15 July 2015
EMA/PDCO/351567/2015
Procedure Management and Committees Support Division

Paediatric Committee (PDCO)

Minutes for the meeting on 17-19 June 2015

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

17 June 2015, 08:30- 19:00, room 3A

18 June 2015, 08:30- 19:00, room 3A

19 June 2015, 08:30- 13:00, room 3A

Disclaimers

Some of the information contained in this agenda 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).

Note on access to documents

Some documents mentioned in the agenda 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

2.1. Opinions on Products

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

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.4. Opinions on Re-examinations

No re-examinations for the month of June.

2.5. Finalisation and adoption of opinions

The opinions adopted during the Paediatric Committee meeting of June 2015 are published in the same month's meeting report published on the EMA website:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/document_listing/document_listing_000192.jsp&mid=WC0b01ac0580028eab

3. Discussion of applications

3.1. Discussions on Products D90-D60-D30

The PDCO discussed 75 procedures in total[1], of which:

- 27 paediatric investigation plan applications;
- 10 product-specific waiver applications;
- 12 compliance check procedures (interim and final);
- 26 requests for modifications of an agreed paediatric investigation plan.

4. Nominations

4.1. List of letters of intent received for submission of applications with start of procedure August 2015 for Nomination of Rapporteur and Peer reviewer

Summary of committee discussion:

The PDCO approved the list of Rapporteurs.

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 list of Rapporteurs.

4.3. Nominations for other activities

[1] The procedures discussed by the PDCO are on-going and therefore are considered confidential. Additional details on these procedures will be disclosed 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).

4.3.1. Re-nomination of two PDCO representatives to the PaedForm project: Professor Anthony Nunn and Doctor Siri Wang

Summary of committee discussion:

The Paediatric Formulary Group of the European Pharmacopoeia (PaedForm project) is run under the auspices of the European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) in close collaboration with the European Commission to improve accessibility to suitable and age-appropriate formulations for children. The PDCO re-nominated Professor Anthony Nunn and Doctor Siri Wang as PDCO representatives to the PaedForm project.

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.

5.1. Discussions on first reports of SAWP products with paediatric interest

5.2. Discussions on SAWP products following a discussion meeting with companies

6. Discussion on the applicability of class waivers

6.1. Discussions on the applicability of class waiver for products

6.1.1. G-5745 (Recombinant humanized anti-MMP9 mAb IgG4) - EMEA-19-2015

Gilead Sciences International Ltd; Treatment of gastric adenocarcinoma/ First-line treatment of patients with inoperable, locally advanced, or metastatic gastric or gastroesophageal junction adenocarcinoma, in combination with standard of care chemotherapy

Rapporteur: Paolo Paolucci

Summary of committee discussion:

The applicability of the class waiver to the planned therapeutic indication was confirmed. Potential paediatric interest of this medicine suggested by PDCO: ulcerative colitis, Crohn's disease, cystic fibrosis, Duchenne muscular dystrophy, juvenile idiopathic arthritis and solid tumours (glioblastoma multiforme, soft tissue sarcomas, neuroblastoma).

6.1.2. Glycopyrronium Bromide - EMEA-21-2015

Pearl Therapeutics, Inc.; Treatment of chronic obstructive pulmonary disease (COPD)

(excluding chronic lung diseases associated with long-term airflow limitation, such as asthma, bronchopulmonary dysplasia, primary cilia dyskinesia, obstructive lung disease related to graft-versus-host disease after (bone-marrow) transplantation)/Maintenance bronchodilator treatment in adult patients with COPD

Rapporteur: Angelika Siapkara;

Summary of committee discussion:

The applicability of the class waiver to the planned therapeutic indication was confirmed. Potential paediatric interest of this medicine suggested by PDCO: treatment of asthma.

6.1.3. Aducanumab - EMEA-23-2015

Biogen Idec Ltd; Treatment of Alzheimer's disease/ Treatment of early symptomatic Alzheimer's disease

Rapporteur: Fernando de Andrés Trelles

Summary of committee discussion:

The applicability of the class waiver to the planned therapeutic indication was confirmed.

6.1.4. binimetinib – EMEA-30-2015

Novartis Europharm Ltd; 1) treatment of melanoma (from 0 to less than 12 years old)/treatment of patients with unresectable or metastatic melanoma harbouring NRAS mutations, treatment of adult patients with unresectable or metastatic melanoma harbouring BRAF V600 mutations in combination with encorafenib; 2) treatment of recurrent or persistent low-grade serous carcinomas of the ovary, fallopian tube or primary peritoneum/ treatment of ovarian carcinoma (excluding rhabdomyosarcoma and germ cell tumours), treatment of fallopian tube carcinoma (excluding rhabdomyosarcoma and germ cell tumours) and treatment of peritoneal carcinoma (excluding blastomas and sarcomas)

Rapporteur: Maaike van Dartel

Summary of committee discussion:

1) The applicability of the class waiver to the planned therapeutic indication reported at point 1, for the age group from birth to less than 12 years of age, was confirmed during the assessment of the procedure EMEA-001454-PIP03-15 (listed in the Agenda PDCO 17-19 June 2015 under point 3.1.22).

