23 April 2014
EMA/PDCO/129787/2014
Human Medicines Research & Development Support Division

Paediatric Committee (PDCO)

Minutes of the 19-21 March 2014 meeting

Chair: Dirk Mentzer - Vice-chair: Koenraad Norga

I Introduction

I.1 Adoption of the minutes from previous meeting

Adopted.

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

I.2 Adoption of the Agenda

Adopted with modifications.

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

I.3 Declaration of Conflict of Interest

See Annex I

I.4 External attendance

Please refer to the March 2014 PDCO monthly 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

I.5 Leaving/New Members and Alternates

Please refer to the March 2014 PDCO monthly 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

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

II Opinions

II.1 Opinions on Products

II.2 Opinions on Compliance Check

II.3 Opinions on Modification of an Agreed Paediatric Investigation Plan

Please refer to the March 2014 PDCO monthly report published in the EMA Website:

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III Discussion of applications

The PDCO discussed 97 procedures in total[1], of which:

- 39 paediatric investigation plan applications;
- 13 product-specific waiver applications;
- 4 compliance check procedures (interim and final);
- 40 requests for modifications of an agreed paediatric investigation plan;
- 1 re-examination request.

IV Nomination of Rapporteurs and Peer reviewers

• List of letters of intent received for submission of applications with start of procedure May 2014[1] for Nomination of Rapporteur and Peer reviewer • Nomination of Rapporteur for requests of confirmation on the applicability of the EMA decision on class waiver	The PDCO approved the lists of Rapporteurs and Peer Reviewers.

V Update and finalisation of opinions and requests for modification

All opinions taken at this meeting (relating to adoption of opinions, recommendations, requests for modifications and applicability of class waivers) were made in the presence of the required quorum of members.

The opinions adopted during the Paediatric Committee meeting of March 2014 are published in the same month's meeting report published in the EMA website: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/document_listing/document_listing_000192.jsp&mid=WC0b01ac0580028eab.

[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).

VI Discussion on the applicability of class waiver

Active substance	Proposed indication	Condition	Outcome	Potential paediatric interest of this medicine suggested by PDCO
MPDL3280A	Treatment of patients with inoperable locally advanced or metastatic PD-L1 positive urothelial bladder cancer, after failure of a platinum-containing chemotherapy regimen	Treatment of ureter and bladder carcinoma	Confirmed	Solid tumours and haematologic malignancies
Patritumab	In combination with erlotinib, for the treatment of heregulin (HRG) high, EGFR inhibitor therapy naïve, EGFR wild type patients with locally advanced or metastatic non-small cell lung cancer after progression on at least one prior systemic therapy	Treatment of lung carcinoma (non-small cell carcinoma)	Confirmed	Insufficient preclinical data are currently available to exclude potential use in children
Bavituximab	Treatment of previously treated non-squamous non-small cell lung cancer	Treatment of lung carcinoma (small cell and non-small cell carcinoma)	Confirmed	Insufficient preclinical data are currently available to exclude potential use in children
GS-9973	Treatment of chronic lymphocytic leukaemia	Treatment of chronic lymphocytic leukaemia	Confirmed	Non-Hodgkin lymphoma and diffuse large B-cell lymphom
GS-9973	Treatment of follicular lymphoma	Treatment of follicular lymphoma	Confirmed	Non-Hodgkin lymphoma and diffuse large B-cell lymphoma

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

No requests were received for the month of March.

VIII Annual reports on deferrals

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan drug	Difficulties progressing the PIP?	Outcome
EMEA-000696-PIP02-10	Eslicarbazepine acetate	Zebinix	No	Yes	The PDCO was informed of the delay due to the need of further PK exploration. The applicant is planning a modification of the agreed PIP.
EMEA-000116-PIP01-07	Retigabine	Trobalt	No	No	The PDCO noted the report.
EMEA-000434-PIP01-08	ambrisentan	Volibris	Yes	Yes	PDCO was informed on the delay for the PIP due to safety concerns.
EMEA-000637-PIP02-10	Lanthanum carbonate hydrate	Fosrenol - Foznol	No	No	The PDCO noted the report.
EMEA-000817-PIP02-11	Purified antigen fractions of inactivated split virion Influenza manufactured in...	Influsplit Tetra and associated names	No	No	The PDCO noted the report. Study 3 has been completed.
EMEA-000170-PIP01-07	Eltrombopag	Revolade	Yes	No	The PDCO noted the report.
EMEA-000170-PIP02-10	Eltrombopag	Revolade	Yes	No	The PDCO noted the report.

