25 May 2016
EMA/PDCO/244355/2016
Procedure Management and Committees Support Division

Paediatric Committee (PDCO)

Minutes for the meeting on 27-29 April 2016

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

27 April 2016, 08:30- 19:00, room 3A

28 April 2016, 08:30- 19:00, room 3A

29 April 2016, 08:30- 13:00, room 3A

Disclaimers

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

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

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

Note on access to documents

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

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1. Introductions

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

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

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

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

1.2. Adoption of agenda

The agenda was adopted with amendments.

1.3. Adoption of the minutes

The minutes 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. Bexagliflozin - EMEA-001841-PIP01-15

Theracos Sub, LLC; Type 2 Diabetes Mellitus

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

During its April 2016 plenary and based on the final assessment of this application the PDCO adopted a positive opinion for a PIP for bexagliflozin for the treatment of type 2 diabetes mellitus in children from 10 to less than 18 years of age. A waiver for the age group from birth to less than 10 years was agreed.

2.1.2. Recombinant humanized anti-MMP9 monoclonal antibody IgG4 - EMEA-001813-PIP01-15

Gilead Sciences International Ltd; Crohn's Disease, Ulcerative Colitis

Day 120 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The PDCO discussed this procedure on D120. The response to the issues raised on D90 was considered acceptable. A positive opinion was adopted.

2.1.3. sulfate hydrate / cilastatin sodium / imipenem monohydrate - EMEA-001809-PIP01-15

Merck Sharp & Dohme (Europe), Inc.; Treatment of bacterial infections caused by Gram-negative bacteria

Day 120 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO discussed the remaining issues. The PDCO adopted a positive opinion.

2.1.4. Methyl {(2S,3R)-1-[(2S)-2-{5-[(2R,5R)-1-{3,5-difluoro-4-[4-(4-fluorophenyl)piperidin-1-yl]phenyl}-5-(6-fluoro-2-{(2S)-1-[N-(methoxycarbonyl)-O-methyl-L-threonyl]pyrrolidin-2-yl}-1H-benzimidazol-5-yl)pyrrolidin-2-yl]-6-fluoro-1H-benzimidazol-2-yl}pyrrolidin-1-yl]-3-methoxy-1-oxobutan-2-yl}carbamate (AbbVie internal name: ABT-530) / (3aR,7S,10S,12R,21E,24aR)-7-tert-butyl-N-[(1R,2R)-2-(difluoromethyl)-1-{[(1-methylcyclopropyl)sulfonyl]carbamoyl}cyclopropyl]-20,20-difluoro-5,8-dioxo-2,3,3a,5,6,7,8,11,12,20,23,24a-dodecahydro-1H,10H-9,12-methanocyclopenta[18,19][1,10,17,3,6]trioxadiazacyclononadecino[11,12-b]quinoxaline-10-carboxamide - EMEA-001832-PIP01-15

AbbVie Ltd; Treatment of Chronic Hepatitis C / Treatment of Chronic Hepatitis C

Day 120 opinion

Infectious Diseases

Summary of committee discussion:

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

Committee including contributions of external expert(s), the PDCO agrees with the applicant's modified PIP proposal. A positive opinion was adopted.

2.1.5. pimavanserin - EMEA-001688-PIP02-15

ACADIA Pharmaceuticals Inc.; Treatment of schizophrenia and other psychotic disorders

Day 120 opinion

Psychiatry

Summary of committee discussion:

The PDCO did not find the PIP in its current form approvable despite the additional information received after Day 90.
In conclusion, the PDCO has adopted a negative opinion refusing the proposed PIP.

2.1.6. Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1) - EMEA-001715-PIP01-14

Seqirus S.r.l.; Influenza / Prevention of influenza

Day 120 opinion

Vaccines

Summary of committee discussion:

The PDCO re-discussed the proposed plan for the adjuvanted quadrivalent influenza vaccine also taking into account the applicant’s responses provided after the D90 discussion and the comments received by the applicant on the draft opinion.
The PDCO adopted a positive opinion with a deferral and a waiver for influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1) in the condition “prevention of influenza”.

Note: the applicant was changed from Novartis Vaccines Influenza S.r.l.(until Day 60) to Seqirus S.r.l.

2.1.7. Rosuvastatin (Calcium) / Olmesartan medoxomil - EMEA-001914-PIP01-15

Daewoong Pharmaceutical Co., Ltd.; Hypertension, Dyslipidaemia, Cardiovascular events / Treatment of dyslipidaemia/hypercholesterolaemia, Prevention of cardiovascular events, Treatment of hypertension

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 Rosuvastatin (calcium) / Olmesartan (medoxomil) for all subsets of the paediatric population (0 to 18 years of age) in the condition of Hypertension, Dyslipidaemia, Cardiovascular events.

2.1.8. Imetelstat - Orphan - EMEA-001910-PIP01-15

Janssen-Cilag International N.V; Treatment of Myelofibrosis

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the proposed product-specific waiver for imetelstat in the condition “treatment of myelofibrosis” also taking into consideration the additional information provided by the applicant the PDCO recommended granting a waiver for imetelstat for all subsets of the paediatric population (from birth to less than 18 years of age) .
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.

