10 September 2014
EMA/PDCO/491868/2014
Procedure Management and Business Support Division

Paediatric Committee (PDCO)

Minutes of the 13 – 15 August 2014 meeting

Chair: Dirk Mentzer - Vice-chair: Koenraad Norga

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).

Disclaimers

Some of the information contained in the PDCO discussions is considered commercially confidential or sensitive and therefore not disclosed in the present minutes. With regards to therapeutic indications 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. The procedures discussed by the PDCO are on-going and therefore certain aspects of them 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). Documents mentioned in these minutes cannot be released at present as they are currently in draft format or are classified as confidential. They will become public when adopted in their final form or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006). Of note, this set of minutes is a working document primarily designed for PDCO members and the work the Committee undertakes.

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I Introduction

I.1 Adoption of the minutes from previous meeting

The Minutes of the PDCO plenary session held on 16-18 July 2014 were 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

The agenda was adopted with amendments.
http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/document_listing/document_listing_000192.jsp&mid=WC0b01ac0580028eab

All decisions taken at this meeting were made in presence of a quorum of members – i.e. 23 or more members were present in the room.

I.3 Declaration of Conflict of Interest

See Annex I

I.4 External attendance

Please refer to the August 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 August 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

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 August 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

III Discussion of applications

The PDCO discussed 85 procedures in total[1], of which:

- 41 paediatric investigation plan applications;
- 2 product-specific waiver applications;
- 5 compliance check procedures (interim and final);
- 37 requests for modifications of an agreed paediatric investigation plan.

IV Nomination

IV.1 Nomination of Rapporteurs and Peer reviewers

• List of letters of intent received for submission of applications with start of procedure October 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.

IV.2 Nomination for other activities

• No requests for nominations were received	

V Update and finalisation of opinions and requests for modification

The opinions adopted during the Paediatric Committee meeting of August 2014 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.

VI Discussion on the applicability of class waiver

Active substance	Proposed indication	Condition	Outcome	Potential paediatric interest of this medicine suggested by PDCO
Elotuzumab	Treatment of multiple myeloma in combination with lenalidomide and dexamethasone in patients who have received one or more prior therapies.	Treatment of multiple myeloma	Confirmed	Not applicable

[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).

Active substance	Proposed indication	Condition	Outcome	Potential paediatric interest of this medicine suggested by PDCO
Margetuximab	Treatment of advanced HER2-positive adenocarcinoma of the stomach or gastroesophageal junction	Treatment of gastric adenocarcinoma	Confirmed	Not applicable
Anti PD-L1 monoclonal antibody (MEDI4736)	Treatment of squamous cell cancer of head and neck	Treatment of oropharyngeal, laryngeal or nasal epithelial carcinoma (excluding nasopharyngeal carcinoma or lympho-epithelioma)	To be re-discussed at September PDCO	

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

No requests were received for the month of August.

VIII Annual reports on deferrals

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan	Difficulties progressing the PIP?	Outcome
EMEA-000498-PIP01-08	linagliptin	Trajenta	No	Yes	The PDCO noted the report. A Modification is planned.
EMEA-000556-PIP01-09	velaglucerase alfa	Vpriv	No	No	The PDCO noted that there are no issues as regards the progression of the PIP studies.
EMEA-001178-PIP01-11	Regorafenib	Stivarga	No	Yes	The PDCO noted the report and the recent Modification procedure.
EMEA-000482-PIP01-08	Teduglutide ([gly2] recombinant human glucagon-like peptide)	Revestive	Yes	Yes	The PDCO noted the report. A Scientific Advice procedure is currently on-going and a Modification procedure is planned.
EMEA-001019-PIP01-10	Poly(oxy-1,2-ethanediyl),alpha-hydro-omega-methoxy-133 ester with granulocyte co...	Lonquex	No	No	The PDCO noted that there are no issues as regards the progression of the PIP studies.
EMEA-000312-PIP01-08	Human coagulation Factor VIII (plus von Willebrand Factor) / Human coagulation F...	Biostate	No	Yes	The PDCO noted the report. A modification of the agreed PIP has already been submitted.
EMEA-000362-PIP01-08	Aliskiren	Rasilez	No	Yes	The PDCO noted the recent modification.
EMEA-000174-PIP01-07	Plerixafor	Mozobil	Yes	No	The PDCO noted that there are no issues as regards the progression of the PIP studies.

