18 June 2014
EMA/PDCO/290625/2014
Human Medicines Research & Development Support Division

Paediatric Committee (PDCO)

Minutes of the 21-23 May 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.

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

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
An agency of the European Union

I.2 Adoption of the Agenda

Adopted.

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 May 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 May 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 May 2014 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

III Discussion of applications

The PDCO discussed 76 procedures in total[1], of which:

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

[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).

IV Nominations

IV.1 Nomination of Rapporteurs and Peer reviewers

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

• Nomination of PDCO representative in the establishment of a joint PDCO/PRAC Working Group • Nomination of clinical peer reviewer for fructose and sorbitol for the Excipients Drafting Group	2 PDCO members were nominated to take part in the establishment of a joint PDCO/PRAC working group. A PDCO member was nominated to act as peer-reviewer for the monograph on fructose and sorbitol drafted by the Excipients Drafting Group.

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 May 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.

VI Discussion on the applicability of class waiver

Active substance	Proposed indication	Condition	Outcome	Potential paediatric interest of this medicine suggested by PDCO
RO6867461	Treatment of wet age-related macular degeneration	Treatment of age-related macular degeneration	Confirmed	• Retinopathy of Prematurity (ROP) • Solid tumors • Choroidal neovascularization • Macular oedema

Active substance	Proposed indication	Condition	Outcome	Potential paediatric interest of this medicine suggested by PDCO
Talaporfin sodium & light activation therapy device	Treatment of the signs and symptoms of benign prostatic hyperplasia	Treatment of benign prostatic hyperplasia	Confirmed	N/A
AMG 337	Treatment of unresectable, locally advanced or metastatic gastric, gastro-oesophageal junction and oesophageal adenocarcinoma	Treatment of gastric adenocarcinoma	Confirmed	Possible paediatric interest in various paediatric solid malignant tumours
BI 691751	Reduction of major CV events in patients with established atherosclerotic disease in multiple vascular beds	Treatment of coronary atherosclerosis	Confirmed	Kawasaki disease
BI 691751	Reduction of major CV events in patients with established atherosclerotic disease in multiple vascular beds	Treatment of peripheral atherosclerosis	Confirmed	Familial hypercholesterolaemia

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

No requests were received for the month of May.

VIII Annual reports on deferrals

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan	Difficulties progressing the PIP?	Outcome
EMEA-000308-PIP01-08	rituximab	MabThera	No	No	The report was noted.
EMEA-000118-PIP02-10	Abatacept	ORENCIA	No	No	The report was noted.

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan	Difficulties progressing the PIP?	Outcome
EMEA-000412-PIP01-08	Insulin detemir	Levemir	No	No	The PDCO has been informed that there are no issues as regards the progression of the PIP studies.
EMEA-000601-PIP01-09	pazopanib	VOTRIENT	Yes	No	The report was noted.
EMEA-001149-PIP01-11	Human Fibrinogen / Human Thrombin	EVARREST, EVICEL	No	Yes	The report was noted.
EMEA-000970-PIP01-10	elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil (as fumarate)	Stribild	No	No	The PDCO has been informed that there are no issues as regards the progression of the PIP studies.
EMEA-000872-PIP01-10	Recombinant human hyaluronidase / Human normal immunoglobulin	HyQvia	No	Yes	The issues with this product in context with the CHMP discussions on tolerability were noted.
EMEA-000183-PIP01-08	Apixaban	Eliquis	No	No	No delay in PIP progression.
EMEA-000183-PIP02-12	apixaban	Eliquis	No	No	No delay in PIP progression.
EMEA-000365-PIP01-08	Oseltamivir (phosphate)	Tamiflu	No	Yes	Procedures concerning the medicinal product are ongoing at the PDCO and the CHMP. PDCO noted the

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan	Difficulties progressing the PIP?	Outcome
					deferral report and the plan to conduct the studies in compliance with the agreed PIP.
EMEA-000429-PIP01-08	N. meningitidis serogroup Y polysaccharide conjugated to tetanus toxoid / N. men...	Nimenrix	No	Yes	Delay in availability of immunogenicity results for co-administered antigens for study 6 due to issues related to quality assay. A request for modification will be submitted by the applicant.

