12 August 2015
EMA/PDCO/471874/2015
Procedure Management and Committees Support Division

Paediatric Committee (PDCO)

Minutes for the meeting on 15-17 July 2015

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

15 July 2015, 08:30- 19:00, room 3A

16 July 2015, 08:30- 19:00, room 3A

17 July 2015, 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).

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 and addition of a topic under point 10.3.

1.3. Adoption of the minutes

The minutes were adopted with amendments and will be published on the EMA website.

2. Opinions[1]

Disclosure of 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

2.2. 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

[1] Please refer to the 15-17 July 2015 PDCO monthly report published on the EMA Website, see PDCO meeting reports

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.4. Opinions on Re-examinations

2.5. Finalisation and adoption of opinions

3. Discussion of applications

Disclosure of 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

3.2. 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

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

4. Nominations

4.1. List of letters of intent received for submission of applications with start of procedure September 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

4.3.1. Nomination of PDCO experts for comments on the 'Draft Guidance document on Uncertainty in Scientific Assessment' developed by the European Food Safety Authority (EFSA)

Summary of committee discussion:

EFSA's Scientific Committee has developed this guidance document to offer a tool-box of methodologies – both quantitative and qualitative – for analysing scientific uncertainties in all its scientific assessments. EFSA invites input on this draft from other scientific advisory bodies as well as academic or applied experts in uncertainty analysis, particularly on the proposed methods contained in the tool box.

Johannes Taminiau, Sylvie Benchetrit, Karl-Heinz Huemer and Brian Aylward expressed their interest to provide comments on the draft document.

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. Edaravone - EMEA-24-2015

Mitsubishi Tanabe Pharma Europe Ltd.; Treatment of amyotrophic lateral sclerosis/ Treatment of amyotrophic lateral sclerosis

Rapporteur: Fernando de Andres Trelles

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: acute ischaemic stroke.

6.1.2. Nintedanib - EMEA-25-2015

Boehringer Ingelheim International GmbH; Treatment of adenocarcinoma of the colon

and rectum/ Treatment of metastatic colorectal carcinoma

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: brain tumours (glioblastoma multiforme, low grade astrocytoma), neuroblastoma, Wilms tumour, haemangioma and acute myeloid leukaemia.

6.1.3. REGN910-3 (REGN910:aflibercept) - EMEA-26-2015

Regeneron Pharmaceuticals, Inc.; Treatment of age-related macular degeneration and diabetic macular oedema/ Treatment of neovascular (wet) age-related macular degeneration and diabetic macular oedema

Rapporteur: Jacqueline Carleer

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: retinopathy of prematurity.

6.1.4. Imetelstat (sodium) - EMEA-27-2015

Janssen-Cilag International N.V; Treatment of primary myelofibrosis/ Treatment of primary myelofibrosis

Rapporteur: Sylvie Benchetrit

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: myelodysplastic syndromes, acute myeloid leukaemia, neuroblastoma, Wilms tumour, hepatoblastoma, Ewing sarcoma and central nervous system tumours.

6.1.5. BAY 949343 - EMEA-28-2015

Bayer Pharma AG; Treatment of mesothelioma/ Treatment of patients with locally advanced or metastatic, mesothelin-overexpressing, malignant mesothelioma

Rapporteur: Koenraad Norga

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: it was concluded that further studies are needed to assess the presence of the drug target in paediatric malignancies.

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 July.

8. Annual reports on deferrals

8.1.1. deferasirox – Exjade - EMEA-001103-PIP01-10 - Orphan

Novartis Europharm Limited

Difficulties progressing the PIP? No

Summary of committee discussion:

The PDCO noted the report.

8.1.2. Ceftaroline fosamil (established INN) – Zinforo - EMEA-000769-PIP01-09

AstraZeneca AB

Difficulties progressing the PIP? No

Summary of committee discussion:

The PDCO noted the report.

8.1.3. boceprevir – Victrelis - EMEA-000583-PIP01-09

SP Europe

Difficulties progressing the PIP? Yes

Summary of committee discussion:

The PDCO noted the report.

8.1.4. Liraglutide – Victoza - EMEA-000128-PIP01-07

Novo Nordisk A/S

Difficulties progressing the PIP? Yes

Summary of committee discussion:

The company reported recruitment issues in their paediatric clinical study.