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan drug	Difficulties progressing the PIP?	Outcome
EMEA-001066-PIP02-11	Aciclovir	Sitavir	No	No	The PDCO noted the report.
EMEA-000081-PIP01-07	Dabigatran etexilate	Pradaxa	No	Yes	The PDCO noted the report.
EMEA-000087-PIP01-07	Fingolimod hydrochloride	Gilenya	No	No	The PDCO noted the report.

IX Other topics

Guidelines	
HIV guideline – feedback from PENTA	PDCO discussed the feedback from PENTA, with participation of EMA staff from the IDWP secretariat. Overall PDCO could agree to the 24 week duration (primary endpoint) for licensing in children, as proposed by the draft GL but it should be linked to an obligation to generate long-term data. Initial acceptance of 24-week data takes into account that the aim is not to delay the availability of these drugs to the paediatric population, but that 24 weeks are insufficient to gather all necessary information. Longer follow-up (particularly on safety, including growth & development, durability of virological suppression and acceptability/palatability of the paediatric formulations) is necessary and this should be stated more clearly in the G, which currently states only that long-term post-marketing and pharmaco-epidemiological studies are “encouraged”. The need for longer follow-up will be taken into account when the finalisation of the GL will be discussed by IDWP following the end of the consultation period. It is to be noted that this follow-up could not be part of the PIP (since it is to be conducted during or after the assessment for approval).
Concept paper on the revision of the guideline on conduct of pharmacovigilance for medicines used by the paediatric population*	Postponed to next PDCO meeting.
Working groups	
Paediatric inventory	The working group discussed the therapeutic area of ophthalmology.

Paediatric oncology	The working group discussed the revision of the class waivers.
Extrapolation	The working group agreed to proceed with a framework and publish submission guidance for PIP on extrapolation, and the need to define role and responsibilities between PDCO and SAWP when extrapolation measures are in the PIP.
Formulation	No non-product related issues where reported to the Committee.
Non-Clinical	The PDCO was informed of the ICH plans to generate a guideline on juvenile animal testing (please see below).
Other topics	
CHMP update on paediatric topics	The PDCO members were informed about the final CHMP opinions on medicinal products with paediatric interest adopted in February 2014.
Update on Enpr-EMA activities	No updates were to be reported.
Revision of class waivers	The revision of the class waivers was restarted by the PDCO. It had been suspended at the 12-14 June 2013 meeting of the PDCO. The PDCO discussed the steps until the next meeting and over the following months. The revision will be supported by a small task force of the PDCO and the EMA. Preliminary options for handling applications for agreement of a PIP or a product-specific waiver when there are paediatric needs in the absence of a class-waiver were discussed.
Edited revised draft of the Commission Guideline on the format and content of PIP applications*	The Committee and the EMA Secretariat discussed the comments and suggestions provided by stakeholders on the proposed new EC Guideline on the Format and Content of PIP applications. Many of the comments and suggestions were deemed as useful changes or additions to the Guideline; as per request of the European Commission, a revised proposed draft of the final guideline has been prepared by the PDCO and the EMA Secretariat, and will be submitted to the EC promptly.
Overview of waiver-requests and outcomes at PDCO/EMA and FDA (up to 2013)	Statistics about full waiver requests at PDCO/EMA and FDA were presented to the Committee.
Inclusion of young adults into paediatric type 2 diabetes studies: FDA and EMA views	Postponed to next PDCO meeting.
PDCO nominations for Inter-committee Scientific Advisory Group Oncology (IC SAG-O)	The PDCO adopted a list of external experts for nomination as core members and additional members of the IC SAG-O, reflecting the participants of the EMA Paediatric oncology task force.