2.1.9. Ciclosporin - EMEA-001916-PIP01-15

Laboratoires Théa; Keratoconjunctivitis sicca

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 Ciclosporin for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of keratoconjunctivitis sicca.

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.

2.1.10. Tramadol / Ibuprofen - EMEA-001887-PIP01-15

FARMALIDER, S.A.; Acute pain

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 Ibuprofen arginine / Tramadol hydrochloride for all subsets of the paediatric population (0 to 18 years of age) in the condition of acute pain.
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. Peanut flour - EMEA-001753-PIP02-15 – early adoption of opinion

Cambridge Allergy Ltd; Treatment of peanut allergy Z91.010

Day 60 discussion

Pneumology - Allergology

Summary of committee discussion:

The PDCO concluded that all issues raised at Day 30 have been addressed and resolved satisfactorily.
The PDCO adopted a positive opinion.

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. maraviroc - EMEA-C-000020-PIP01-07-M05

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

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO re-discussed the compliance request on 27 April 2016 also taking into account the clarifications provided by the applicant after the D30 discussion.
The PDCO adopted on 29 April 2016 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0237/2015) of 30/10/2015.

2.2.2. Sirukumab - EMEA-C2-001043-PIP01-10-M02

Janssen-Cilag International N.V.; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis)

Day 30 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO discussed the completed study and considered that these are compliant with the latest Agency's Decision (P/0020/2016) of 29/01/2016.
The PDCO finalised on 29 April 2016 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. Riociguat- EMEA-C3-000718-PIP01-09-M05

Bayer Pharma AG; Treatment of pulmonary hypertension

Cardiovascular Diseases

Summary of committee discussion:

The committee noted the positive outcome the opinion adopted via written procedure on 18 April 2016.

2.2.4. Dasatinib - EMEA-C3-000567-PIP01-09-M04

Bristol-Myers Squibb Pharma EEIG; Treatment of Philadelphia chromosome (BCR-ABL translocation)-positive acute lymphoblastic leukaemia

Day 30 opinion

Oncology

Summary of committee discussion:

The PDCO, taking into account the supplementary information, discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0118/2013) of 02 May 2013.
The PDCO finalised on 29 April 2016 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.

2.2.5. midostaurin - EMEA-C2-000780-PIP01-09-M02 – early adoption of opinion

Novartis Europharm Limited; Treatment of acute myeloid leukaemia

Day 30 opinion

Oncology

Summary of committee discussion:

The PDCO discussed the completed Study and considered that this was compliant with the latest Agency's Decision (P/0039/2016) of 19 February 2016.
The PDCO finalised on 29 April 2016 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.

2.2.6. Tobramycin - EMEA-C-000184-PIP02-14 – early adoption of opinion

Novartis Europharm Limited; Treatment of P. aeruginosa pulmonary infection/colonisation in patients with cystic fibrosis

Day 30 discussion

Infectious Diseases

Summary of committee discussion:

The PDCO adopted on 29 April 2016 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0184/2014) of 6 August 2014.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Liraglutide - EMEA-000128-PIP02-09-M02

Novo Nordisk A/S; E66 Obesity / Treatment of obesity

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO agreed with the proposed changes.
Based on the review of the rationale submitted by the application 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/0086/2015 of 8 May 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.2. retosiban - EMEA-001359-PIP01-12-M03

GlaxoSmithKline Trading Services Limited; Treatment of spontaneous preterm labour / Treatment of spontaneous preterm labour to improve neonatal outcomes by prolonging pregnancy in women with an uncomplicated singleton pregnancy between 24 and less than 34 weeks gestation

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the review of the rationale submitted by the application 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/0194/2015 of 04/09/2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.3. Tolvaptan - EMEA-001231-PIP02-13-M03

Otsuka Pharmaceutical Europe Ltd.; Polycystic Kidney Disease (PKD), Dilutional hyponatraemia / Treatment of chronic (>48 hours) dilutional hyponatraemia resistant to fluid restriction (i.e., euvolemic and hypervolemic hyponatremia) associated with heart failure, cirrhosis or SIADH, Treatment of progression of ADPKD, Treatment of progression of ARPKD

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the review of the rationale submitted by the application 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/0045/2016 of 26 February 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.4. potassium sulphate / magnesium sulphate heptahydrate / sodium sulphate anhydrous - EMEA-000816-PIP02-10-M01

IPSEN Pharma; Diagnostic of organic and/or functional bowel diseases / In adults and children from 6 months of age for bowel cleansing prior to any procedure requiring a clean bowel (e.g. bowel visualisation including endoscopy and radiology or surgical procedure). The product is not a treatment for constipation

Day 60 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan and the further information received, the PDCO considered that the majority of the 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/214/2011 of 2/9/2011).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. efmorocotocog alfa - EMEA-001114-PIP01-10-M03

Biogen Idec Ltd; Hereditary Factor VIII Deficiency - D66 / Treatment and prophylaxis of bleeding in patients with severe Haemophilia A (congenital FVIII deficiency)