8.1.5. Liraglutide – Saxenda - EMEA-000128-PIP02-09

Novo Nordisk A/S

Difficulties progressing the PIP? No

Summary of committee discussion:

The PDCO noted the report.

8.1.6. ponatinib – Ponatinib - EMEA-001186-PIP01-11 - Orphan

ARIAD Pharma, Ltd.

Difficulties progressing the PIP? Yes

Summary of committee discussion:

The PDCO noted the report and is still awaiting a request for modification of the agreed PIP.

8.1.7. N-[3-[3-cyclopropyl-5-[(2-fluoro-4-iodophenyl)amino]- 6,8-dimethyl-2,4,7-trioxo-... – Mekinist - EMEA-001177-PIP01-11

GlaxoSmithKline Trading Service Limited

Difficulties progressing the PIP? Yes

Summary of committee discussion:

The PDCO noted the report.

8.1.8. Obinutuzumab – Gazyvaro - EMEA-001207-PIP01-11 - Orphan

Roche Registration Limited

Difficulties progressing the PIP? Yes

Summary of committee discussion:

The PDCO noted the report.

8.1.9. Belimumab – Benlysta - EMEA-000520-PIP01-08

Glaxo Group Limited

Difficulties progressing the PIP? No

Summary of committee discussion:

The paediatric development progresses according to plan.

8.1.10. Sunitinib malate - Sutent- EMEA-000342-PIP01-08 - Orphan

Pfizer Limited

Difficulties progressing the PIP? Yes

Summary of committee discussion:

The PDCO noted the report.

8.1.11. Belatacept – Nulojix - EMEA-000157-PIP01-07

Bristol-Myers Squibb International Corporation

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

None

9.1.1. PDCO Opinion on revision of class waiver list

Rapporteur: Hendrik van den Berg, Koenraad Norga

Summary of committee discussion:

The PDCO acknowledged the consolidated comments received from the pharmaceutical industry stakeholders and then adopted an opinion on the revision of the list of class waivers.

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 4 products, Kanuma, Raxone, Strensiq and Levemir, for which the CHMP adopted a positive opinion recommending paediatric indications during their meeting in June 2015. A new oral powder formulation as a replacement for the currently marketed Norvir oral solution was approved for the paediatric population.

At request of the Committee, background document on the CHMP opinion on Heparesc will be circulated in the post meeting mailing.

9.2.2. sodium-glucose co-transporter-2 (SGLT2) inhibitors

Treatment of type 2 diabetes

PRAC review following referral under Article 20 of Regulation (EC) 726/2004 following a safety signal of diabetic ketoacidosis (DKA)

Summary of committee discussion:

Following reports of diabetic ketoacidosis in patients on SGLT-2 inhibitor treatment for

type 2 diabetes the European Medicines Agency (EMA) has started a review for this class of medicinal products:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/SGLT2_inhibitors/human_referral_prac_000052.jsp&mid=WC0b01ac05805c516f

The PDCO discussed this potential safety risk with regards to the currently agreed PIPs in this class of medicinal products for type 1 and type 2 diabetes. Following these discussions, the PDCO decided to pro-actively contact companies who have PIPs agreed in this class of medicinal products and recommend inclusion of a relevant safety parameter within their paediatric clinical studi(es) to monitor the potential risk of diabetic ketoacidosis in the paediatric population (i.e. once daily ketone body measurements in the urine or once daily blood ketones self-measurement). The PDCO believes that this is an important measure to allow early detection of this potential safety risk.

Furthermore, the PDCO agreed to liaise internally with the Pharmacovigilance Risk Assessment Committee (PRAC) for a general recommendation for paediatric developments in this class of products in terms of monitoring measures (pre- and/or post-marketing).

9.2.3. Draft Scientific guidance on Post-Authorisation Efficacy Studies (PAES)

Summary of committee discussion:

The PDCO noted the first draft of Scientific Guidance on Post-authorisation Efficacy Studies (PAES). This guidance is intended to provide scientific guidance for MAHs and for competent authorities regarding PAES in the EU on the general need for such studies, on general methodological considerations, on specific situations and on study conduct. The guideline has been released for 3 months public consultation. PDCO was invited to send comments during the consultation period.

