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 Diclofenac sodium for all subsets of the paediatric population (0 to 18 years of age) in the conditions Treatment of pain and Treatment of inflammation.
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.

2.2. 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. Raltegravir - EMEA-C-000279-PIP01-08-M05

Merck Sharp & Dohme (Europe) Inc., Treatment of Human Immunodeficieny Virus (HIV-1) infection

Opinion adopted via written procedure on 19 June 2017

Infectious Diseases

Summary of committee discussion:

The PDCO noted the adoption of the revised opinion.

2.2.2. Meropenem trihydrate / Vaborbactam - EMEA-C1-001731-PIP01-14

Rempex Pharmaceuticals, a wholly owned subsidiary of The Medicines Company; Treatment of Gram-negative bacterial infections

Day 30 letter

Infectious Diseases

Summary of committee discussion:

The completed non-clinical studies were checked for compliance.
The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0229/2015) of 22 October 2015.
The PDCO finalised on 23 June 2017 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.

2.2.3. Meropenem trihydrate / Vaborbactam - EMEA-C1-001740-PIP01-14

Rempex Pharmaceuticals, a wholly owned subsidiary of The Medicines Company; Treatment of Gram-negative bacterial infections

Day 30 letter

Infectious Diseases

Summary of committee discussion:

The completed non-clinical studies were checked for compliance.
The PDCO discussed the completed studies, and considered that these are compliant with the latest Agency's Decision (P/0230/2015) of 22 October 2015.
The PDCO finalised on 23 June 2017 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. Tofacitinib - EMEA-C1-000576-PIP03-12

Pfizer Limited; Treatment of Ulcerative Colitis

Day 60 letter

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The completed studies were checked for compliance.
The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0195/2014) of 8 August 2014.
The PDCO finalised on 21 June 2017 this partially completed compliance procedure.

2.2.5. Human normal immunoglobulin - EMEA-C1-001797-PIP01-15

Octapharma Pharamzeutika Produktionsges.m.b.H; Treatment of primary immunodeficiency

Day 60 letter

Immunology-Rheumatology-Transplantation / Haematology-Hemostaseology

Summary of committee discussion:

The completed studies were checked for compliance.

The PDCO discussed the completed studies.
The PDCO finalised this negative compliance check on 21 June 2017.

2.2.6. Ibrutinib - EMEA-C1-001397-PIP03-14-M02

Janssen-Cilag International N.V.; Treatment of mature B-cell neoplasm

Day 60 letter

Oncology

Summary of committee discussion:

The PDCO considered the study compliant with the latest Agency's Decision (P/0100/2017) of 11 April 2017.
The PDCO finalised on 23 June 2017 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.

2.2.7. Ataluren - EMEA-C2-000115-PIP01-07-M08

PTC Therapeutics International Limited; Treatment of dystrophinopathy

Day 30 letter

Neurology

Summary of committee discussion:

The PDCO discussed the completed studies.
The committee considered that these are compliant with the latest Agency's Decision (P/0283/2016) of 04 November 2016.
The PDCO finalised on 23 June 2017 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.

2.2.8. nivolumab - EMEA-C1-001407-PIP02-15-M01

Bristol-Myers Squibb Pharma EEIG; Treatment of malignant neoplasms of the central nervous system

Day 30 letter

Oncology

Summary of committee discussion:

The ongoing study was checked for compliance.
The PDCO finalised on 23 June 2017 this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be initiated until this date.

2.2.9. Split influenza virus, inactivated containing antigen equivalent to A/H3N2-like strain / Split influenza virus, inactivated containing antigen equivalent to B-like strain (B/Yamagata lineage) / Split influenza virus, inactivated containing antigen equivalent to B-like strain (B/Victoria lineage) / Split influenza virus, inactivated containing antigen equivalent to A/H1N1-like strain - EMEA-C-001254-PIP01-11-M02

Sanofi Pasteur SA; Prevention of influenza infection

Day 30 opinion

Vaccines

Summary of committee discussion:

The PDCO discussed the compliance request on 22 June 2017.
The completed study was checked for compliance.
The PDCO adopted on 23 June 2017 an opinion confirming the compliance of all studies in

the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0129/2017) of 8 May 2017.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Apremilast - Orphan - EMEA-000715-PIP05-13-M01

Celgene Europe Limited; Treatment of Behcets Disease / Treatment of patients with active oral ulcers (with or without genital ulcers) associated with Behcets Disease, who are candidates for systemic therapy

Revised opinion adopted via written procedure on 14 June 2017

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO noted the adoption of the revised opinion.