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-000019-PIP06-09	everolimus	Certican and associated names	No	No	The PDCO noted that there are no issues as regards the progression of the PIP studies.
EMEA-001147-PIP01-11	N-{3-[5-(2-Amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluoro...	Tafinlar	No	No	The PDCO noted the report.
EMEA-000145-PIP01-07	denosumab	Prolia, XGEVA (previously Amgiva)	No	Yes	The PDCO noted the delay of the estimated completion date of the PIP. A PIP modification is planned in September 2014.
EMEA-000145-PIP02-12	denosumab	Prolia, XGEVA (previously Amgiva)	No	No	The PDCO noted that there are no issues as regards the progression of the PIP studies.
EMEA-000769-PIP01-09	Ceftaroline fosamil (established INN)	Zinforo	No	No	The PDCO noted that there are no issues as regards the progression of the PIP studies.

IX Other topics

Guidelines	
Draft guideline on influenza vaccines: non-clinical and clinical module	Guideline adopted and published on EMA external website for 6-month consultation.

Working groups	
Paediatric inventory	The following therapeutic areas were discussed: Nephro-Urology, Oncology and Ophthalmology.
Paediatric oncology	Breakout session took place in the margins of the PDCO plenary meeting.
Extrapolation	Breakout session took place in the margins of the PDCO plenary meeting.
Neonatal	Cancelled and postponed.
Paediatric consultation meeting – update and way forward	Breakout session took place in the margins of the PDCO plenary meeting.
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	
Induction to new EMA premises Wednesday, 13 August 2014, 08:45 – 09:00	The PDCO noted the presentation.
Art.31 referral of Hydroxyzine, PDCO responses to PRAC List of Questions – TC with HEALTH CANADA Sylvie Benchetrit	The PDCO re-discussed and adopted the responses to the PRAC LoQ on the use of hydroxyzine in the paediatric population. Health Canada listened to the PDCO discussion.
Discussion on comments to the Questions and Answers draft document on the excipient Sodium (update of the Excipients guideline)	The PDCO members were reminded that they can comment on the document by 29 August 2014.
Comparative analysis COMP Orphan Designation versus PDCO PIP condition	The PDCO noted the presentation.
CHMP update on paediatric topics	The PDCO members were informed about the CHMP opinions on 3 medicinal products with paediatric indication and corresponding PIPs adopted in July 2014.

PIP for DTaP-containing combination vaccine Marta Granström	The document, endorsed by the CHMP in July with VWP comments, has now been adopted by PDCO for public consultation. EMA will liaise with the EC to disseminate the information through the Health Security Committee. EMA shall also inform CMDh in September, the VWP who has a WHO representative, FDA and Vaccines Europe for Industry.
Organ maturation tables (lung, GI tract)	The purpose of the organ maturation tables is to potentially better inform the judgement from paediatric queries on Eudravigilance signals for medicinal products. These overview tables are based on published literature and reviewed by experts in the field before adoption by the PDCO. The maturation table for the lung was adopted. The maturation table for the GI-tract will be reviewed again by the PDCO member Dr Jan Taminiau before adoption.
Serious adverse events and safety concerns for clofarabine combined with chemotherapy in children with acute lymphoblastic leukaemia Sylvie Benchetrit	At the meeting held in July, the PDCO discussed safety issues related the use of clofarabine, alone and in combination with other anti-cancer medicines, for the treatment of acute lymphoblastic leukaemia in children and adolescents. The main safety concerns were related to the frequency and severity of adverse drug reactions, which seem to be higher when clofarabine is used in combination with other agents than when it is used as a single agent. It was also noted that in clinical trials the dose of clofarabine used in combination seems to be not clearly defined; moreover, in clinical practice, clofarabine is not used in accordance with the modalities reported in the Summary of Product Characteristics, but as a combined regimen in second line therapy (and more rarely in first line therapy). Comments were received by several PDCO Members and the Committee concluded that:

	1. the therapeutic strategies based on the use of clofarabine in combined regimen should be reconsidered and redefined in view of the emerging safety concerns in combined regimen with etoposide and cyclophosphamide; 2. the off-label use of clofarabine in combination with etoposide and cyclophosphamide should be discouraged; 3. Clinical trials should address the question of posology and toxicity in combined regimens. It was highlighted that the combination of clofarabine with etoposide and cyclophosphamide does not seem to have been tested in non-clinical studies; therefore the available data cannot confirm superiority of the combination, compared to monotherapy, whereas possible additional safety concerns cannot be excluded. It was also considered that a revision of the Product Labelling (and in particular of section 4.2 and section 4.4) could be useful, as well as the inclusion of any patient treated with clofarabine in the European Registry Programme (a registry aimed at further characterization of the clofarabine safety profile and assessment of its risk/benefit ratio in routine clinical practice).
Paediatric development life cycle	The PDCO was updated and exchanged views on this project.
Paediatric inventory	The inventories of paediatric therapeutic needs for Ophthalmology and for Nephro-Urology were adopted for publication.
PDCO response to the questions from PRAC on the Chlorhexidine procedure Angeliki Siapkara, Dina Apele-Freimane	Adopted at July PDCO.
D30 Products identified for the Non-Clinical Working Group Jacqueline Carleer	Documents tabled for information.