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that only some of the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0077/2014 of 2 April 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.6. Secukinumab - EMEA-000380-PIP02-09-M03

Novartis Europharm Limited; Chronic Idiopathic Arthritis / Treatment of juvenile psoriatic arthritis, Treatment of enthesitis-related arthritis JIA

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

Based on the review of the rationale submitted by the application 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/0247/2014 of 30 September 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.7. raltegravir - EMEA-000279-PIP01-08-M05

Merck Sharp & Dohme (Europe), Inc.; Human Immunodeficiency Virus (HIV-1) infection / In combination with other anti-retroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infection

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the application 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/0187/2015 of 4 September 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. Alemtuzumab - EMEA-001072-PIP01-10-M02

Genzyme Europe B.V.; Multiple sclerosis / For paediatric patients with relapsing remitting multiple sclerosis (RRMS) with active disease on prior disease modifying treatment (DMT) defined by clinical or imaging features

Day 60 opinion

Neurology

Summary of committee discussion:

The PDCO re-discussed the issues highlighted at D30 taking into account the further requested clarification. Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that 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/0286/2011 of 30 November 2011). The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.9. Clostridium Botulinum neurotoxin type A (150 kD), free from complexing proteins - EMEA-001039-PIP02-12-M02

Merz Pharmaceuticals GmbH; Treatment of sialorrhea / Treatment of chronic troublesome sialorrhea associated with neurological conditions (e.g. cerebral palsy, traumatic brain injury) and/or intellectual disability in children and adolescents aged 2 – 17 years.

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/0005/2016 of 25/01/2016). The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.10. Melatonin - Orphan - EMEA-000440-PIP02-11-M04

RAD Neurim Pharmaceuticals EEC Ltd; Insomnia - children, Insomnia - adults / Insomnia

Day 60 opinion

Neurology

Summary of committee discussion:

Based on the review of the rationale submitted by the application 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/0244/2015 of 30 October 2015). The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.11. ibrutinib - Orphan - EMEA-001397-PIP03-14-M01

Janssen-Cilag International N.V.; Treatment of mature B-cell neoplasm / Treatment of children from 1 year to less than 18 years of age with newly-diagnosed and relapsed/refractory mature B-cell lymphoma, that is, diffuse large B-cell lymphoma or Burkitt and Burkitt-like lymphoma.

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO discussed the request for modification of the PIP agreed for ibrutinib taking into account the supplementary information received which clarified the issues mentioned during the previous discussion.
Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision. The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.12. darbepoetin alfa - EMEA-000329-PIP02-09-M05

Amgen Europe B.V.; Drug-induced aplastic anaemia, Treatment of anaemia due to chronic disorders / Treatment of symptomatic anaemia in adult and paediatric cancer patients with non-myeloid malignancies receiving chemotherapy, Treatment of symptomatic anaemia associated with chronic renal failure (CRF) in adults and paediatric patients

Day 60 opinion

Oncology / Uro-nephrology

Summary of committee discussion:

Based on the review of the rationale submitted by the application 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/0241/2015 of 30 October 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.13. tafluprost - EMEA-001187-PIP01-11-M03

Santen Oy; Glaucoma (ICD: H40) / Tafluprost preservative-free is indicated for the treatment

of elevated intraocular pressure in paediatric patients 1 month post-natal to less than 18 years of age

Day 60 opinion

Ophthalmology

Summary of committee discussion:

The PDCO discussed the comments provided by the applicant to the PDCO D30 minutes and supported the points raised by the Rapporteur and Peer reviewer.
In conclusion, based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes cannot be accepted.
The PDCO therefore adopted a negative Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0216/2015 of 2 October 2015).

2.3.14. Clostridium Botulinum neurotoxin type A (150 kD), free from complexing proteins - EMEA-001039-PIP01-10-M02

Merz Pharmaceuticals GmbH; Treatment of muscle spasticity, Treatment of dystonia, Treatment of muscle induced wrinkles / Treatment of spasticity of the upper and/or lower limb in children and adolescents (aged 2 - 17 years) with cerebral palsy

Day 60 opinion

Ophthalmology / Dermatology / 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/0005/2016 of 25/01/2016)/ The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. Atrasentan hydrochloride - EMEA-001666-PIP01-14-M01

AbbVie, Ltd; Nephropathies / Treatment of multidrug-resistant nephrotic syndrome (MDR-NS)

Day 60 opinion

Uro-nephrology

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, and following the discussions at D30 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/0175/2015 of 07 August 2015). The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.16. Ferric citrate (coordination complex) - EMEA-001213-PIP02-12-M02

Keryx Biopharma UK Ltd.; Treatment of hyperphosphataemia / The control of

hyperphosphataemia in patients with chronic kidney disease (CKD)

Day 60 opinion

Uro-nephrology

Summary of committee discussion:

Based on the review of the rationale submitted by the application 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/0218/2014 of 3 September 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.17. Eltrombopag - EMEA-000170-PIP01-07-M04 – early adoption of opinion

Novartis Europharm Limited; Treatment of Idiopathic Thrombocytopenia Purpura (ITP) / Treatment of Chronic Idiopathic thrombocytopenic purpura (ITP)

Day 30 discussion

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/0307/2012 of 21/12/2012).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.4. Opinions on Re-examinations

2.4.1. Coagulation Factor VIIa (Recombinant) - EMEA-001203-PIP02-14-M01

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 30 opinion

Haematology-Hemostaseology

Summary of committee discussion:

On 7 April 2016 LFB SA submitted to the European Medicines Agency a written request including detailed grounds for a re-examination of the Opinion issued on 26 February 2016 on the request for modification of the agreed paediatric investigation plan.