2.3.2. apixaban - EMEA-000183-PIP01-08-M05

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 PEG L-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:

The committee confirmed the main conclusions from the Day 30 discussion.
The PDCO discussed the clarification provided by the applicant.
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/0254/2016 of 19/08/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.3. Allantoin - Orphan - EMEA-001590-PIP01-13-M04

Scioderm, Inc.; Treatment of epidermolysis bullosa

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/0361/2016 of 21 December 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.4. Asfotase alfa - Orphan - EMEA-000987-PIP01-10-M03

Alexion Europe SAS; Treatment of hypophosphatasia

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

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/0176/2014 of 2 July 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. Canagliflozin - EMEA-001030-PIP01-10-M07

Janssen-Cilag International NV; Treatment of Type 2 Diabetes Mellitus

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

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/0217/2016 of 12/08/2016) on 23 June 2017.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.6. Liraglutide - EMEA-000128-PIP01-07-M08

Novo Nordisk A/S; Treatment of type 2 diabetes mellitus

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

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/0176/2016 of 01/07/2016) on 23 June 2017.

2.3.7. semaglutide - EMEA-001441-PIP02-15-M01

Novo Nordisk; Type 2 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 for semaglutide for the treatment of type 2 diabetes mellitus, 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/0217/2016 of 12/08/2016) on 23 June 2017.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. Sodium zirconium cyclosilicate - EMEA-001539-PIP01-13-M02

AstraZeneca AB; Treatment of Hyperkalaemia

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

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/0296/2016 of 4 November 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.9. sotagliflozin - EMEA-001517-PIP01-13-M01

sanofi-aventis R&D; Type 2 diabetes mellitus / Treatment of type 2 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 for sotagliflozin for the treatment of type 2 diabetes mellitus, 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/0287/2014 of 28/10/2014) on 23 June 2017.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.10. sotagliflozin - EMEA-001517-PIP02-14-M01

sanofi-aventis R&D; Treatment of type 1 diabetes mellitus

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO re-discussed the request modification for sotaglifozin for the treatment of type 1 diabetes taking into account the applicant's clarifications and the revised studies submitted after D30.

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0150/2015 of 10 July 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.11. Obeticholic Acid (6 alpha-ethylchenodeoxycholic acid) - Orphan - EMEA-001304-PIP02-13-M03

Intercept Pharma Ltd.; Primary Biliary Cirrhosis (PBC) / Biliary Atresia

Day 60 opinion

Gastroenterology-Hepatology

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/0310/2015 of 21 December 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.12. Coagulation Factor VIIa (Recombinant) - EMEA-001203-PIP02-14-M02

LFB SA; Treatment of congenital coagulation disorders, Treatment of acquired haemophilia / Treatment of bleeding and prevention of bleeding in those undergoing surgery or invasive procedures in patients with haemophilia A or B with inhibitors to Factors VIII or IX, Treatment of bleeding and prevention of bleeding in those undergoing surgery or invasive procedures in patients with acquired haemophilia

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan for Coagulation Factor VIIa (Recombinant) for the treatment of congenital coagulation disorders, 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/0103/2016 of 04/05/2016) on 23 June 2017.

2.3.13. Damoctocog alfa pegol - Orphan - EMEA-001229-PIP01-11-M03

Bayer AG; Treatment of hereditary factor VIII deficiency / Treatment and prophylaxis of bleeding in patients with haemophilia A (hereditary factor VIII deficiency)

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan for damoctocog alfa pegol for the treatment of hereditary factor VIII deficiency (hemophilia A), 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/0025/2016 of 29/01/2016) on 23 June 2017.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.14. Luspatercept - Orphan - EMEA-001521-PIP01-13-M01

Celgene Europe Ltd; Treatment of myelodysplastic syndromes, Treatment of beta-thalassaemia/ Treatment of anaemia in patients with b-thalassaemia intermedia and major

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO re-discussed this procedure during the June 2017 plenary.
The PDCO therefore adopted a favourable Opinion on modification of the agreed PIP as set in the Agency's latest decision (P/0245/2014 of 29 September 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. Recombinant fusion protein linking coagulation factor IX with albumin - Orphan - EMEA-001107-PIP01-10-M03

CSL Behring GmbH; Treatment of hereditary factor IX deficiency

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO re-discussed the applicant's request taking into account the supplementary information. The committee endorsed its view 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/0269/2014 of 27 October 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.16. Recombinant Fusion Protein Linking Coagulation Factor VIIa with Albumin (rVIIa-FP) - Orphan - EMEA-001886-PIP01-15-M01

CSL Behring GmbH; Treatment of Haemophilia B, Treatment of Haemophilia A / Treatment of Haemophilia B with Inhibitors, Treatment of Haemophilia A with Inhibitors

Day 60 opinion

Haematology-Hemostaseology

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/0342/2016 of 2 December 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.17. Recombinant Fusion Protein Linking Coagulation Factor VIIa with Albumin (rVIIa-FP) - Orphan - EMEA-001886-PIP02-15-M01

CSL Behring GmbH; Treatment of congenital Factor VII Deficiency

Day 60 opinion

Haematology-Hemostaseology

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/0343/2016 of 2 December 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.18. Romiplostim - Orphan - EMEA-000653-PIP01-09-M05

Amgen Europe B.V.; Treatment of disease-related thrombocytopenia in myelodysplastic syndrome, Treatment of immune thrombocytopenia (idiopathic thrombocytopenic purpura) / Treatment of chronic immune thrombocytopenia (idiopathic thrombocytopenic purpura; ITP) in paediatric patients who are refractory or intolerant to other treatments (e.g., glucocorticosteroids, immunoglobulins, splenectomy)

Day 60 opinion

Haematology-Hemostaseology

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/0114/2014 of 06/05/2014) on 23 June 2017.

