17 April 2013
EMA/PDCO/154253/2013
Human Medicines Development and Evaluation

Paediatric Committee (PDCO)

Minutes of the 13-15 March 2013 meeting

Chair: Daniel Brasseur

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 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 March 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 March 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

III Discussion of applications

The PDCO discussed 70 procedures in total[1], of which:

- 34 paediatric investigation plan applications;
- 7 product-specific waiver applications;
- 3 compliance check procedures (interim and final);
- 25 requests for modifications of an agreed paediatric investigation plan;
- 1 re-examination requests.

IV Nomination of Rapporteurs and Peer reviewers

• List of letters of intent received for submission of applications with start of procedure May 2013[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 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

Class waiver number	Active substance	Condition	Proposed indication	Outcome
EMEA-01-2013	Panobinostat (LBH589)	Treatment of Multiple Myeloma	Treatment of Multiple Myeloma	Confirmed

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

PIP number	Active substance	Condition	Proposed indication	Outcome
EMEA-000200-PIP01-08	Saxagliptin	Treatment of patients with type 2 Diabetes Mellitus	Reduction of major CV events in patients with Type 2 diabetes who also have CV risk factors or established CV disease	Pending
EMEA-000467-PIP01-08	Perampanel	Treatment of treatment-resistant epilepsies	1) Adjunctive therapy in patients with PGTC seizures 2) Adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut syndrome	Confirmed
EMEA-000549-PIP01-09-M01	Infliximab	Rheumatoid arthritis Juvenile idiopathic arthritis Psoriatic arthritis Ankylosing spondylitis Psoriasis Crohn's disease Ulcerative colitis	Prevention/reduc-tion of post-operative recurrence of Crohn's disease	Confirmed

VIII Annual reports on deferrals

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan drug	Difficulties progressing the PIP?	Outcome
EMEA-000178-PIP01-07-M02	purified antigen fractions of inactivated split virion Influenza A/Indonesia/5/05/ (H5N1) (Pumarix),	Pumarix	No	No	No action required
EMEA-000087-PIP01-07-M02	Fingolimod hydrochloride	Gilenya	No	No	No action required

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan drug	Difficulties progressing the PIP?	Outcome
EMEA-000673-PIP01-09-M06	Pneumococcal polysaccharide serotype 23F conjugate...	Synflorix	No	Yes	N/A
EMEA-000347-PIP01-08-M02	Bilastine	Bilaxten and associated names	No	Yes	No action required
EMEA-000637-PIP02-10-M02	Lanthanum carbonate hydrate	"Fosrenol" in the RMS (Sweden) and associated name "Foznol"	No	Yes	Modification procedure planned by applicant. EMA will contact Enpr-EMA or paediatric nephrologist for input
EMEA-000081-PIP01-07-M05	Dabigatran etexilate	Pradaxa	No	Yes	The PDCO noted that for one study, clinical trial authorisation and favourable ethics committee opinions were not achieved for all planned sites.
EMEA-000170-PIP02-10-M01	Eltrombopag (eltrombopag olamine)	Revolade	Yes	No	No action required
EMEA-000170-PIP01-07-M03	Eltrombopag (eltrombopag olamine)	Revolade	No	No	No action required
EMEA-000533-PIP01-08-M04	Tenofovir disoproxil (as fumarate)	Viread	No	No	No action required
EMEA-000653-PIP01-09-M02	Romiplostim	Nplate	Yes	Yes	Modification procedure ongoing
EMEA-001181-PIP01-11	Agomelatine	Valdoxan, Thymanax	No	No	No action required

IX Other topics

Guidelines	
Clinical Investigation of	The PDCO received the FDA comments on the proposed concept paper

Medicinal Products in the Paediatric Population, E-11	on amending ICH E-11. The PDCO agreed answers* to the comments, to be submitted to the FDA.
Revision of the Note for Guidance on Clinical Investigation of Medicinal Products for Treatment of Asthma	The PDCO discussed the comments / requests for clarification made by the guideline consistency group regarding the paediatric chapter in the revised asthma guideline: 1) "The chapter is considered too detailed": the PDCO disagreed, and reiterated the need on very specific and detailed recommendations, which are based on the recommendations from an expert meeting held at the Agency. 2) The PDCO agrees with the request to clarify the current wording regarding study design and study duration. A revised wording has been proposed.
Revision of the Reflection paper on Immune Tolerance Induction in haemophilia A patients with inhibitors	The PDCO agreed with the comments made to this reflection paper during public consultation. The reflection paper was adopted by the PDCO.
Working groups	
Paediatric inventory	The Working Group discussed the status of the inventory for the therapeutic areas nephro-urology and neurology.
Paediatric oncology	The PDCO members discussed in the pre-plenary meeting the EuroDIA meeting, the FDA meeting on minimal residual disease assessment in acute myeloid leukaemia, the organisation of participation in scientific meetings in the remainder of 2013 and innovative aspects of designs of studies in paediatric oncology.
Extrapolation	The group discussed the finalisation of the Concept paper on extrapolation of efficacy and safety in medicine development following comments from external stakeholders with a view to the publication of the final version of the concept paper and the overview of the comments from external stakeholders. The majority of the comments related to the future reflection paper which will be the next step in the process.
Formulation	No non-product related issues where reported to the Committee.
Non-Clinical	No non-product related issues where reported to the Committee.
Other topics	
Feedback from the PDCO informal meeting in Dublin 06-08 March 2012	A report on the presentations and discussions held at the informal PDCO was illustrated.
Draft 'Letter to the Editor' of the journal *Haemophilia* responding to Mannucci article 'Evolution of the European guidelines for the clinical development of	The draft EMA joint letter was presented and adopted by the PDCO. It will be submitted to the journal *Haemophilia.*