The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.5. 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. Eleclazine - EMEA-001697-PIP01-14

Treatment of congenital long QT syndromes / Indicated for the treatment of long QT syndrome type 2 (LQT2), Indicated for the treatment of long QT syndrome type 3 (LQT3)

Day 90 discussion

Cardiovascular Diseases

3.1.2. Eleclazine - EMEA-001697-PIP02-14

Treatment of hypertrophic cardiomyopathy / Indicated for the treatment of symptomatic hypertrophic cardiomyopathy (HCM)

Day 90 discussion

Cardiovascular Diseases

3.1.3. Metreleptin - Orphan - EMEA-001701-PIP01-14

Aegerion Pharmaceuticals Ltd; Treatment of lipodystrophy

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.4. Humanized monoclonal modified immunoglobulin G4 (IgG4) antibody with bispecific structure targeting factors IX, IXa, X and Xa - Orphan - EMEA-001839-PIP01-15

Roche Registration Limited; Treatment of Hereditary FVIII Deficiency / indicated for the routine prophylaxis to reduce the frequency of or prevent bleeding episodes in paediatric patients with hemophilia A with FVIII inhibitors

Day 90 discussion

Haematology-Hemostaseology

3.1.5. Cadazolid - EMEA-001108-PIP02-15

Enterocolitis due to Clostridium difficile / Treatment of Clostridium difficile-associated diarrhea

(CDAD)

Day 90 discussion

Infectious Diseases

3.1.6. cytarabine 100 mg (liposome combination) daunorubicin HCl 44mg (liposome combination) - Orphan - EMEA-001858-PIP01-15

Celator (UK) Ltd; Acute myeloid leukemia / treatment of acute myeloid leukemia

Day 90 discussion

Oncology

3.1.7. Glycopyrronium bromide (dose expressed as free base) / Mometasone furoate / Indacaterol acetate (dose expressed as free base) - EMEA-001812-PIP01-15

Treatment of asthma

Day 90 discussion

Pneumology - Allergology

3.1.8. A phosphorothioate oligonucleotide targeted to apolipoprotein C-III - Orphan - EMEA-001915-PIP01-15

Ionis Pharmaceuticals; Familial Chylomicronemia Syndrome

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.9. efpeglenatide - EMEA-001903-PIP01-15

Type 2 diabetes mellitus

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.10. Antithrombin alfa - EMEA-001154-PIP02-15

Treatment of congenital antithrombin deficiency, Treatment of acquired antithrombin deficiency (Preeclampsia), Treatment of acquired antithrombin deficiency (ECMO) / Prophylaxis of peri-partum thromboembolic events in congenital antithrombin deficient patients., Antithrombin supplementation during ECMO procedure, Treatment of pregnant women less than 30 weeks GA with preeclampsia to prolong gestation and decrease foetal and neonatal morbidity and mortality

Day 60 discussion

Haematology-Hemostaseology

3.1.11. abatacept - EMEA-000118-PIP03-15

Treatment of childhood-onset SLE / Treatment of childhood-onset lupus nephritis caused by childhood-onset SLE with abatacept in combination with MMF or CY, and CS in pediatric patients 5 years of age and older who have had an insufficient response to MMF or CY, and CS

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.12. Ciprofloxacin Hydrochloride - EMEA-001563-PIP02-15

Treatment of cystic fibrosis related bronchiectasis associated with P. aeruginosa infection, Treatment of non-cystic fibrosis related bronchiectasis associated with P. aeruginosa infection (NCFBEPA+)

Day 60 discussion

Infectious Diseases

3.1.13. synthetic surfactant protein B analogue / synthetic surfactant protein C analogue / 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoglycerol sodium salt / dipalmitoylphosphatidylcholine - Orphan - EMEA-001780-PIP01-15

Chiesi Farmaceutici SpA; treatment of respiratory distress syndrome (RDS) / treatment of respiratory distress syndrome (RDS) in preterm neonates of less than 37 weeks of gestational age

Day 60 discussion

Neonatology - Paediatric Intensive Care

3.1.14. benzodiazepine - EMEA-001918-PIP01-15

ICD10 F84: Treatment of autism spectrum disorder

Day 60 discussion

Neurology

3.1.15. N. meningitidis serogroup W polysaccharide conjugated to tetanus toxoid / N. meningitidis serogroup Y polysaccharide conjugated to tetanus toxoid / N. meningitidis serogroup C polysaccharide conjugated to tetanus toxoid / N. meningitidis serogroup A polysaccharide conjugated to tetanus toxoid - EMEA-001930-PIP01-16