2.3.19. Treosulfan - Orphan - EMEA-000883-PIP01-10-M04

medac Gesellschaft für klinische Spezialpräparate mbH; Conditioning treatment prior to haematopoietic progenitor cell transplantation

Day 60 opinion

Immunology-Rheumatology-Transplantation / 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/0059/2017 of 17 March 2017).

The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.20. Lamivudine (3TC) / Abacavir (ABC) / Dolutegravir (DTG) - EMEA-001219-PIP01-11-M03

ViiV Healthcare UK Limited; Treatment of Human Immunodeficiency Virus (HIV-1) infection / Treatment Human Immunodeficiency Virus (HIV-1) infection in paediatric population

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

Additional clarifications were provided by the applicant.

As all the issues raised at Day 30 were satisfactorily resolved, 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/0308/2015 of 21 December 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.21. Tenofovir Alafenamide / Emtricitabine / Cobicistat / Elvitegravir - EMEA-001460-PIP01-13-M02

Gilead Sciences International Ltd.; Treatment of human immunodeficiency virus (HIV-1) infection / treatment of HIV-1 infection in paediatric patients from 6 years to less than 18 years.

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/0195/2015 of 4 September 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.22. zanamivir - EMEA-001318-PIP01-12-M02

GlaxoSmithKline Trading Services Limited; Treatment of influenza, Prevention of influenza / Treatment of influenza A and B virus infection, Prevention of influenza A and B virus infection

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

An oral explanation took place on the Wednesday 21st June.

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/0094/2015 of 8 May 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.23. Bivalent anti-human myostatin adnectin recombinant human IgG1-Fc fusion protein - EMEA-001793-PIP01-15-M02

Bristol-Myers Squibb International Corporation; Treatment of Duchenne Muscular Dystrophy / Treatment of Duchenne Muscular Dystrophy in patients from 2 to less than 18 years of age

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/0084/2017 of 16 March 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.24. Brentuximab vedotin - Orphan - EMEA-000980-PIP01-10-M05

Takeda Pharma A/S; Treatment of Hodgkin lymphoma / Treatment of paediatric patients with newly diagnosed, relapsed or refractory Hodgkin lymphoma (from 5 years of age)

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the applicant's request taking into account the supplementary information
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/0211/2016 of 12 August 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.25. decitabine - Orphan - EMEA-000555-PIP01-09-M06

Janssen-Cilag International NV; Treatment of acute myeloid leukemia / Treatment of paediatric patients with acute myeloid leukaemia who have high-risk cytogenetics, or are refractory to, or have a relapse after first-line treatment

Day 60 opinion

Oncology

Summary of committee discussion:

The committee's view expressed on day 30 was re-discussed and endorsed.

Based on the assessment of this application the PDCO agrees with the applicant's request for a modification.

2.3.26. Isopropyl Alcohol / Chlorhexidine Gluconate - EMEA-000989-PIP01-10-M02

3M Health Care Limited; Prevention of infection

Day 60 opinion

Other

Summary of committee discussion:

The PDCO confirmed the outcome of the Day 30 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 not be accepted and that a full waiver should be granted instead.
The PDCO therefore adopted an Opinion on the refusal of a modification of an agreed Paediatric Investigation Plan and on the granting of a product-specific waiver.
The new PDCO Opinion on the product-specific waiver supersedes the previous PDCO Opinion.

2.3.27. ivacaftor / lumacaftor - EMEA-001582-PIP01-13-M06

Vertex Pharmaceuticals (Europe) Limited; cystic fibrosis / Treatment of cystic fibrosis

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/0086/2017 of 16 March 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.28. Recombinant Varicella Zoster Virus (VZV) glycoprotein E - EMEA-001426-PIP01-13-M01

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

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, 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/0168/2013 of 29 July 2013).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.4. Opinions on Re-examinations

2.4.1. Ivacaftor - EMEA-001640-PIP01-14-M02

Vertex Pharamceuticals (Europe) lTd; Treatment of Cystic Fibrosis

Day 30 opinion

Pneumology - Allergology

Summary of committee discussion:

The committee discussed the applicant's grounds for re-examination. The PDCO agreed to revise its opinion following the re-examination and adopted a positive Opinion on the PIP Modification request.

2.4.2. rivaroxaban - EMEA-000430-PIP01-08-M10

Bayer Pharma AG; Treatment of thromboembolic events, Prevention of thromboembolic events / Treatment (secondary prevention) of venous thromboembolism

Day 30 opinion

Cardiovascular Diseases

Summary of committee discussion:

The Paediatric Committee, following the re-examination, adopted a positive Opinion on the PIP Modification request.