IX Other topics

Guidelines	
Guideline on clinical investigation of hepatitis B immunoglobulin (updated with comments after public consultation) Marianne Orholm	PDCO members have contributed to the revision of the draft guideline after the public consultation with specific comments on issues of paediatric interest. The guideline has been agreed by the PDCO for CHMP adoption.
Working groups	
Paediatric inventory	The group discussed the status of the inventory for the therapeutic area of oncology.
Paediatric oncology	The working group discussed the organisation of contributions and comments to the oncology inventory and the forthcoming scientific public meetings.
Extrapolation	No meeting
Formulation	No non-product related issues were reported to the Committee.

Non-Clinical	No non-product related issues where reported to the Committee
White paper drafting group: The paediatric regulation beyond 2017 Koenraad Norga	The group convened and continued working with a view to providing input to the European Commission for the revision of the Paediatric Regulation.
Other topics	
Review and Reconnect: Rationalisation of Committees Secretariat	The PDCO was informed of the progress of a specific project within the Review and Reconnect exercise for the rationalisation of the Agency's Committees Secretariat service. A centralised Scientific Committee Secretariat Service is now operating with the objective to focus on the provision of an efficient and high quality technical/regulatory support, operate to best practice using simplified, optimised and harmonised processes, tools and templates. The PDCO will be informed during all phases of project implementation, in particular regarding organisational and process changes. Committee's members will be involved in user tests of new tools.
CHMP update on paediatric topics	The PDCO members were informed about the final CHMP opinions on medicinal products with paediatric relevance adopted in April 2014.
Debriefing on the workshop on paediatric PBPK models Ine Rusten	Intensive scientific and regulatory work is carried out in the area of modelling pharmacokinetic and other data, as reflected in public scientific meetings this year. The PDCO supports such works and is interested in proposals that include tools such as physiology-based pharmacokinetic models (PBPK), in order to optimise paediatric clinical trials and to strengthen the data on medicines for children.
Gaucher disease – a Strategic Collaborative Approach from EMA and FDA Adopted via written procedure on 12 May 2014	The Committee was informed that the document is now published and open for a 3-months consultation period. The outcome of the comments will be presented to the PDCO, SAWP and CHMP.
Opinion for Insulin degludec EMEA-000456-PIP01-08-M02 Adopted via written procedure on 15 May 2014	The committee was informed about the adoption of the opinion by written procedure.

Inventory of paediatric therapeutic needs - Infectious diseases (final adopted list) Draft inventory of paediatric therapeutic needs - Neurology (list open for public consultation) Draft inventory of paediatric therapeutic needs - Ophthalmology (list open for public consultation)	The PDCO was updated on the status of the inventory of paediatric therapeutic needs.
Project 2014 - Move to Churchill Place	The PDCO was informed of practicalities concerning the relocation of EMA to the new premises.
ICH E11 Concept Paper	The two EMA delegates in the ICH E11 Drafting group (the PDCO Chair and Daniel Brasseur from CHMP) updated the PDCO on the joint concept paper finalised for the ICH by the Rapporteur (Industry). Several points have been identified by the drafting group: • Extrapolation: more guidance to developers is necessary. • Modelling and simulation: general principles will be introduced in the modified ICH E11; however detailed and comprehensive guidance should not be included in the guideline as the field is evolving rapidly. • Formulations: guidance on these aspects should be included in E11. • Methodology: innovative/special statistical approaches and non competitive trials are to be discussed and potentially encouraged. The final completion of the revision activities is not expected to be completed before 2016. The update will be either an addendum, or a Questions & Answers (Q&A) document (still to be decided). The EMA coordinators clarified that specific PDCO members will be involved according to expertise, and the Committee will be regularly updated on the proceedings. It was also suggested that some topics could be discussed in the framework of the Paediatric Cluster teleconference, where Canada and Australia regulatory authorities are also represented (even if Industry is not).