Prevention of Meningococcal Disease

Day 60 discussion

Vaccines

3.1.16. alvimopan - EMEA-001922-PIP01-15

Postoperative ileus

Day 30 discussion

Gastroenterology-Hepatology

3.1.17. Ascorbic Acid / Sodium Ascorbate / Potassium Chloride / Sodium Chloride / Sodium Sulfate / Macrogol 3350 - EMEA-001705-PIP02-15

Diagnosis of large intestine disorders / For bowel cleansing prior to any clinical procedures requiring a clean bowel e.g. bowel endoscopy or radiology

Day 30 discussion

Gastroenterology-Hepatology

3.1.18. Susoctocog alfa - EMEA-000753-PIP02-16

Congenital haemophilia A with antibodies (inhibitors) to human factor VIII / Peri-operative management in patients with congenital haemophilia A with antibodies (inhibitors) to human FVIII, On-demand treatment and control of bleeding episodes in patients with congenital haemophilia A with antibodies (inhibitors) to human FVIII

Day 30 discussion

Haematology-Hemostaseology

3.1.19. Fc- and CDR-modified humanized monoclonal antibody against C5 - EMEA-001943-PIP01-16

Atypical Haemolytic Uremic Syndrome / Treatment of atypical Haemolytic Uremic Syndrome

Day 30 discussion

Uro-nephrology / Haematology-Hemostaseology

3.2. Discussions on Compliance Check

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

3.2.1. Ciclosporin - EMEA-C-000575-PIP01-09-M03

SANTEN OY; Treatment of vernal keratoconjunctivitis

Day 30 discussion

Ophthalmology

Summary of committee discussion:

The PDCO discussed the compliance request and concluded that compliance with all measures

and timelines of the PIP can be confirmed. A positive opinion has been adopted.

3.2.2. cinacalcet - EMEA-C-000078-PIP01-07-M07

Amgen Europe B.V.; treatment of secondary hyperparathyroidism in patients with end-stage renal disease

Day 30 discussion

Uro-nephrology

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Landiolol hydrochloride - EMEA-001150-PIP02-13-M01

AOP Orphan Pharmaceuticals AG; Treatment of supraventricular arrhythmias / Treatment of sinus tachycardia or supraventricular tachyarrhythmias, including junctional ectopic tachycardia (JET), atrial flutter (AF), atrial fibrillation (AFL), focal atrial tachycardia (FAT), atrioventricular re-entrant tachycardia (AVRT), and atrioventricular nodal re- entrant tachycardia (AVNRT), peri-operatively (during an induction phase, intra-operatively, and during the weaning phase), or when in the phycisian's judgement control of the heart rate is required.

Day 30 discussion

Cardiovascular Diseases

3.3.2. rCFP-10 (recombinant 10 kD culture filtrate protein) / rdESAT-6 (recombinant dimer of 6 kD early secretory antigenic target) - EMEA-001156-PIP01-11-M07

Statens Serum Institut; Diagnosis of tuberculosis / To diagnose individuals suspected to be infected with Mycobacterium tuberculosis from 28 days of age

Day 30 discussion

Diagnostic

3.3.3. Canagliflozin - EMEA-001030-PIP01-10-M06

Janssen-Cilag International NV; Renal Disease in Patients with Type 2 Diabetes Mellitus, Type 2 Diabetes Mellitus / Treatment of Type 2 Diabetes Mellitus, Treatment of Renal Disease in Patients with Type 2 Diabetes

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.4. corifollitropin alfa - EMEA-000306-PIP01-08-M03

Merck Sharp & Dohme Limited; Inability to achieve pregnancy, female / hypogonadotropic hypogonadism

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.5. dulaglutide - EMEA-000783-PIP01-09-M04

Eli Lilly & Company; Type 2 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.6. Liraglutide - EMEA-000128-PIP01-07-M07

Novo Nordisk A/S; E11 Non-insulin-dependent diabetes mellitus / Treatment of type 2 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.7. Naloxegol (as naloxegol oxalate) - EMEA-001146-PIP01-11-M02

AstraZeneca AB; Treatment of opioid induced constipation

Day 30 discussion

Gastroenterology-Hepatology

3.3.8. caplacizumab (anti-von Willebrand Factor Nanobody) - Orphan - EMEA-001157-PIP01-11-M01

Ablynx NV; Treatment of thrombotic thrombocytopenic purpura / Treatment of acquired thrombotic thrombocytopenic purpura

Day 30 discussion

Haematology-Hemostaseology

3.3.9. Deferasirox - Orphan - EMEA-001103-PIP01-10-M03

Novartis Europharm Limited; Treatment of chronic overload requiring chelation therapy / Treatment of chronic iron overload due to blood transfusions when deferoxamine therapy is contraindicated or inadequate in patients with others anemias, Treatment of chronic transfusional iron overload in patients with beta thalassemia major, Treatment of chronic iron overload in patients with non-transfusion-dependent thalassemia