2.5. Finalisation and adoption of opinions

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. Birch bark extract - Orphan - EMEA-001299-PIP02-16

Birken AG; Treatment of epidermolysis bullosa

Day 90 discussion

Dermatology

3.1.2. Selonsertib - EMEA-001868-PIP03-16

K75.8 Other specified inflammatory liver diseases (non-alcoholic steatohepatitis [NASH]) / Treatment of Non-Alcoholic Steatohepatitis (NASH) with moderate to severe fibrosis (F2-F4) in paediatric subjects, 8 to < 18 years of age

Day 90 discussion

Gastroenterology-Hepatology

3.1.3. Atacicept - EMEA-002004-PIP01-16

Treatment of systemic lupus erythematosus

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.4. Lefamulin - EMEA-002075-PIP01-16

Treatment of community-acquired pneumonia

Day 90 discussion

Infectious Diseases

3.1.5. fenfluramine hydrochloride - Orphan - EMEA-001990-PIP01-16

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

Day 90 discussion

Neurology

3.1.6. Sarizotan hydrochloride - Orphan - EMEA-001808-PIP02-16

Newron Pharmaceuticals SpA; Treatment of Rett syndrome

Day 90 discussion

Neurology

3.1.7. Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor - Orphan - EMEA-001862-PIP01-15

Kite Pharma EU B.V.; Treatment of B lymphoblastic leukaemia/lymphoma

Day 90 discussion

Oncology

3.1.8. Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor - Orphan - EMEA-002010-PIP01-16

Kite Pharma EU B.V.; Treatment of B-cell neoplasm

Day 90 discussion

Oncology

3.1.9. Recombinant protein derived from the saliva of Ornithodoros moubata tick - EMEA-002100-PIP01-16

Atypical haemolytic uraemic syndrome

Day 60 discussion

Haematology-Hemostaseology

3.1.10. Recombinant protein derived from the saliva of Ornithodoros moubata tick - Orphan - EMEA-002100-PIP02-16

Akari Therapeutics plc; Paroxysmal nocturnal haemoglobinuria

Day 60 discussion

Haematology-Hemostaseology

3.1.11. Cefiderocol - EMEA-002133-PIP01-17

Treatment of Gram-negative bacterial infections

Day 60 discussion

Infectious Diseases

3.1.12. 5-[4-[2-(5-(1-hydroxyethyl)-2-pyridinyl)ethoxy]benzyl]-2,4-thiazolidinedione hydrochloride - Orphan - EMEA-002106-PIP01-16

Minoryx Therapeutics SL; Treatment of adrenoleukodystrophy / Treatment of X-linked adrenoleukodystrophy

Day 60 discussion

Neurology

3.1.13. Adeno-associated viral vector serotype rh.10 carrying the human N-sulfoglucosamine sulfohydrolase cDNA - Orphan - EMEA-002122-PIP02-17

LYSOGENE; Mucopolysaccharidosis type IIIA

Day 60 discussion

Neurology

3.1.14. Entrectinib - Orphan - EMEA-002096-PIP01-16

Ignyta, Inc.; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms), Treatment of malignant neoplasms of the central nervous system / Treatment of primary brain tumours with NTRK1/2/3, ROS1 or ALK gene fusions, Treatment of extracranial solid tumours with NTRK1/2/3, ROS1 or ALK gene fusions

Day 60 discussion

Oncology

3.1.15. Pevonedistat - EMEA-002117-PIP01-17

Acute Myeloid Leukemia (AML), Myelodysplastic Syndromes (MDS) / The treatment of paediatric patients with relapsed or refractory (R/R) MDS (including juvenile myelomonocytic leukemia), The treatment of paediatric patients with relapsed or refractory (R/R) AML.

Day 60 discussion

Oncology

3.1.16. EMEA-002121-PIP01-17

Treatment of insomnia / Treatment of attention deficit hyperactivity disorder (ADHD)-related insomnia

Day 60 discussion

Psychiatry

3.1.17. Recombinant Clostridium difficile Toxoid B / Recombinant Clostridium difficile Toxoid A - EMEA-002112-PIP01-16

Prevention of Clostridium difficile infection (CDI) / Active immunization for the prevention of primary Clostridium difficile infection in children and adolescents 2 to 18 years of age

Day 60 discussion

Vaccines

3.1.18. tralokinumab - EMEA-001900-PIP02-17

Treatment of Atopic Dermatitis

Day 30 discussion

Dermatology

3.1.19. EMEA-002162-PIP01-17

type 2 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.20. Maralixibat Chloride - Orphan - EMEA-001475-PIP03-17

Shire Pharmaceuticals Ireland Limited; Treatment of Progressive Familial Intrahepatic Cholestasis

Day 30 discussion

Gastroenterology-Hepatology

3.1.21. Non-Pathogenic Bacterial Lysate of Escherichia coli (DSM 17252) and Enterococcus faecalis (DSM 16440) - EMEA-002155-PIP01-17