Questions from PDCO to PKWP - BA/BE demonstration for BCS II and IV compounds	The PDCO was informed about the answers provided by the CHMP to four questions raised by the PDCO regarding formulation performance of low solubility compounds.
Excipient drafts for consultation on Benzalkonium chloride and Gluten*	PDCO were asked to comment on the reports and Q&A prepared for these two excipients.
Plans for a juvenile animal ICH guideline	The PDCO was informed of the ICH plans to generate a guideline on juvenile animal testing. Europe, the US and Japan have their own a guidelines on juvenile animal testing. However, it appears that this has led to conflicting recommendations on the nonclinical development program among regulatory bodies. Therefore, a need for harmonization of the standards for the conditions was seen under which juvenile animal testing is considered informative and necessary for the safety of pediatric clinical trial subjects and to provide guidance on the design and timing of the studies. PhRMA produced the first draft of a Concept Paper. The NcWG of the PDCO will now provide comments on this draft Concept Paper by 03 April 2014 the latest. These comments will then be adopted by PDCO during their April 2014 plenary. The ICH Steering Committee will meet next at 15 April 2014 to discuss comments on the draft Concept Paper. Once the concept paper is adopted 2 experts from Europe/EMA (one from CHMP/SWP and one from PDCO/NcWG) will be nominated to be part of the ICH Expert Working Group (EWG). The EWG will produce the ICH guideline on juvenile animal testing. Their first face-to-face meeting is planned in November 2014.
Paracetamol exposure in pregnancy and risk of ADHD in children	The PDCO was informed of an ongoing PRAC evaluation of two epidemiological studies regarding the paracetamol use during pregnancy and the potential influence on child development and development of ADHD-like symptoms.
Debriefing on - Minutes of PDCO-COMP Working Group*	The PDCO was informed about the working group activities.
Project 2014 - Move to Churchill Place	Topic cancelled. The presentation has been added to the postmail.

Any other business

- Access to D30 Summary Reports (PIPs only) of next PDCO meeting in MMD (time of postmail of previous meeting): this will be started from the next month.
- Assignment of rapporteurship (rapporteur and peer-reviewer) from the same member state: the Committee was reminded that, in principle, it is desirable that the Rapporteur and the Peer Reviewer for any procedure are chosen from different Member States, to ensure a broader representation of differing viewpoints.

- Update on the Centralisation of the Committee Secretariats: the Committee was informed that the Agency is officially centralising the administrative support to the PDCO to the Scientific Committee Support Department in the Procedure Management and Business Support Division. This involves the transfer to the new Department of two assistants from the Paediatric Medicines Office to the new Department. No immediate change in the current procedures or interaction of PDCO members with the Secretariat is expected.
- Resolution of the EP on off-label use, and EC response: the Committee was informed of the European Parliament resolution of 22 October 2013 on the report from the Commission to the Council on the basis of Member States' reports on the implementation of the Council Recommendation (2009/C 151/01) on patient safety, including the prevention and control of healthcare-associated infections, and the relative response from the European Commission.
- Inventory of paediatric therapeutic needs: the PDCO was informed of the possibility to provide comments on the draft inventory for ophthalmology which will be distributed in the postmail.

Note on access to documents

Some documents mentioned in the agenda/minutes cannot be released at present following a request for access to documents under 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).

Annex I to the Minutes of the PDCO of March 2014

Documentation on Declaration of interest of members, alternates 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 Committee members for the upcoming discussions.

In accordance with the Agency's revised Policy and Procedure on the handling of conflicts of interests, participants in this meeting were asked to declare any conflict of interests on the matters for discussion (in particular any changes, omissions or errors to the already declared interests).

Member, alternate, expert name	Outcome restriction following evaluation of electronic evaluation form	Topics on the current Committee Agenda for which this restriction applies
Adriana Ceci	Restriction level XR	EMEA-001333-PIP02-13
Jaroslav Sterba	Restriction level DP	EMEA-001372-PIP02-13
Jaroslav Sterba	Restriction level DP	EMEA-000019-PIP10-13
Marek Migdal	Restriction level DP	EMEA-000325-PIP01-08-M03
Marina Dimov Di Giusti	Restriction level DC	EMEA-001545-PIP01-13
Violeta Iotova	Restriction level XP	EMEA-001030-PIP01-10-M02

Note: the procedures identified in the table above are on-going and therefore considered commercially 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).

No new or additional conflicts were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Scientific Committee members and, where relevant, experts attending the plenary meeting, as announced by the Scientific Committee Secretariat at the start of meeting.

Restriction levels:

Evaluation of the conflict of interest	
Outcome	Impact
R-P	To be replaced for the discussions, final deliberations and voting as appropriate in relation to the relevant product or a competitor product.