Day 30 discussion

Haematology-Hemostaseology

3.3.10. Eltrombopag - EMEA-000170-PIP03-13-M01

Novartis Europharm Limited; Bone Marrow Depression and Hypoplastic Anaemia / Treatment of cytopenias in paediatric patients with severe aplastic anaemia who are no receiving hematopoietic stem cell transplant

Day 30 discussion

Haematology-Hemostaseology

3.3.11. baricitinib - EMEA-001220-PIP01-11-M01

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

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.12. belimumab - EMEA-000520-PIP01-08-M05

Glaxo Group Limited; Systemic lupus erythematosus / Treatment of systemic lupus erythematosus

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.13. Eculizumab - Orphan - EMEA-000876-PIP05-15-M01

Alexion Europe SAS; Myasthenia Gravis / Treatment of Refractory Generalized Myasthenia Gravis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.14. letermovir - Orphan - EMEA-001631-PIP01-14-M01

Merck Sharp & Dohme (Europe), Inc.; Prevention of cytomegalovirus infection / Prevention of CMV viremia and/or disease in at-risk patients having undergone an allogeneic HSCT or SOT

Day 30 discussion

Infectious Diseases

3.3.15. EMEA-001411-PIP01-12-M03

Gilead Sciences International Ltd; Chronic Viral Hepatitis C infection / Chronic Viral Hepatitis C

infection

Day 30 discussion

Infectious Diseases

3.3.16. Brivaracetam - Orphan - EMEA-000332-PIP01-08-M10

UCB Pharma SA; 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

Day 30 discussion

Neurology

3.3.17. Decitabine - Orphan - EMEA-000555-PIP01-09-M05

Janssen-Cilag International NV; Acute Myeloid Leukaemia / 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 30 discussion

Oncology

3.3.18. Regorafenib - EMEA-001178-PIP01-11-M02

Bayer Pharma; Treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue) / Treatment of paediatric patients with a solid malignant tumour(s) integrated with anti-cancer therapy

Day 30 discussion

Oncology

3.3.19. Methoxyflurane - EMEA-000334-PIP01-08-M04

Medical Developments UK Ltd; treatment of acute pain

Day 30 discussion

Pain

3.3.20. 1-(2,2-difluoro-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl}cyclopropanecarboxamide / Ivacaftor - Orphan - EMEA-001640-PIP01-14-M01

Vertex Pharamceuticals (Europe) Ltd; Cystic Fibrosis / Treatment of Cystic Fibrosis

Day 30 discussion

Pneumology - Allergology

3.3.21. AGOMELATINE - EMEA-001181-PIP01-11-M03

Les Laboratoires Servier; Major Depressive Episodes / Major Depressive Episodes

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 21 June 2016 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:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

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. Seribantumab - EMEA-11-2016

Merrimack Pharmaceuticals U.K. Limited; Treatment of breast carcinoma/ In combination with exemestane or fulvestrant for the treatment of postmenopausal women and men with ER positive, HER2 negative, HRG positive advanced breast cancer following prior cyclin-dependent kinase inhibitor therapy for advanced or metastatic disease

Summary of committee discussion:

The applicability of the class waiver as referred to in the Agency's Decision CW/1/2011 to the planned therapeutic indication was confirmed.

Other potential paediatric interest of this medicine suggested by PDCO: currently none.

6.1.2. EMEA-12-2016

Bayer Pharma AG; Androgen receptor modulator medicinal products for treatment of prostate malignant neoplasms/ Treatment of patients with high risk non-metastatic castration-resistant prostate cancer (nmCRPC) as defined by a prostate specific antigen (PSA) doubling time of $\leqslant$ 10 months

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 interest of this medicine suggested by PDCO: currently none.

6.1.3. Rovalpituzumab tesirine - EMEA-13-2016

Stemcentrx, Inc.; Treatment of lung carcinoma (small cell and non-small cell carcinoma)/ Treatment of adult patients with DLL3-expressing extensive stage small cell lung cancer which have received at least two prior systemic therapies, including a platinum-based regimen; or as maintenance therapy in patients who have achieved clinical benefit from front-line platinum-based chemotherapy

Summary of committee discussion:

The applicability of the class waiver as referred to in the Agency's Decision CW/1/2011 to the planned therapeutic indication was confirmed.

Other potential paediatric interest of this medicine suggested by PDCO: paediatric cancers for which there is evidence that aberrations of DLL3 and of other targets in the NOTCH pathway are relevant (e.g. in public repositories of clinically annotated genomic data (e.g., R2), datasets from patients with a neuroblastoma indicate a strong adverse prognostic relevance of high DLL3 expression for overall survival. In addition, DLL3 amplifications and have been found in high-grade glioma in paediatric patients (e.g., Bax et al. 2010)).

Note: in case of removal from the list of class waivers listed in the Agency's Decision CW/1/2011, the requirements set out in Article 7 and 8 of Regulation (EC) No 1901/2006 of the Agency's Decision CW/0001/2015 shall apply after 36 months from the date of the removal

from the list of class waivers.