Irritable bowel syndrome (IBS)

Day 30 discussion

Gastroenterology-Hepatology

3.1.22. Hydroxycarbamide - EMEA-002156-PIP01-17

Sickle Cell Syndrome

Day 30 discussion

Haematology-Hemostaseology

3.1.23. Risankizumab - EMEA-001776-PIP02-17

Chronic Idiopathic Arthritis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.24. Human normal immunoglobulin for intravenous use - EMEA-002163-PIP01-17

Replacement therapy: D80-D84 Primary Immunodeficiency Syndromes with failure of antibody production. Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed. Hypogammaglobulinaemia and recurrent bacterial infections in plateau phase multiple myeloma patients who have failed to respond to pneumococcal immunisation. Hypogammaglobulinaemia in patients after allogeneic haematopoietic stem cell transplantation (HSCT). / Primary Immunodeficiency Syndromes with failure of antibody production.

Day 30 discussion

Immunology-Rheumatology-Transplantation / Haematology-Hemostaseology

3.1.25. EMEA-002080-PIP01-16

Treatment of Influenza

Day 30 discussion

Infectious Diseases

3.1.26. Obiltoxaximab - EMEA-002144-PIP01-17

Treatment of bacillary infection, Prevention of bacillary infection / Treatment of inhalation anthrax following exposure to Bacillus anthracis in combination with appropriate antibacterial drugs, Post-exposure prophylaxis of inhalation anthrax when alternative therapies are not available or are not appropriate, Prophylaxis of inhalation anthrax when alternative therapies are not available or are not appropriate

Day 30 discussion

Infectious Diseases

3.1.27. Insulin human - EMEA-002116-PIP01-17

Intestinal malabsorption in preterm infants / Treatment of intestinal malabsorption in preterm infants

Day 30 discussion

Neonatology - Paediatric Intensive Care / Gastroenterology-Hepatology

3.1.28. Insulin human - Orphan - EMEA-002116-PIP02-17

Nutrinia, Ltd.; Short bowel syndrome / Treatment of infants with Short Bowel Syndrome following surgical resection to improve intestinal absorption of nutrients and fluids

Day 30 discussion

Neonatology - Paediatric Intensive Care / Gastroenterology-Hepatology

3.1.29. anetumab ravtansine - Orphan - EMEA-002123-PIP01-17

Bayer AG; Treatment of acute myeloid leukaemia, Treatment of mesothelioma/ Treatment of patients from 2 to less than 18 years of age with relapsed and/or refractory mesothelin-positive acute myeloid leukaemia

Day 30 discussion

Oncology

3.1.30. Autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 - Orphan - EMEA-001654-PIP02-17

Novartis Europharm Limited; Mature B-cell neoplasm / Treatment of paediatric patients with relapsed or refractory mature B-cell non-Hodgkin's lymphoma

Day 30 discussion

Oncology

3.1.31. daratumumab - Orphan - EMEA-002152-PIP01-17

Janssen-Cilag International N.V.; Acute Lymphoblastic Leukemia / Daratumumab in combination with standard chemotherapy is indicated for the treatment of pediatric patients aged 1 month to 18 years with acute lymphoblastic leukemia.

Day 30 discussion

Oncology

3.1.32. daratumumab - Orphan - EMEA-002152-PIP02-17

Janssen-Cilag International N.V.; Mature T-cell and Natural Killer-cell Neoplasms, Mature B-cell Neoplasms

Day 30 discussion

Oncology

3.1.33. Carotuximab - Orphan - EMEA-002138-PIP01-17

TRACON Pharma Limited; Treatment of angiosarcoma

Day 30 discussion

Oncology

3.1.34. fully human monoclonal antibody (mAb) directed against the human PD-1 receptor - EMEA-002007-PIP02-17

Treatment of Solid Tumours / Treatment of newly diagnosed diffuse intrinsic pontine gliomas (DIPG) and recurrent high-grade gliomas (HGG)

Day 30 discussion

Oncology

3.1.35. Talacotuzumab - EMEA-002158-PIP01-17

Acute myeloid leukaemia / Talacotuzumab, in combination with anti-cancer therapy is indicated for the treatment of pediatric patients, 28 days to 18 years of age with acute myeloid leukaemia

Day 30 discussion

Oncology / Haematology-Hemostaseology

3.1.36. Burosumab - EMEA-001659-PIP02-16

Tumor-induced osteomalacia

Day 30 discussion

Other

3.1.37. Fluticasone propionate - EMEA-002140-PIP01-17

Treatment of asthma (mild, moderate, and severe) / Prophylactic management in children who require prophylactic medication, including patients not controlled on currently available prophylactic medication

Day 30 discussion

Pneumology - Allergology

3.1.38. Salmeterol xinafoate / Fluticasone propionate - EMEA-002177-PIP01-17

Treatment of asthma (mild, moderate and severe) / Regular treatment of asthma where use of a combination product (long-acting β2 agonist and inhaled corticosteroid) is appropriate: • patients not adequately controlled with inhaled corticosteroids and “as needed” inhaled short-acting β2 agonist or • patients already adequately controlled on both inhaled corticosteroid and long-acting β2 agonist