Draft standard PIP on DTaP-containing combination vaccine & Letter to the VWP	The Committee endorsed the latest draft PIP for DTaP-containing combination vaccine. It was agreed to send this document to the VWP for comments, together with a cover letter raising specific questions.
Initial Consultation on Paediatric Development: draft procedure	The Committee was again informed that the EMA Secretariat is working on a new procedure, the "Initial Consultation on Paediatric Development", to allow applicants to obtain advice from the PDCO without committing to a full PIP application (which could then be done at a more mature development stage). The procedure could also be a module of a broader global early interaction procedure between prospective applicants and the EMA. Concerns were expressed by PDCO members on workload implications, the role of the Formulation Working Group and the Non-Clinical Working Group, the level of formality of the procedure and on ways to ensure the involvement of the whole Committee. The draft documents prepared so far (WIN, timelines, Q&A guidance, press release, and the outcome document) were sent to PDCO members for comments and re-discussion at the June meeting.
Draft agenda of the EMA Human Scientific Committees' Working Parties with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP) joint meeting (3 June 2014)	Documents tabled for information
PDCO dates for 2016	PDCO meeting dates for 2016-2018 to be adopted at PDCO June 2014 meeting.

Any other business

- Fast track compliance procedure for Insulin degludec (EMEA-C-000456-PIP01-08-M02); adoption of opinion

Annex I to the Minutes of the PDCO of May 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
Jaroslav Sterba	Restriction level DP	EMEA-000227-PIP03-13
Jaroslav Sterba	Restriction level DP	EMEA-001450-PIP01-13
Paolo Rossi	Restriction level XR	EMEA-000576-PIP03-12

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 May 2014

List of Participants

Chair

Dirk MENTZER

Members appointed by Member States or CHMP

Karl Heinz HUEMER	Austria
Koenraad NORGA	Belgium
Violeta IOTOVA	Bulgaria
George SAVVA	Cyprus
Jaroslav STERBA	Czech Republic
Marianne ORHOLM	Denmark
Irja LUTSAR	Estonia
Pirjo LAITINEN-PARKONNEN	Finland
Sylvie BENCHETRIT	France
Birka LEHMANN	Germany
Grigorios MELAS	Greece
Agnes GYURASICS	Hungary
Gylfi OLKARSSON	Iceland
Paolo ROSSI	Italy
Dina APELE-FREMIANE	Latvia
Carine de BEAUFORT	Luxembourg
Hendrik van den BERG	The Netherlands
Siri WANG	Norway
Marek MIGDAL	Poland
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

Jacqueline CARLEER	Belgium
Marta GRANSTRÖM	Denmark
Immanuel BARTH	Germany
Brian AYLWARD	Ireland
Francesca ROCCHI	Italy
Herbert LENICKER	Malta
Ine Skottheim RUSTEN	Norway
Jolanta WITKOWSKA-OZOGOWSKA	Poland
Hugo TAVARES	Portugal
Maria Jesus FERNANDEZ CORTIZO	Spain
Ninna GULLBERG	Sweden
Martina RIEGL	United Kingdom

Members representing patients' organisations

Tsveta SCHYNS-LIHARSKA, European Network for Research on Alternating Hemiplegia, Belgium

Members representing health care professionals

Anthony James NUNN, Alder Hey Children's Hospital, UK

Alternates representing health care professionals

Paolo PAOLUCCI, Polyclinic of Modena, Italy

Experts

Anastasia MOUNTAKI, National Organization for Medicines, Greece

Masakazu HIRATA, Pharmaceuticals and Medical Devices Agency, Japan

European Medicines Agency support

Meeting run with relevant support from the EMA staff