6.1.4. Chimeric monoclonal antibody against claudin-18 splice variant 2 - EMEA-14-2016

GANYMED Pharmaceuticals AG; Treatment of gastric adenocarcinoma/ Treatment of adult patients with advanced metastatic CLDN18.2-positive, HER2-negative adenocarcinoma of the stomach and gastroesophageal junction (including Siewert type I, II, III tumors) on top of on top of platinum and fluoropyrimidine-based standard of care chemotherapy

Summary of committee discussion:

The applicability of the class waiver as referred to in the Agency's Decision CW/1/2011 to the planned therapeutic indication was confirmed.

Other potential paediatric interest of this medicine suggested by PDCO: currently none.

Note: in case of removal from the list of class waivers listed in the Agency's Decision CW/1/2011, the requirements set out in Article 7 and 8 of Regulation (EC) No 1901/2006 of the Agency's Decision CW/0001/2015 shall apply after 36 months from the date of the removal from the list of class waivers.

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

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

None

8. Annual reports on deferrals

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

9. Organisational, regulatory and methodological matters

9.1. Mandate and organisation of the PDCO

None

9.2. Coordination with EMA Scientific Committees or CMDh-v

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

Summary of committee discussion:

The PDCO members were informed about 5 products, Flixabi, Galafold, Pandemic influenza vaccine H5N1 MedImmune, Strimvelis and Humira, for which the CHMP adopted positive opinions recommending paediatric indications during their meeting in March 2016.

9.2.2. Draft Agenda for the Strategic Review and Learning Meeting to be held on 1-3 June 2016 in Utrecht, the Netherlands

PDCO member: Hendrik van den Berg, Maaike van Dartel

Summary of committee discussion:

The Committee noted the draft agenda of the meeting.

9.2.3. Canagliflozin – INVOKANA (CAP); canagliflozin, metformin – VOKANAMET (CAP)

Applicant: Janssen-Cilag International N.V; Treatment of type 2 diabetes mellitus

PRAC Rapporteur: Valerie Strassmann

Scope: Article 20 procedure to PRAC was triggered by European Commission on 15 April 2016, Signal of potential increased risk of lower limb amputations

Summary of committee discussion:

The PDCO was informed by the PRAC Rapporteur about the ongoing review of canagliflozin (Article 20 of Regulation (EC) No 726/2004) following data on toe amputations in ongoing CANVAS study (CANagliflozin cardioVascular Assessment Study), a long-term cardiovascular outcome study.

Furthermore, Elke Stahl from the Clinical Trials Facilitation Group (CFTG) was invited to update the PDCO on ongoing clinical trials with canagliflozin.

It was agreed that the PRAC will keep the PDCO informed about the on-going review.

The importance of PRAC/CHMP considering the paediatric population as regards arising safety issues was emphasized.

9.2.4. Concept paper on the need for revision of the guideline on the clinical development of medicinal products for the treatment of cystic fibrosis

Summary of committee discussion:

The Committee was informed that the CHMP respiratory drafting group is currently preparing the concept paper on the need to revise the CF guideline. The draft concept paper will be circulated in the PDCO post-mail with the request to review and to notify the respiratory drafting group in case of important deficiencies.

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

PDCO member: Dina Apele-Freimane

Summary of committee discussion:

The concept paper was discussed and adopted by the PDCO.

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

9.3.1. Non-clinical Working Group: D30 Products identified

PDCO member: Jacqueline Carleer

Summary of committee discussion:

The chair of the NcWG identified the products which will require NcWG evaluation and discussion.

9.3.2. Formulation Working Group

PDCO member: Brian Aylward

Summary of committee discussion:

Relevant products for FWG discussion were identified.

9.3.3. Inventory of paediatric therapeutic needs – respiratory

PDCO member: Ninna Gullberg, Sabine Scherer

Summary of committee discussion:

The committee discussed whether fixed dose combinations of inhaled corticosteroids with long acting beta-2 agonists for the treatment of asthma, should be included in the respiratory inventory. Swedish data demonstrating the off-label use of in children under the age of 5 were presented.

The committee adopted the respiratory inventory for a two month public consultation.

9.4. Cooperation within the EU regulatory network

9.4.1. Reflection on the late submission of PIPs

PDCO Chair: Dirk Mentzer

Summary of committee discussion:

The Committee discussed with concern the problem of very late submissions of PIP applications from some pharmaceutical companies, which may lead to difficulties for the companies and a delay in the marketing authorisation. EMA scientific staff reported that companies are routinely informed of the need to submit a PIP/waiver application according to the legislation and published guidelines, in all pre-authorisation interactions, such as development pipeline meetings, PRIME eligibility procedures, orphan designation pre-submission meetings, and in several other instances. A discussion of this concern and its implications will be included in a general report to the European Commission.

9.4.2. EU Network Training Centre (EU NTC) Paediatric Curriculum

Summary of committee discussion:

The PDCO was informed about the set-up of an 'EU NTC Paediatric Curriculum'.

The EU Network Training Centre (EU NTC) is a new initiative on training for the European Medicines Regulatory Network (EMRN). One of the aims is to provide continuous professional development for staff of national regulatory agencies and EMA.