Day 30 discussion

Pneumology - Allergology

3.1.39. Vilanterol trifenatate / Umeclidinium bromide / Fluticasone furoate - EMEA-002153-PIP01-17

ICD-10 J45.5x severe persistent asthma

Day 30 discussion

Pneumology - Allergology

3.1.40. Litoxetine (as benzoate) - EMEA-002151-PIP01-17

Bladder and urethral symptoms / Treatment of Mixed Urinary Incontinence (women), Treatment of Urinary Incontinence post prostatectomy (men)

Day 30 discussion

Uro-nephrology

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

None

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Captopril - EMEA-001544-PIP01-13-M01

Proveca Limited; Heart failure / Treatment of heart failure in children aged 2 to 18 years

Day 30 discussion

Cardiovascular Diseases

3.3.2. Tilmanocept - EMEA-001255-PIP01-11-M02

Norgine BV; Visualisation of lymphatic drainage of solid malignant tumours for diagnostic purposes / Visualisation of lymphatic drainage of rhabdomyosarcoma and melanoma for diagnostic purposes

Day 30 discussion

Diagnostic / Oncology

3.3.3. exenatide - EMEA-000689-PIP01-09-M07

AstraZeneca AB; Non insulin dependent diabetes mellitus (treatment including thiazolidinediones), Non insulin dependent diabetes mellitus (excluding treatment with thiazolidinediones), Non insulin dependent diabetes mellitus - in combination with insulin (with or without oral antidiabetics) / Treatment of type 2 Diabetes Mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.4. Human Fibrinogen - EMEA-001208-PIP01-11-M03

Octapharma Pharmazeutika Produktionsges. m. b. H; Treatment of congenital fibrinogen deficiency

Day 30 discussion

Haematology-Hemostaseology

3.3.5. cobicistat / darunavir - EMEA-001280-PIP01-12-M01

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

in pediatric patients from 3 to less than 18 years.

Day 30 discussion

Infectious Diseases

3.3.6. doravirine - EMEA-001676-PIP01-14-M02

Merck Sharp & Dohme (Europe), Inc.; Treatment of human immunodeficiency virus-1 (HIV-1) infection / Antiretroviral therapy, in combination with other antiretroviral agents, for the treatment of HIV-1 infection in children aged from birth to 18 years

Day 30 discussion

Infectious Diseases

3.3.7. elbasvir / grazoprevir - EMEA-001604-PIP01-13-M03

Merck Sharp & Dohme (Europe), Inc.; treatment of chronic hepatitis C infection / Treatment of chronic hepatitis C genotype 1 infection with the combination regimen in children and adolescents from 3 years to less than 18 years of age who are previously untreated or who have failed previous Peg-Interferon/Interferon therapy with ribavirin.

Day 30 discussion

Infectious Diseases

3.3.8. Fidaxomicin - EMEA-000636-PIP01-09-M06

Astellas Pharma Europe B.V.; Treatment of enterocolitis caused by clostridium difficile / Treatment of Clostridium difficile infections (CDI) also known as C. difficile-associated diarrhoea (CDAD)

Day 30 discussion

Infectious Diseases

3.3.9. tenofovir alafenamide / emtricitabine / cobicistat / darunavir - EMEA-001825-PIP01-15-M01

Janssen-Cilag International NV; Treatment of human immunodeficiency virus type-1 (HIV-1) infection / Treatment of HIV-1 infection in paediatric subjects weighing 25 kg or more above 6 years of age

Day 30 discussion

Infectious Diseases

3.3.10. Tenofovir disoproxil (as fumarate) - EMEA-000533-PIP01-08-M07

Gilead Sciences International Ltd; Treatment of human immunodeficiency virus (HIV-1) infection, Treatment of chronic viral hepatitis B / For treatment of chronic hepatitis B in

paediatric patients from 2 years of age with compensated liver disease., In combination with other antiretroviral medicinal products for the treatment of HIV-1 infection in antiretroviral treatment experienced paediatric patients.

Day 30 discussion

Infectious Diseases

3.3.11. tenofovir disoproxil fumarate / lamivudine / doravirine - EMEA-001695-PIP01-14-M02

Merck Sharp & Dohme (Europe), Inc.; Treatment of human immunodeficiency virus-1 (HIV-1) infection / Antiretroviral combination therapy, for the treatment of HIV-1 infection in adults and children aged 2 to 18 years

Day 30 discussion

Infectious Diseases

3.3.12. Brivaracetam - Orphan - EMEA-000332-PIP01-08-M12

UCB Pharma S.A.; treatment of paediatric epilepsy syndromes, Treatment of epilepsy with partial onset seizures, Treatment of neonatal seizures / Treatment of neonatal seizures with adjunctive administration of brivaracetam, Treatment of paediatric patients with partial onset seizures, treatment of refractory paediatric epilepsy syndromes with adjunctive administration of brivaracetam