XP	Where Individual product involvement is declared - PRODUCT INDICATION: - No involvement with respect to procedures involving the relevant product or a competitor product in the relevant indication i.e. no part in discussions, final deliberations and voting as appropriate as regards these medicinal products. - Cannot act as Rapporteur for these products - [Cannot act as Rapporteur for development of guidelines in concerned therapeutic area].
XC	Where cross product / general involvement is declared - COMPANY: - No involvement (as outlined above) with respect to products from the specified company. - Cannot act as Rapporteur for products from the relevant company(ies).
DP	Where Individual product involvement is declared - PRODUCT INDICATION: - Involvement in discussions only with respect to procedures involving the relevant product or a competitor product i.e. no part in final deliberations and voting as appropriate as regards these medicinal products. - Cannot act as Rapporteur for these products.
DC	Where cross product / general involvement is declared - COMPANY: - Involvement in discussions only with respect to products from the specified company. - Cannot act as Rapporteur on products from the relevant company(ies).
XR	Committee member cannot act as Rapporteur or Peer reviewer in relation to any medicinal product from the relevant company.
R-C	To be replaced for the discussions, final deliberations and voting as appropriate in relation to any medicinal product from the relevant company

Annex II to the Minutes of the PDCO of March 2014

List of Participants

Chair

Dirk MENTZER

Members appointed by Member States or CHMP

Karl Heinz HUEMER	Austria
Koenraad NORGA	Belgium
Violeta IOTOVA	Bulgaria
Marina DIMOV DI GUSTI	Croatia
George SAVVA	Cyprus
Jaroslav STERBA	Czech Republic
Marianne ORHOLM	Denmark
Irja LUTSAR	Estonia
Pirjo LAITINEN-PARKONNEN	Finland
Sylvie BENCHETRIT	France
Birka LEHMANN	Germany
Agnes GYURASICS	Hungary
Gylfi OLKARSSON	Iceland
Kevin CONNOLLY	Ireland
Paolo ROSSI	Italy
Dina APELE-FREMIANE	Latvia
Carine de BEAUFORT	Luxembourg
Hendrik van den BERG	The Netherlands
Siri WANG	Norway
Helena FONSECA	Portugal
Dana Gabriela MARIN	Romania
Stefan GROSEK	Slovenia
Fernando DE ANDRÉS TRELLES	Spain
Viveca Lena ODLIND	Sweden
Angeliki SIAPKARA	United Kingdom

Alternates appointed by Member States or CHMP

Christoph MALE	Austria
Jacqueline CARLEER	Belgium
Peter SZITANYI	Czech Republic
Marta GRANSTRÖM	Denmark
Immanuel BARTH	Germany
Brian AYLWARD	Ireland
Francesca ROCCHI	Italy
Herbert LENICKER	Malta
Jolanta WITKOWSKA-OZOGOWSKA	Poland
Hugo TAVARES	Portugal
Ninna GULLBERG	Sweden
Martina RIEGL	United Kingdom

Members representing patients' organisations

Tsveta SCHYNS-LIHARSKA

Alternates representing patients' organisations

Gerlind BODE

Members representing health care professionals

Adriana CECI

Anthony James NUNN

Alternates representing health care professionals

Paolo PAOLUCCI

Observers

Fiona BICKELL	Guy's and St Thomas' NHS Foundation Trust, United Kingdom
Katherine MCGINN	Medicines and Healthcare Products Regulatory Agency, United Kingdom

European Medicines Agency

Jordi LLINARES GARCIA	Head of Product Development Scientific Support Department
Paolo TOMASI	Head of Paediatric Medicines
Andrea ECKER	Scientific Officer, Paediatric Medicines
Benjamin PELLE	Scientific Officer, Paediatric Medicines

Cecile OLIVIER	Scientific Officer, Paediatric Medicines
Chrissi PALLIDIS	Scientific Officer, Paediatric Medicines
Dobromir PENKOV	Scientific Officer, Paediatric Medicines
Emilie DESFONTAINE	Scientific Officer, Paediatric Medicines
Giovanni LESA	Scientific Officer, Paediatric Medicines
Gunter EGGER	Scientific Officer, Paediatric Medicines
Irmgard EICHLER	Scientific Officer, Paediatric Medicines
Janina KARRES	Scientific Officer, Paediatric Medicines
Peter KÁROLYI	Scientific Officer, Paediatric Medicines
Ralf HEROLD	Scientific Officer, Paediatric Medicines
Ralph BAX	Scientific Officer, Paediatric Medicines
Richard VESELY	Scientific Officer, Paediatric Medicines
Thorsten OLSKI	Scientific Officer, Paediatric Medicines
Ramona ZEMACHE	Assistant, Paediatric Medicines
Aurelie HERVIEU	Assistant, Paediatric Medicines
Spiros VAMVAKAS	Head of Scientific Advice
Thomas GIRARD	Regulatory Affairs Officer, Regulatory Affairs Office
Georgia GAVRIILIDOU	Legal Officer, Legal Department