2) The applicability of the class waiver to the planned therapeutic indication was confirmed during the assessment of the procedure EMEA-001454-PIP03-15 (listed in the Agenda PDCO 17-19 June 2015 under point 3.1.22).

6.1.5. encorafenib – EMEA-31-2015

Novartis Europharm Ltd; Treatment of melanoma (from 0 to less than 12 years old)/ Treatment of adult patients with unresectable or metastatic melanoma harbouring BRAF V600 mutations in combination with binimetinib

Rapporteur: Maaike van Dartel

Summary of committee discussion:

The applicability of the class waiver to the planned therapeutic indication, for the age group from birth to less than 12 years of age, was confirmed during the assessment of the procedure EMEA-001588-PIP01-13 (listed in the Agenda PDCO 17-19 June 2015 under point 3.1.21).

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

No requests were received for the month of June 2015.

8. Annual reports on deferrals

8.1.1. Rituximab – MabThera – EMEA-000308-PIP01-08

Roche Registration Ltd

Difficulties progressing the PIP? Yes

Summary of committee discussion:

The committee noted the report and the progress of the large international trial.

8.1.2. Rituximab – MabThera – EMEA-000308-PIP02-11

Roche Registration Ltd

Difficulties progressing the PIP? No

Summary of committee discussion:

The report was noted by the Committee.

8.1.3. Artemether (20mg) and lumefantrine (120mg) – RIAMET (in all EU), Coartem in some countries such as US, Switzerland, Australia, African countries...- EMEA-000777-PIP01-09

Novartis Europharm Limited

Difficulties progressing the PIP? Yes

Summary of committee discussion:

The PDCO noted the report. The issues have already been addressed in the modification to

the agreed PIP (M05).

8.1.4. Denosumab – XGEVA (previously Amgiva), Prolia – EMEA-000145-PIP01-07

Amgen Europe B.V.

Difficulties progressing the PIP? No

Summary of committee discussion:

The PDCO noted the report.

8.1.5. Denosumab – XGEVA (previously Amgiva), Prolia – EMEA-000145-PIP02-12

Amgen Europe B.V.

Difficulties progressing the PIP? No

Summary of committee discussion:

The PDCO noted the report.

8.1.6. Aripiprazole – Abilify – EMEA-000235-PIP02-10

Otsuka Pharmaceutical Europe Ltd.

Difficulties progressing the PIP? No

Summary of committee discussion:

The PDCO noted the report.

8.1.7. Icatibant acetate – Firazyr – EMEA-000408-PIP01-08 – Orphan

Jerini AG

Difficulties progressing the PIP? No

Summary of committee discussion:

The PDCO noted the report.

9. Organisational, regulatory and methodological matters

9.1. Mandate and organisation of the PDCO

9.1.1. Review of PDCO meeting agenda (feedback from Strategic Review and Learning Meeting in Frankfurt 28-29 May 2015)

PDCO member: Dirk Mentzer

Summary of committee discussion:

The PDCO Chair gave a presentation on optimisation of plenary discussions based on collection of data over 6 months.

9.1.2. Communication of PDCO activities/outcomes to the public (feedback from Strategic Review and Learning Meeting in Frankfurt 28-29 May 2015)

PDCO member: Koenraad Norga

Summary of committee discussion:

The PDCO Vice-Chair reported from the Strategic Review and Learning Meeting discussion held in Frankfurt on 29 May 2015 highlighting the need for PDCO to enhance regular communication to stakeholders on PDCO activities and outcomes.

9.1.3. Full waivers for fixed-dose combination for antihypertensive drugs

Summary of committee discussion:

The Committee heard a presentation from the EMA coordinator on recent literature published on antihypertensive drugs. In light of increasing prevalence of hypertension in children, there might be a need for authorised fixed dose combination of antihypertensive drugs at least in adolescents. A group of interested PDCO members will start discussion if the current position of the PDCO to always grant full waivers for this type of medicines might need to be reconsidered.

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, Repatha, Unituxin, Fycompa, Kuvan and Stelara, for which the CHMP adopted a positive opinion recommending paediatric indications during their meeting in May 2015.

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:

Documents tabled for information.

9.3.2. Formulation Working Group: D30 Products identified

PDCO member: Brian Aylward

Summary of committee discussion:

Documents tabled for information.

9.3.3. Paediatric Investigation Plan for DTaP-containing combination vaccine

PDCO member: Marta Granström

Summary of committee discussion:

The PDCO adopted the final document, after revisions implementing some of the public comments received and final comments from the Vaccine Working Party (VWP). The PDCO also adopted the answers to the public comments.

Both documents will be presented at CHMP plenary in June 2015 and will be published on EMA website after CHMP adoption.