factor VIII products: little progress towards improved patient management' that is critical of revised European guidance for FVIII and FIX products)*	
Revision of Rules of procedure of the Paediatric Committee (PDCO)	Minor revisions of the rules of procedure of the Paediatric Committee have been adopted. The revised document will be published on the website after adoption by the relevant bodies (including the EMA Management Board).
Standard Allergen PIP	The need to demonstrate long-term, i.e. disease modifying effect, in at least one allergen product in the paediatric population as proof of concept was stressed again. The Revision of the standard allergen PIP will be discussed by a working group, including PDCO members, EMA staff, Paul-Ehrlich-Institut (PEI) representatives as well as representatives of EMA Scientific Advice and CHMP.
Reflection on revocation of the EMA decision on the list of class waivers	The PDCO continued the discussion and review of the data and grounds for individual waivers, including new data from disease registries.
EMEA-000463-PIP01-08-M0x (Glivec) – PDCO opinion on design of follow-up study to evaluate the long-term safety of imatinib	The PDCO discussed the request by the CHMP and reviewed the proposal by the applicant for the generation of further data. The PDCO defined its recommendations for further data to be generated to follow-up on endpoints indicating safety and efficacy aspects. The PDCO adopted an opinion as response to the CHMP request, including the requested review and the requested recommendations for the design of a registry or single-arm study.
Analysis done for the purpose of the Annual Report 2012 to EC*	A brief report on the information contained in Annual reports on deferred measures was presented to the PDCO, including the outcome that more than half of the annual reports stated that paediatric development was progressing in accordance with the agreed PIP.
Revision of the off-patent priority list	The PDCO discussed the comments provided for the revision of the off-patent priority list. In order to address the issues which are still open in more detail it was agreed to re-circulate the list and comments for a further discussion at the next PDCO meeting.
Questionnaire for children and young people*	As part of the goal to involve children and young people in the work of the PDCO the PDCO were presented with a draft questionnaire written with colleagues from the Patient Information team, as a basis to initiate interaction with children and young people. It was explained that a video clip was to be produced to explain the work of EMA/PDCO that will be used as an introduction for completing this questionnaire on-line. Many PDCO members agreed that asking for the input and opinion of their own children would be beneficial. It was also agreed that PDCO

	members should translate the questionnaire to their own language, which would help facilitate the understanding of the questions, and ultimately facilitate enabling the questionnaire to be used by all children across EU. Discussion was held about the need to formally validate the questionnaire before it can be used in order to ensure scientific robustness. This item will be tabled in the April agenda of the PDCO for further discussion and possible adoption.
Vaccine schedules in PIPs: action plan	The PDCO aims at defining the "best" vaccine schedules to be included in the PIPs to avoid unnecessary paediatric clinical trials in children and multiple blood sampling. It plans to set up a working group with the European Centre for Disease prevention and Control, the European Commission and Member States representatives to review scientific evidence.
CHMP update on paediatric topics	The PDCO members were informed about the final CHMP opinions adopted in February 2013 on medicinal products with paediatric interest.
Draft plan for indicators to be measured, benchmarked and interpreted on the question, what are the public health benefits of the Paediatric Regulation*	A working group of the PDCO progressed with drafting a plan for data collecting in the coming year that can be used for the 10-year report on the Paediatric Regulation.
Update on the Workshop on paediatric investigation plans in type-2 diabetes mellitus on 25 February 2013	The topic was postponed to the April PDCO agenda.
Enpr-EMA annual workshop	The committee was informed about the annual workshop will be held on 27&28 June 2013 at the Agency and was asked to propose topics for the agenda. Two issues were considered of high importance to be addressed: 1) The need for a better communication and cooperation between PDCO and national ethic committees. 2) To increase knowledge and awareness on the need for paediatric research among practising paediatricians. Paediatricians traditionally are used to prescribe medicines off-label in children; thus they frequently do not see the need for clinical studies to increase the evidence base of medicines for children.
Guidance for Summary of PDCO Opinion*	The adoption of the guidance was postponed to April, due to comments/suggestions expected from the Medical Information Sector of the Agency.