For more details see: http://www.hma.eu/otsg.html?&L=0

A draft outline of the EU NTC Paediatric Curriculum was presented to the PDCO. This course will provide an overview of the EU Paediatric Regulation and the Paediatric Investigation Plan (PIP) lifecycle. Furthermore, special scientific topics in paediatric drug development will be covered. These include lectures on paediatric formulations, non-clinical requirements to support the development of paediatric medicines as well as lectures related to the conduct of clinical trials in the paediatric population (general and disease specific, including also methodological considerations when the number of patients is limited). Also, a lecture on pharmacovigilance considerations in paediatric drug development will be part of this curriculum.

Topics will be presented through pre-recorded lectures by experts in the field. Individual lectures will be 20-60min and the overall curriculum will be about 1-2 days. The envisaged timeline for the completion of this curriculum is December 2016. The curriculum is modular and can be complemented over time by additional lectures.

The PDCO welcomed this initiative of an EU NTC Paediatric Curriculum. It was noted by several PDCO members that training material on paediatric drug development has also been generated through the Global Research in Paediatrics (GRiP) scientific network. It was agreed to investigate if and how this training material could be used to further complement the EU NTC Paediatric Curriculum. PDCO members reminded to not waste resources by duplicating existing training material.

PDCO members will be given 2 weeks to comment on the outline of the EU NTC Paediatric Curriculum. The feedback will be re-discussed at the May 2016 PDCO plenary.

9.4.3. 10-year Report to the European Commission (EC)

Summary of committee discussion:

The report was presented to the committee and the next steps were outlined.

9.5. Cooperation with International Regulators

None

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

None

9.7. PDCO work plan

None

9.8. Planning and reporting

None

9.9. PDCO ORGAM

9.9.1. PDCO ORGAM Draft Minutes for 16 March 2016

Summary of committee discussion:

The PDCO ORGAM minutes for the meeting held on 16 March 2016 were adopted by the PDCO.

9.10. Other

9.10.1. EMA Workshop on the use of Single Arm Trials in Oncology products to be held on 30 June 2016

Summary of committee discussion:

The draft agenda of the workshop was presented to the Committee.

10. Any other business

10.1. None

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

The participation in the Oncology working party and in forthcoming workshops was prepared. The exchange with external stakeholders was discussed. The discussion of an anti-cancer medicine in the plenary of the Paediatric Committee was prepared.

11.1.2. Neonatology

Summary of committee discussion:

The participation at the International Neonatal Consortium was discussed as well as the concept paper on the planned revision of the Neonatal Guideline.

11.1.3. Inventory

Summary of committee discussion:

This session was cancelled.

The Chair thanked the participants and closed the 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 PDCO 29 March – 1 April 2016 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	
Christoph Male	Alternate	Austria	No participation in final deliberations and voting on the following products or a rival product:	EMEA-001114-PIP01-10-M03 EMEA-001839-PIP01-15 EMEA-000753-PIP02-16 EMEA-001203-PIP02-14-M01
Koenraad Norga	Member (Vice-Chair)	Belgium	No restrictions applicable to this meeting	
Jacqueline Carleer	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Suzana Mimica Matanovic	Alternate	Croatia	No participation in discussions, final deliberations and voting on:	EMEA-001839-PIP01-15 EMEA-001918-PIP01-15
Jaroslav Sterba	Member	Czech Republic	No interests declared	
Marianne Orholm	Member	Denmark	No interests declared	
Jana Lass	Alternate	Estonia	No interests declared	
Ann Marie Kaukonen	Member	Finland	No interests declared	
Sylvie Benchetrit	Member	France	No interests declared	
Immanuel Barth	Member	Germany	No interests declared	
Sabine Scherer	Alternate	Germany	No interests declared	
Grigorios Melas	Member	Greece	No interests declared	
Francesca Rocchi	Alternate	Italy	No restrictions applicable to this meeting	
Dina Apele-Freimane	Member	Latvia	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No restrictions applicable to this meeting	
Herbert Lenicker	Alternate	Malta	No interests declared	
Maaike van Dartel	Alternate	Netherlands	No interests declared	
Siri Wang	Member	Norway	No interests declared	
Ine Skottheim Rusten	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	
Stefan Grosek	Member	Slovenia	No interests declared	
Maria Jesús Fernández Cortizo	Alternate	Spain	No interests declared	
Ninna Gullberg	Member	Sweden	No interests declared	
Angeliki Siapkara	Member	United Kingdom	No interests declared	
Martina Riegl	Alternate	United Kingdom	No interests declared	
Riccardo Riccardi	Member	Healthcare Professionals' Representative	No participation in discussions, final deliberations and voting on:	EMEA-001072-PIP01-10-M02
Paolo Paolucci	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	
Tsvetana Schyns-Liharska	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Kerry Leeson-Beevers	Alternate	Patients' Organisation Representative	No restrictions applicable to this meeting	
Sara Homer	Expert - in person*	United Kingdom	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Juliana Min	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Valerie Strassmann	Expert -via tele-conference*	Germany	No interests declared	
Elke Stahl	Expert – via tele-conference*	Germany	No restrictions applicable to this 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/