9.4. Cooperation within the EU regulatory network

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

Summary of committee discussion:

The committee was informed about the annual Enpr-EMA workshop. Both PDCO and Enpr-EMA members agree to start generic discussions (not related to specific PIPs) in specific therapeutic areas. Cystic fibrosis (CF) was selected as first therapeutic area. A dedicated Enpr-EMA CF-working group shall be established with members from the Cystic Fibrosis Society - Clinical Trials Network (ECFS-CTN) and PDCO members. PDCO members were invited to express their interest in becoming a member of this working group.

9.4.2. Debriefing from the European Parliament Workshop on the Paediatric Regulation held on 16 June 2015

PDCO member: Koenraad Norga

Summary of committee discussion:

The Committee was informed about the proceedings of a workshop entitled "The Paediatric Regulation: are children still missing out on potentially life-saving treatments?" organised by the European parliament's Health Working Group. The committee noted that a recording of the event can be viewed at http://www.europarl.europa.eu/ep-live/en/committees/video?event=20150616-1030-COMMITTEE-ENVI

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

None

10. Any other business

10.1. EMA 20th anniversary event on innovation and early dialogue with experts and staff

Wednesday 17 June 2015, 13:00-14:00, Promenade lounge (-1)

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

The participants discussed a strategy for future interactions with stakeholders.

11.1.2. Neonatology

Summary of committee discussion:

The outcome of the workshop launching the International Neonatal Consortium which took place at the EMA 18-19 May 2015 was discussed.

11.1.3. Inventory

Summary of committee discussion:

The group met to discuss vaccines as part of the immunology inventory list.

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 17-19 June 2015 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	To be replaced for discussions, final deliberations and voting when chairing the meeting	EMEA-000431-PIP01-08-M08 EMEA-001749-PIP01-15 EMEA-001569-PIP01-13 EMEA-001359-PIP01-12-M02 EMEA-C1-000520-PIP01-08-M04 EMEA-C1-000520-PIP02-13-M01
Jacqueline Carleer	Alternate	Belgium	No restrictions applicable to this meeting	
Violeta Iotova	Member	Bulgaria	No participation in discussions, final deliberations and voting	EMEA-000694-PIP01-09-M05 EMEA-001755-PIP01-15
Marina Dimov Di Giusti	Member	Croatia	No interests declared	
Georgios Savva	Member	Cyprus	No interests declared	
Jaroslav Sterba	Member	Czech Republic	No interests declared	
Marianne Orholm	Member	Denmark	No interests declared	
Marta Granström	Alternate	Denmark	No interests declared	
Irja Lutsar	Member	Estonia	No interests declared	
Ann Marie Kaukonen	Member	Finland	No interests declared	
Maija Pihlajamaki	Member	Finland	No interests declared	
Sylvie Benchetrit	Member	France	No interests declared	
Birka Lehmann	Member	Germany	No interests declared	
Immanuel Barth	Alternate	Germany	No interests declared	
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
Paolo Rossi	Member	Italy	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Francesca Rocchi	Alternate	Italy	No restrictions applicable to this meeting	
Dina Apele-Freimane	Member	Latvia	No interests declared	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No restrictions applicable to this meeting	
John-Joseph Borg	Member	Malta	No interests declared	
Hendrik van den Berg	Member	Netherlands	No interests declared	
Siri Wang	Member	Norway	No interests declared	
Ine Skottheim Rusten	Alternate	Norway	No interests declared	
Marek Migdal	Member	Poland	No restrictions applicable to this meeting	
Jolanta Witkowska-Ozogowska	Alternate	Poland	No interests declared	
Helena Fonseca	Member	Portugal	No interests declared	
Hugo Tavares	Alternate	Portugal	No interests declared Connected via teleconference for EMEA-001054-PIP01-10-M03 and EMEA-001753-PIP01-15	
Dana Gabriela Marin	Member (CHMP alternate)	Romania	No interests declared	
Stefan Grosek	Member	Slovenia	No interests declared	
Fernando de Andrés Trelles	Member	Spain	No interests declared	
Maria Jesús Fernández Cortizo	Alternate	Spain	No interests declared	
Ninna Gullberg	Member	Sweden	No restrictions applicable to this meeting	
Anna-Karin Hamberg	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 participation in discussions, final deliberations and voting	EMEA-000461-PIP02-11-M01
Paolo Paolucci	Alternate	Healthcare Professionals' Representative	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Doina Plesca	Alternate	Healthcare Professionals' Representative	No participation in discussions, final deliberations and voting	EMEA-C2-001202-PIP02-13 EMEA-C-000319-PIP01-08-M03 EMEA-000431-PIP01-08-M08 EMEA-C4-000467-PIP01-08-M06 EMEA-001617-PIP01-14 EMEA-C1-000696-PIP02-10-M05 EMEA-000402-PIP02-11-M02 EMEA-001217-PIP01-11-M01
Paola Baiardi	Alternate	Patients' Organisation Representative	No interests declared	
Kerry Leeson-Beevers	Alternate	Patients' Organisation Representative	No restrictions applicable to this meeting	
Katherine McGinn	Expert - via telephone*	United Kingdom	No interests declared	
Meeting run with support from relevant EMA staff				

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

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/