4 December 2013
EMA/PDCO/641214/2013
Human Medicines Research & Development Support Division

Paediatric Committee (PDCO)

Minutes of the 06-08 November 2013 meeting

Chair: Dirk Mentzer

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 November 2013 PDCO monthly 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

I.5 Leaving/New Members and Alternates

Please refer to the November 2013 PDCO monthly 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

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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 November 2013 PDCO monthly report published in the EMA Website:

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III Discussion of applications

The PDCO discussed 82 procedures in total[1], of which:

- 39 paediatric investigation plan applications;
- 6 product-specific waiver applications;
- 8 compliance check procedures (interim and final);
- 29 requests for modifications of an agreed paediatric investigation plan.

IV Nomination of Rapporteurs and Peer reviewers

• List of letters of intent received for submission of applications with start of procedure January 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 November 2013 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
Fluticasone Furoate / Umeclidinium / Vilanterol	Treatment of chronic obstructive pulmonary disease (COPD)	Chronic Obstructive Pulmonary Disease (COPD)	Confirmed	Treatment of asthma
Regorafenib	Treatment of patients with advanced hepatocellular carcinoma (HCC) whose disease has progressed after prior treatment with sorafenib.	Treatment of liver and intrahepatic bile duct carcinoma (excluding hepatoblastoma)	Confirmed	Treatment of solid malignant tumours (PIP Decision P/0258/2012)
MK-8931	1. Delay of disability in patients with mild-to-moderate Alzheimer's disease 2. Delay of progression to mild Alzheimer's disease in patients with amnestic mild cognitive impairment due to Alzheimer's disease	Treatment of Alzheimer's disease	Confirmed	N/A
Mepolizumab	Treatment of chronic obstructive pulmonary disease (COPD)	Chronic Obstructive Pulmonary Disease (COPD)	Confirmed	Several PIPs are already agreed for this medicinal product. However atopic dermatitis and nasal polyposis are not covered by a PIP.

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

No requests were received for the month of November.

VIII Annual reports on deferrals

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan	Difficulties progressing the PIP?	Outcome
EMEA-000185-PIP01-08	Catridecacog	NovoThirteen	Yes	No	The PDCO noted the report.
EMEA-000290-PIP01-08	Nilotinib	Tasigna	Yes	No	The PDCO noted the report.
EMEA-000237-PIP01-08	Azilsartan medoxomil	Edarbi	No	Yes	Difficulties in recruitment of patients to the PK study, resulting in delay of

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan	Difficulties progressing the PIP?	Outcome
					initiation additional efficacy and safety studies. A request for modification has been submitted and was already agreed by the PDCO.
EMEA-000430-PIP01-08	Rivaroxaban	Xarelto	No	No	The PDCO noted the report.
EMEA-000694-PIP01-09	Dapagliflozin	Not available at present	No	Yes	Recruitment difficulties into their PK/PD studies. The applicant plans to open more sites (15 total). Also, the applicant has already delayed completion timelines and broadened inclusion criteria in order to facilitate recruitment (M01 and M02 procedures).
EMEA-000927-PIP01-10	Linaclotide	Not available at present	No	No	Studies progressing according to plan.
EMEA-000980-PIP01-10	Brentuximab vedotin	Not available at present	Yes	No	The PDCO noted the report.
EMEA-000060-PIP01-07	Recombinant human monoclonal antibody to human IL-1beta of the IgG1/K class		Yes	Yes	Studies progressing according to plan.
EMEA-000060-PIP02-08	Canakinumab	ILARIS	Yes	No	Recruitment issues regarding children below 2 years of age were reported. However, eventually sufficient children were recruited.
EMEA-000178-PIP01-07	Purified antigen fractions of inactivated split virion Influenza A/Indonesia/ 5/0...	Pumarix	No	No	Studies progressing according to plan.
EMEA-000160-PIP01-07	Purified antigen fractions of inactivated split virion	Pandemrix, Prepandemic influenza vaccine (H5N1) (split	No	No	Studies progressing according to plan.