9.2.4. Report from PDCO-PRAC Strategic Review and Learning Meeting in Frankfurt held on 28-29 May 2015

Resource: Dirk Mentzer

Summary of committee discussion:

The Committee noted a joint report by the PDCO and PRAC Chairs from the PDCO-PRAC Strategic Review and Learning Meeting in Frankfurt held on 28-29 May 2015.

PDCO members were invited to send comments on the summary and proposed action plan which will be endorsed in September 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

PDCO member: Brian Aylward

Summary of committee discussion:

Documents tabled for information.

9.4. Cooperation within the EU regulatory network

9.4.1. EU Network Training Centre

Summary of committee discussion:

The Committee was informed of the launch and objectives of the EU Network Training Centre, a European central platform for exchange of training information across the European Medicines Regulatory Network. Possibilities for Members and for their Agencies to use the network and to contribute to its courses were presented.

9.4.2. List of paediatric rare diseases lacking satisfactory treatments

Summary of committee discussion:

A list of possible paediatric rare diseases to be recommended for EU funding programmes was presented. The committee will assess and review the list to be possibly adopted in the plenary meeting in August.

9.4.3. PDCO support for Enpr-EMA involvement in planned IMI project to develop European paediatric clinical trial network

Summary of committee discussion:

The PDCO adopted a letter in support of Enpr-EMA involvement in a planned IMI2 project to develop a Pan-EU Paediatric Clinical Trials Network. The committee expressed its commitment to support and contribute to Enpr-EMA's involvement in this planned initiative.

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. Public summaries of PDCO opinions on agreed PIPs and waivers

Summary of committee discussion:

The PDCO members were informed about the preparation and publication by the EMA of summaries of PDCO evaluation of PIPs and waivers.

10.2. Enhanced early dialogue to foster development and facilitate accelerated assessment

Summary of committee discussion:

The Committee was informed of development of a new scheme that is designed to facilitate the development and accelerated assessment of innovative medicines of major public health interest, in particular from the viewpoint of therapeutic innovation.

10.3. Communication of PDCO activities/outcomes to the public

PDCO member: Koenraad Norga

Action: For discussion

Summary of committee discussion:

PDCO members were invited to comment on a draft editorial on PDCO activities.

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

During the breakout session, the participants discussed interactions with internal and external stakeholders.

11.1.2. Neonatology Working Group

Summary of committee discussion:

The meeting was cancelled.

11.1.3. Inventory Working Group

Summary of committee discussion:

The Inventory Working Group discussed the responses received to the public consultation of the draft inventory of paediatric needs for Gastroenterology.

List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 15-17 July 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 on products from GlaxoSmithKline when chairing the meeting	EMEA-001359-PIP01-12-M02 EMEA-001569-PIP01-13 EMEA-C1-000520-PIP01-08-M04 EMEA-C1-000520-PIP02-13-M01 EMEA-001792-PIP01-15
Jacqueline Carleer	Alternate	Belgium	No restrictions applicable to this meeting	
Violeta Iotova	Member	Bulgaria	No participation in discussions, final deliberations and voting on	EMEA-000200-PIP01-08-M05 EMEA-000498-PIP01-08-M05 EMEA-000828-PIP01-09-M04 EMEA-001030-PIP01-10-M04
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- via telephone	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	
Grigorios Melas	Member	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian	Member	Ireland	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Aylward				
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	
Herbert Lenicker	Alternate	Malta	No interests declared	
Maaike van Dartel	Alternate	Netherlands	No interests declared	
Siri Wang	Member	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	
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	
Ninna Gullberg	Member	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
Maria Grazia Valsecchi	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
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 participation in discussions, final deliberations and voting	EMEA-000402-PIP02-11-M02 EMEA-001217-PIP01-11-M01

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				CHF 5993 (pMDI)
Günther Auerswald	Member	Patients' Organisation Representative	No participation in discussions, final deliberations and voting	EMEA-C2-000971-PIP01-10-M02 EMEA-C1-001215-PIP01-11-M03 EMEA-001296-PIP01-12-M02 RO5534262, ACE910, CH5534262
Tsvetana Schyns-Liharska	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Dominik Karres	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Martina Weise	Expert - via telephone*	Germany	No restrictions applicable to this meeting	
Marion Haberkamp	Expert - via telephone*	Germany	No restrictions applicable to this meeting	
Henrike Potthast	Expert - via telephone*	Germany	No restrictions applicable to this meeting	
A representative from the European Commission attended the meeting via telephone.				
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/