PDCO survey on preferred submission method	Some PDCO members confirmed that a hard-copy (CD/DVD) of the submission is required by their Agencies. Therefore the current submission policy will not be modified.

Any other business

- Summary of knowledge gaps related to quality and efficacy of current influenza vaccines
  - The PDCO adopted the gap analysis on current knowledge related to quality and efficacy of influenza vaccines (seasonal and pandemic)*. After CHMP adoption, the document will be published.

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 March 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-001003-PIP01-10-M02
Adriana Ceci	Restriction level DP	EMEA-C1-000118-PIP02-10-M01
Alexandra Compagnucci	Restriction level XR	EMEA-001405-PIP01-12
Alexandra Compagnucci	Restriction level DC	EMEA-000627-PIP01-09-M04
Alexandra Compagnucci	Restriction level DC	EMEA-000628-PIP01-09-M04
Carine de Beaufort	Restriction level XR	EMEA-001395-PIP01-12
Christoph Male	Restriction level DP	EMEA-001382-PIP01-12
Dobrin Konstantinov	Restriction level DP	EMEA-000713-PIP02-10-M02
Jaroslav Sterba	Restriction level XP	EMEA-001392-PIP01-12
Jaroslav Sterva	Restriction level XP	EMEA-000713-PIP02-10-M02
Marek Migdal	Restriction level DP	EMEA-001309-PIP01-12
Michal Odermarsky	Restriction level XP	EMEA-001288-PIP01-12

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 2013

List of Participants

Chair

Daniel BRASSEUR

Vice-chair

Dirk MENTZER

Members appointed by Member States or CHMP

Christoph MALE	Austria
Koenraad NORGA	Belgium
Dobrin KONSTANTINOV	Bulgaria
Jaroslav STERBA	Czech Republic
Marianne ORHOLM	Denmark
Irja LUTSAR	Estonia
Pirjo LAITINEN-PARKONNEN	Finland
Dirk MENTZER	Germany
Kevin CONNOLLY	Ireland
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
Vlasta KAKOSOVA	Slovak Republic
Janez JAZBEC	Slovenia
Fernando DE ANDRÉS TRELLES	Spain
Marta GRANSTRÖM	Sweden
Julia DUNNE	United Kingdom

Alternates appointed by Member States or CHMP

Karl Heinz HUEMER	Austria
Jacqueline CARLEER	Belgium
Peter SZITANYI	Czech Republic
Ann Marie KAUKONEN	Finland
Birka LEHMANN	Germany
Francesca ROCCHI	Italy
Rugile PILVINIENE	Lithuania
Herbert LENICKER	Malta
Ine Skottheim RUSTEN	Norway
Hugo TAVARES	Portugal
Dana Gabriela MARIN	Romania
Maria Jesus FERNANDEZ CORTIZO	Spain
Viveca Lena ODLIND	Sweden
Angeliki SIAPKARA	United Kingdom

Members representing patients' organisations

Tsveta SCHYNS-LIHARSKA

Michal ODERMARSKY

Alternates representing patients' organisations

Gerlind BODE

Experts

Peter BAUER	Medical statistician

European Medicines Agency

Agnes SAINT RAYMOND	Head of Sector, Human Medicines Special Areas
Paolo TOMASI	Head of Section, Paediatric Medicines
Sophie OLIVIER	Scientific Administrator, Paediatric Medicines
Anne-Sophie HENRY-EUDE	Scientific Administrator, Paediatric Medicines
Almudena SAIZ HERRANZ	Scientific Administrator, Paediatric Medicines
Benjamin PELLE	Scientific Administrator, Paediatric Medicines
Emilie DESFONTAINE	Scientific Administrator, Paediatric Medicines
Chrissi Pallidis	Scientific Administrator, Paediatric Medicines
Dobromir PENKOV	Scientific Administrator, Paediatric Medicines

Elin Haf DAVIES	Scientific Administrator, Paediatric Medicines
Giovanni LESA	Scientific Administrator, Paediatric Medicines
Gunter EGGER	Scientific Administrator, Paediatric Medicines
Irmgard EICHLER	Scientific Administrator, Paediatric Medicines
Janina KARRES	Scientific Administrator, Paediatric Medicines
Peter KÁROLYI	Scientific Administrator, Paediatric Medicines
Ralf HEROLD	Scientific Administrator, Paediatric Medicines
Ralph BAX	Scientific Administrator, Paediatric Medicines
Richard VESELY	Scientific Administrator, Paediatric Medicines
Thorsten OLSKI	Scientific Administrator, Paediatric Medicines
Alessandro JENKNER	National Expert on Secondment, Paediatric Medicines
Cristina BEJNARIU	Trainee
Aurelie HERVIEU	Assistant, Paediatric Medicines
Isabel PEREZ	Assistant, Paediatric Medicines
Sunni HOLTMAN	Assistant, Paediatric Medicines