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan	Difficulties progressing the PIP?	Outcome
	Influenza A/Vietnam/1194/...	virion, inactivated, adjuvanted) (referring to Informed Consent for Prepandrix), Prepandrix			
EMEA-000373-PIP02-09	Ferumoxytol	Not available at present	No	Yes	Recruitment issues and comparator drug supply issues. However, the applicant expects to meet all the measures and timelines as agreed in M03.
EMEA-000583-PIP01-09	boceprevir	Not available at present	No	Yes	Clinical studies are on hold at the request of the FDA for re-evaluation of the need for developing interferon-containing regimen in children.

IX Other topics

Guidelines	
Revision of the EC guideline on excipients*	The PDCO was reminded of the opportunity to send comments for an additional week to the draft monographs and Questions & Answers documents related to the modification of the Excipients guideline. The PDCO was also informed that the tentative plan for the documents they received is to have them published in early 2014, after adoption by the CHMP.
Working groups	
Paediatric inventory	Meeting cancelled.
Paediatric oncology	The PDCO members discussed the further handling of the responses to the two draft standard PIPs* and a forthcoming public meeting.
Extrapolation	Meeting postponed
Formulation	No non-product related issues were reported to the Committee.
Non-Clinical	No non-product related issues were reported to the Committee.
Other topics	
Election of the PDCO Vice-Chair	Dr Koenraad Norga was elected at the second round as the vice-chair of the PDCO.
Development of effective	The Medicines for Children Research Network (MCRN) Consumer

young people involvement strategies at PDCO	Liaison Manager and two UK adolescents from the MCRN Young Person's Advisory Group came to the PDCO meeting to discuss involvement of young people in clinical research. This topic was divided in 3 parts: • A short DVD involving 2 adolescents taking part in a clinical trial was shown as an introduction to the topic; • A short presentation of the MCRN YPAG followed and the 2 adolescents explained their role in the group and their reasons for joining it; • Finally, an open discussion with the PDCO members took place. This discussion focused mainly on ways to collaborate between PDCO and YPAG in the UK and other similar organisations across Europe.
Report on the 7th DIA/EFGCP/EMA Medicines for Children Conference, held in London	At this year's 7th DIA/EFGCP/EMA Medicines for Children conference, ideas for the future of the PDCO and the implementation of the Paediatric Regulation with the Paediatric Investigation Plans (PIPs) were discussed. The newly elected PDCO chair Dirk Mentzer (PEI, Germany) was introduced. The EU Commission (DG pharmaceuticals) gave an overview about the EC's report and the achievements of the Paediatric Regulation so far. The conference included three highly interactive break-out sessions. Participants had been invited to send in questions prior to the conference; these were answered by Paolo Tomasi in a dedicated session. The concept of collaboration was illustrated with an example of the IMI-project for patient reported outcomes that involves PDCO, academia, industry and patients/parents. The EMA is currently undergoing a major reorganisation. Agnès Saint-Raymond is now responsible for the implementation of the reorganisation, and Jordi Llinares Garcia has been appointed new Head of the Product Development Scientific Support Department (which oversees Paediatric Medicines, Orphan Drugs, and Scientific Advice). He introduced the new agency structure.
CHMP update on paediatric topics	An update on the CHMP final opinions in October on products with paediatric relevance was presented to the PDCO.
Impact of juvenile animal studies' results on paediatric anti-cancer medicine development	The PDCO members were informed about the start of the project.
Obstacles to, and facilitation of early paediatric brain tumour studies	The PDCO supported a document* outline possible obstacles and actions for facilitating access to new anti-cancer medicines for non-clinical and clinical studies for children with brain tumours.
Request of nomination of PDCO representative as core member of Oncology WP	The PDCO agreed that Dr Hendrik van den Berg shall be nominated as member of the Oncology WP.