Day 30 discussion

Neurology

3.3.13. Daclizumab - EMEA-001349-PIP01-12-M02

Biogen Idec Ltd; Multiple Sclerosis / Treatment of relapsing remitting forms of multiple sclerosis

Day 30 discussion

Neurology

3.3.14. Autologous T cells transduced with lentivlral vector containing a chimeric antigen receptor directed against CD19 - Orphan - EMEA-001654-PIP01-14-M02

Novartis Europharm Limited; B cell acute lymphoblastic leukaemia (ALL) / Treatment of CD19+ B cell acute lymphoblastic leukaemia (ALL) in paediatric patients whose disease is refractory to a standard chemotherapy regimen, relapsed after stem cell transplantation (SCT) or are ineligible for allogenic SCT.

Day 30 discussion

Oncology

3.3.15. Dabrafenib (dabrafenib mesilate) - EMEA-001147-PIP01-11-M05

Novartis Europharm Limited; Treatment of solid malignant tumours (excluding melanoma), Treatment of melanoma / Treatment of paediatric patients with solid malignant tumours containing BRAF V600 mutations, Treatment of adolescent patients with melanoma with a BRAF V600 mutation

Day 30 discussion

Oncology

3.3.16. Poly(oxy-1,2-ethanediyl),alpha-hydro-omega-methoxy-133 ester with granulocyte colony-stimulating factor [methionyl,133-[O-[2-(acetylamino]-6-O-[N-[N-carboxyglycyl)amino]-alpha neuraminosyl]-2-deoxy-alpha-D-galactopyranosyl]-L-threonine]] (human) - EMEA-001019-PIP01-10-M04

UAB "Sicor Biotech"; Treatment of chemotherapy-induced neutropenia, Prevention of chemotherapy-induced febrile neutropenia / Treatment of neutropenia and reduction in the incidence of febrile neutropenia in patients treated with chemotherapy for malignancy

Day 30 discussion

Oncology

3.3.17. Sunitinib malate - EMEA-000342-PIP01-08-M06

Pfizer Limited; CD10 code C49.4 malignant neoplasms of connective and soft tissue of abdomen - gastro-intestinal stromal tumours (GIST) / Treatment of gastro-intestinal stromal tumour in paediatric patients aged 6 to less than 18

Day 30 discussion

Oncology

3.3.18. Trametinib (trametinib dimethyl sulfoxide) - EMEA-001177-PIP01-11-M04

Novartis Europharm Limited; treatment of melanoma, Treatment of solid malignant tumours (excluding melanoma) / Treatment of paediatric patients with solid malignant tumours containing BRAF V600 mutations, Treatment of adolescent patients with melanoma with a BRAF V600 mutation

Day 30 discussion

Oncology

3.3.19. sildenafil - Orphan - EMEA-000671-PIP01-09-M08

Pfizer Limited; Treatment of Pulmonary Arterial Hypertension (PAH)

Day 30 discussion

Other

3.3.20. lurasidone hydrochloride - EMEA-001230-PIP01-11-M03

Sunovion Pharmaceuticals Ltd.; Schizophrenia

Day 30 discussion

Psychiatry

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 15 August 2017 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

Summary of committee discussion:

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. Antibody drug conjugate comprised of a humanized anti-HER2 antibody attached by a peptide linker to a novel topoisomerase I inhibitor - EMEA-10-2017

Daiichi Sankyo, Inc.; Class of Her- / Epidermal growth factor-receptor antibody medicinal products for treatment of breast malignant neoplasms/ Treatment of patients with human epidermal growth factor receptor (HER)2-positive metastatic breast cancer that is resistant or refractory to trastuzumab emtansine (T-DM1)

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.

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. Evolocumab - EMEA-001268-PIP01-12-M04

Amgen Europe B.V.; Treatment of elevated cholesterol

Summary of committee discussion:

The PDCO confirmed that the proposed indication is included within the condition of the agreed PIP (Decision P/0101/2017).

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

9.1.1. Inventory

Summary of committee discussion:

A presentation was done by the members of the paediatric inventory group on the potential use of a score to prioritise unmet needs on the basis of licensing status and scientific

evidence.

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 presented the list of procedures with paediatric indications to be evaluated by the CHMP, starting in May 2017.

The members were also informed about 4 medicinal products, Insulin lispro Sanofi, Izba, Renvela and Sevelamer carbonate Zentiva for which the CHMP adopted a positive opinion recommending a paediatric indication during their meeting in May 2017.

A new pharmaceutical form (100 mg and 500 mg powder for oral solution) for Kuvan was approved for use in paediatric patients of all ages.

9.2.2. Joint CHMP/PDCO session

Summary of committee discussion:

The second joint CHMP-PDCO session took place

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.