Any other business

Annex I to the Minutes of the PDCO of August 2014

List of Participants and 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).

The below list includes any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 13 - 15 August 2014 meeting.

PDCO Chair	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product / substance
Dirk Mentzer	Germany	Full involvement	

PDCO Member	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product / substance
Karl-Heinz Huemer	Austria	Full involvement	
Koenraad Norga	Belgium	Full involvement	
Violeta Iotova	Bulgaria	Restriction level XP	EMEA-000496-PIP01-08-M03
			EMEA-001556-PIP01-13
			EMEA-000694-PIP02-14
			EMEA-001517-PIP01-13
Georgios Savva	Cyprus	Full involvement	
Peter Szitanyi	Czech Republic	Full involvement	
Marianne Orholm	Denmark	Full involvement	
Irja Lutsar	Estonia	Full involvement	

PDCO Member	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product/substance
Pirjo Laitinen-Parkkonen	Finland	Full involvement	
Sylvie Benchetrit	France	Full involvement	
Birka Lehmann	Germany	Full involvement	
Grigorios Melas	Greece	Full involvement	
Agnes Gyurasics	Hungary	Full involvement	
Kevin Connolly	Ireland	Restriction level XP	EMEA-001037-PIP02-11-M01
Paolo Rossi	Italy	Connected via TC	
Dina Apele-Freimane	Latvia	Full involvement	
Carola de Beaufort	Luxembourg	Connected via TC	
John Joseph Borg	Malta	Full involvement	
Siri Wang	Norway	Full involvement	
Marek Migdal	Poland	Restriction level DP	EMEA-001599-PIP01-13 EMEA-001639-PIP01-14
Helena Fonseca	Portugal	Full involvement	
Dana Gabriela Marin	Romania	Full involvement	
Michaela Meciakova	Slovakia	Full involvement	
Stefan Grosek	Slovenia	Full involvement	
Fernando de Andrés Trelles	Spain	Full involvement	
Viveca Lena Odlind	Sweden	Full involvement	
Angeliki Siapkara	United Kingdom	Full involvement	

PDCO Alternate	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product/substance
Jacqueline Carleer	Belgium	Full involvement	

PDCO Alternate	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product/substance
Immanuel Barth	Germany	Full involvement	
Brian Aylward	Ireland	Full involvement	
Maaike van Dartel	Netherlands	*Replacing PDCO member* Full involvement	
Ine Skottheim Rusten	Norway	Full involvement	
Jolanta Witkowska-Ożogowska	Poland	Full involvement	
Hugo Tavares	Portugal	Connected via TC	
Maria Jesús Fernández Cortizo	Spain	Full involvement	
Ninna Gullberg	Sweden	Full involvement	
Martina Riegl	United Kingdom	Full involvement	

PDCO Representative of doctors' organisations	Role	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product/substance
Antje Neubert	Member	Representative of doctors' organisations	Full involvement	
Johannes Taminiau	Member	Representative of doctors' organisations	Full involvement	
Doina Plesca	Alternate	Representative of doctors' organisations	Restriction level XP	EMEA-000069-PIP02-10-M04
				EMEA-000402-PIP02-11-M01
				EMEA-C4-000548-PIP01-09-M05
				EMEA-C1-000332-PIP01-08-M08

PDCO Representative of doctors' organisations	Role	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product/substance
Riccardo Riccardi	Member	Representative of doctors' organisations	Full involvement	

PDCO Representative of patients' organisations	Role	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product/substance
Gunther Auerswald	Member	Representative of patients' organisations	Full involvement	
Paola Baiardi	Alternate	Representative of patients' organisations	Full involvement	
Michal Odermarsky	Member	Representative of patients' organisations	Restriction level XP	EMEA-000533-PIP01-08-M05
				EMEA-001577-PIP01-13
				EMEA-001418-PIP01-13

PDCO Expert	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which the expert is invited Product/substance
*Experts were only evaluated against the product they have been invited to talk about.			
Katherine McGinn	United Kingdom	Full involvement	EMEA-001549-PIP02-14 EMEA-001150-PIP02-13 EMEA-001664-PIP01-14
Dominik Karres	United Kingdom	Full involvement	EMEA-001644-PIP01-14

PDCO Expert by phone	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which the expert is invited Product/substance
*Experts were only evaluated against the product they have been invited to talk about.			

PDCO Expert by phone	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which the expert is invited Product/substance
Health Canada representative	Canada	Connected via TC	Art.31 referral of Hydroxyzine

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