Need for CD/DVD submission of applications to PDCO members	PDCO members were asked whether they need CD/DVD submissions in addition to Eudralink email submission. PDCO members were split on this matter as some consider the download from CD/DVD is sometimes more convenient.

Any other business

The PDCO adopted a revision of the previously adopted opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMEA-001173-PIP01-11-M01.

Note on access to documents

Documents marked with an asterisk* in these minutes cannot be released at present as they are currently in draft format. They will become public when adopted in their final form.

Annex I to the Minutes of the PDCO of November 2013

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-000599-PIP01-09-M03
Jean-Pierre Aboulker	Restriction level XR	EMEA-000599-PIP01-09-M03
Alexandra Compagnucci	Restriction level XR	EMEA-000599-PIP01-09-M03
Michal Odermarsky	Restriction level XP	EMEA-001418-PIP01-13
Michal Odermarsky	Restriction level XP	EMEA-001460-PIP01-13
Michal Odermarsky	Restriction level XP	EMEA-001442-PIP01-13
Paolo Rossi	Restriction level XR	EMEA-001442-PIP01-13
Jaroslav Sterba	Restriction level XP	EMEA-001493-PIP01-13
Carine de Beaufort	Restriction level XR	EMEA-001489-PIP01-13
Carine de Beaufort	Restriction level XR	EMEA-001425-PIP01-13
Carine de Beaufort	Restriction level XR	EMEA-001434-PIP01-13
Adriana Ceci	Restriction level DP	EMEA-000380-PIP02-09-M01

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 November 2013

List of Participants

Chair

Dirk MENTZER

Members appointed by Member States or CHMP

Karl Heinz HUEMER	Austria
Koenraad NORGA	Belgium
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
Paolo ROSSI	Italy
Dina APELE-FREMIANE	Latvia
Hendrik van den BERG	The Netherlands
Siri WANG	Norway
Marek MIGDAL	Poland
Helena FONSECA	Portugal
Stefan GROSEK	Slovenia
Fernando DE ANDRÉS TRELLES	Spain
Julia DUNNE	United Kingdom

Alternates appointed by Member States or CHMP

Peter SZITANYI	Czech Republic
Jana LASS	Estonia
Ann Marie KAUKONEN	Finland

Immanuel BARTH	Germany
Brian AYLWARD	Ireland
Francesca ROCCHI	Italy
Herbert LENICKER	Malta
Jolanta WITKOWSKA-OZOGOWSKA	Poland
Hugo TAVARES	Portugal
Dana Gabriela MARIN	Romania
Maria Jesus FERNANDEZ CORTIZO	Spain
Ninna GULLBERG	Sweden
Angeliki SIAPKARA	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

Experts

Peter BAUER	Medical statistician
Johannes OVELGÖNNE	CAT member

Observers

Martina RIEGL	Medicines and Healthcare Products Regulatory Agency, United Kingdom
Jennifer PRESTON	Medicines for Children Research Network, United Kingdom
2 adolescents	Medicines for Children Research Network, Young People Advisory Group, United Kingdom

European Medicines Agency

Paolo TOMASI	Head of Paediatric Medicines
Sophie OLIVIER	Scientific Officer, Paediatric Medicines

Benjamin PELLE	Scientific Officer, Paediatric Medicines
Chrissi PALLIDIS	Scientific Officer, Paediatric Medicines
Dobromir PENKOV	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 VESELÝ	Scientific Officer, Paediatric Medicines
Thorsten OLSKI	Scientific Officer, Paediatric Medicines
Cecile OLIVIER	Scientific Officer, Paediatric Medicines
Alessandro JENKNER	National Expert on Secondment, Paediatric Medicines
Ramona ZEMACHE	Assistant, Paediatric Medicines
Aurelie HERVIEU	Assistant, Paediatric Medicines