9.3.3. Revision of the Guidelines on the clinical investigation and core SmPC of recombinant and human plasma-derived factor VIII products

Summary of committee discussion:

The PDCO was updated on the planned revisions of the Guidelines on the clinical

investigation and core SmPC of recombinant and human plasma-derived factor VIII. Overall, the PDCO supported the changes to be introduced in the revision of the guideline and core SmPC.

9.3.4. Guideline on the clinical evaluation of medicinal products indicated for the prophylaxis or treatment of respiratory syncytial virus (RSV) disease

Summary of committee discussion:

The PDCO reviewed the comments received from members of the Committee and adopted a final version including all agreed comments.

9.3.5. Paediatric Addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections

PDCO member: Maria Fernandez Cortizo

Summary of committee discussion:

The committee was informed that an updated proposal to cover some of the issues raised at the May PDCO discussion has been sent to the Infectious Disease Working Party (IDWP) for comments, which will be re-discussed at the July TC of IDWP. The PDCO agreed to circulate the version following the IDWP Discussion to all PDCO members for their comments and to re-discuss it at next month PDCO meeting.

The committee re-iterated that paediatric drug development programmes are increasingly multiregional. To ensure efficient paediatric drug development and timely delivery of safe and effective medicines for children, there is a need for early interactions with other regulatory authorities to facilitate agreement on a common scientific approach to paediatric development programmes.

9.3.6. Draft Agenda of the PCWP/HCPWP joint meeting to be held on 27-28 June 2017

Summary of committee discussion:

The document was tabled for information.

9.4. Cooperation within the EU regulatory network

None

9.5. Cooperation with International Regulators

9.5.1. Gaucher disease - A strategic collaborative approach from EMA and FDA

PDCO member: Sylvie Benchetrit

Summary of committee discussion:

Strategic Collaborative Approach document was adopted by the PDCO.

9.5.2. Report on the EMA/FDA/Health Canada workshop on paediatric pulmonary arterial hypertension (PAH)' held on 12 June 2017 at EMA

Summary of committee discussion:

EMA reported on the EMA/FDA/Health Canada workshop on paediatric pulmonary arterial hypertension which took place in June at EMA premises.

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. Strategic Review and Learning Meeting (SRLM) to be held in Estonia on 4-6 October 2017

PDCO member: Irja Lutsar

Summary of committee discussion:

The draft agenda will be circulated to PDCO members and discussed next month during the July PDCO plenary.

10. Any other business

10.1.1. Paediatric applications to PDCO members: proposal for simplification

PDCO Chair: Dirk Mentzer

Summary of committee discussion:

PDCO delegates were asked to indicate whether they should continue to receive the PIP submissions on CDs, together with a justification in case they wish to continue.

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

Due to time constraints the break-out session was cancelled.

11.1.2. Neonatology

Summary of committee discussion:

Due to time constraints the break-out session was cancelled. A TC will be organised before the next Plenary Meeting.

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 20-22 June 2017 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	EMEA-002153-PIP01-17 EMEA-001426-PIP01-13-M01 EMEA-001318-PIP01-12-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	
Suzana Mimica Matanovic	Alternate	Croatia	No interests declared	
Georgios Savva	Member	Cyprus	No interests declared	
Jaroslav Sterba	Member	Czech Republic	No interests declared	
Peter Szitanyi	Alternate	Czech Republic	No interests declared	
Marianne Orholm	Member	Denmark	No interests declared	
Marta Granström	Alternate	Denmark	No interests declared	
Irja Lutsar	Member via TC	Estonia	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ann Marie Kaukonen	Member	Finland	No interests declared	
Maija Pihlajamaki	Alternate	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	
Alessandro Jenkner	Alternate	Italy	No interests declared	
Dina Apele-Freimane	Member	Latvia	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	
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	
Stefan Grosek	Member	Slovenia	No interests declared	
Fernando de Andrés	Member via TC	Spain	No interests	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Trelles			declared	
Maria Jesús Fernández Cortizo	Alternate via TC	Spain	No interests declared	
Ninna Gullberg	Member	Sweden	No interests declared	
Eva Agurell	Alternate	Sweden	No restrictions applicable to this meeting	
Angeliki Siapkara	Member	United Kingdom	No interests declared	
Martina Riegl	Alternate	United Kingdom	No interests declared	
Riccardo Riccardi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Jorrit Gerritsen	Alternate	Healthcare Professionals' Representative	No interests declared	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
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 participation in final deliberations and voting on:	EMEA-002153-PIP01-17 EMEA-001426-PIP01-13-M01 EMEA-001318-PIP01-12-M02
Michal Odermarsky	Member	Patients' Organisation Representative	No interests declared	
Tsveta Schyns-Liharska	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Anneliese Hilger	Expert - via telephone*	Germany	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Kristine Moll Harboe	Expert - in person*	Denmark	No interests declared	
Catriona Elizabeth Baker	Expert - in person*	United Kingdom	No interests declared	
Shiva Ramroop	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Sara Homer	Expert - in person*	United Kingdom	No interests declared	
Eva Segovia	Expert - via telephone*	Spain	No interests declared	

* 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/