6 November 2013
EMA/PDCO/592586/2013
Human Medicines Research & Development Support Division

Paediatric Committee (PDCO)

Minutes of the 09-11 October 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 October 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 October 2013 PDCO monthly report published in the EMA Website:

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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 October 2013 PDCO monthly report published in the EMA Website:

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III Discussion of applications

The PDCO discussed 86 procedures in total[1], of which:

- 28 paediatric investigation plan applications;
- 13 product-specific waiver applications;
- 12 compliance check procedures (interim and final);
- 32 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 December 2013 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 October 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
Darapladib	Treatment of visual impairment due to diabetic macular oedema	Treatment of diabetic macular oedema	Confirmed	The PDCO considers that there could be a therapeutic benefit of this product in children with asthma.
RO4602522	Adjunctive therapy for the treatment of patients with moderate severity Alzheimer's disease	Treatment of Alzheimer's disease	Confirmed	N/A
Bevacizumab	in combination with paclitaxel plus topotecan or paclitaxel plus cisplatin, for the treatment of persistent, recurrent or Stage IVB carcinoma of the cervix	Treatment of cervix and corpus uteri carcinoma	Confirmed	The PDCO noted the ongoing paediatric developments for treatment of rhabdo-myosarcoma, non-rhabdomyosarcoma soft tissue tumour and high-grade glioma. In addition, modifiers of tumour vasculature are of interest, for example for treatment of Wilms tumour and hepatoblastoma.
Momelotinib	1. Treatment of Primary Myelofibrosis (PMF) 2. Treatment of Post-Polycythemia Vera or Post-Essential Thrombocythemia Myelofibrosis (Post-PV/ET MF)	Treatment of primary myelofibrosis	Confirmed for the indication Treatment of Primary Myelofibrosis. Not confirmed for the indication Treatment of Post-Polycythemia Vera or Post-Essential Thrombocythemia Myelofibrosis.	The PDCO considers that there could be a therapeutic benefit in children with leukaemia.

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

No requests were received for the month of October

VIII Annual reports on deferrals

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan	Difficulties progressing the PIP?	Outcome
EMEA-000468-PIP02-12	Posaconazole	Noxafil	No	Yes	The PDCO noted the reported delayed progress of the PIP compared to the planned completion date and the planned modification procedure to address this.
EMEA-001071-PIP02-12	Certolizumab pegol	Cimzia	No	No	The PDCO noted the report.
EMEA-000035-PIP02-09	Tiotropium bromide (monohydrate)	Spiriva Respimat 2.5 microgram, solution for inhalation, Spiriva 18 microgram, inhalation powder, hard capsule	No	Yes	The PDCO noted the reported delayed progress of the PIP compared to the planned completion date and the planned modification procedure to address this.
EMEA-000265-PIP01-08	Golimumab	Simponi	No	Yes	Difficulties in the development of the formulation. Request for the modification was submitted.
EMEA-000265-PIP02-11	Golimumab	Simponi	No	Yes	Difficulties in recruitment of patients to the PK study, which has not been initiated yet. Expected start in October 2013, request for modification is to be submitted.
EMEA-000671-PIP01-09	Sildenafil citrate	Revatio	Yes	Yes	Initiation of the PPHN study was delayed due to difficulties obtaining EC approval in France, in particular. Overall timelines of the study

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan	Difficulties progressing the PIP?	Outcome
					will be re-evaluated in early 2014.
EMEA-000452-PIP02-10	Tadalafil	Cialis, Adcirca	No	No	The PDCO noted the report.
EMEA-000627-PIP01-09	Ivabradine hydrochloride	Corlentor	No	No	The PDCO noted the report.
EMEA-000628-PIP01-09	Ivabradine hydrochloride	Procoralan	No	No	The PDCO noted the report.
EMEA-000200-PIP01-08	Saxagliptin	Onglyza	No	Yes	The PDCO noted the report.
EMEA-000367-PIP01-08	Human recombinant C1 inhibitor	Rhucin	Yes	Yes	The applicant reports recruitment difficulties and will request modification of the agreed PIP.
EMEA-000827-PIP01-09	Aztreonam	Cayston	Yes	No	The PDCO noted the report.

IX Other topics

Guidelines	
Revision of the EC guideline on excipients	The PDCO was updated on the status of the proposals for the revision of the EC guideline on excipients. Committee members were also asked to comment on the Questions and Answers documents prepared for ethanol, benzyl alcohol, benzoic acid and cyclodextrins, before the next PDCO meeting.
Working groups	
Paediatric inventory	The working group discussed the draft paediatric inventory for neurology and infectious diseases.
Paediatric oncology	The working group discussed the Addendum on Paediatric oncology and the preparation of contributions to forthcoming external meetings.
Extrapolation	No meeting in October.
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	
PDCO/COMP workshop on conditions in rare diseases	Both committees met together to discuss the determination of the condition in rare diseases. It has been recognised that although the definition of condition is identical in the respective EC guidelines, the different scopes and aims of the two (orphan and paediatric) legislations cause different approaches to its application by the two committees. While paediatric need drives the PDCO towards a broader scope of the PIPs, COMP deals with individual orphan diseases with a strong focus on their low prevalence. Examples of past and recent representative cases were shown, when these different approaches led to different determination of the condition. An overview of the scientific and regulatory aspects and possible consequences of this situation was provided by EMA. Members of both committees discussed how to address optimally the public health needs in both rare diseases and children's health. Both committees acknowledged the importance of the problem and committed themselves to work together more tightly to improve their opinions. Creation of the inter-active working group was agreed, where members of both committees would regularly meet to: • minimise the risks of unnecessarily different wording of the conditions in PDCO and COMP opinions; • identify situations when scientific committees cannot avoid divergent conclusions; • identify ways to achieve the best service to public health in both fields of rare diseases and children's health with respect to both legislations. Creation of the inter-active PDCO/COMP working group is planned at next plenary meetings in November. Members of both Committees who intend to contribute to the work of this working group have been invited to express their interest to their committee secretariat.
Draft inventory of paediatric therapeutic needs Therapeutic area neurology	The PDCO discussed and adopted the draft inventory of paediatric therapeutic needs in neurology. The list will now be released for public consultation.
Draft inventory of paediatric therapeutic needs Therapeutic area infectious diseases	The PDCO discussed the comment received during public consultation and adopted the final inventory of paediatric therapeutic needs for infectious diseases.
Reorganisation communication to the PDCO Zaide Frias	The new Head (ad interim) of the Division Human Medicines Research & Development Support explained the process and structural changes that are currently being implemented in the European Medicines Agency. The new structure of the Agency is now available on the public website. PDCO members appreciated that the new "Department Product Development Scientific

	Support" includes the Paediatric Medicines, Orphan Medicines and Scientific Advice Offices, due to the frequent interactions between the respective Committees; the PDCO also supported the matrix approach to processes, which is scheduled to facilitate interactions with the CHMP and the new Agency offices providing its secretariat, even if situated in different Divisions.
Nomination of PDCO representative in SAWP	The PDCO nominated as its representative in the SAWP: Kevin Connolly (Ireland). The PDCO considered that its representation in the SAWP should be increased to be the same as that of the COMP, i.e. a minimum of 2 and a maximum of 3 members. The Agency will explore this possibility.
Request of nomination of PDCO representative as core member of Oncology WP	Postponed to November PDCO.
CHMP update on paediatric topics	The PDCO members were informed about the final CHMP opinions on medicinal products with paediatric interest adopted in September 2013. No new paediatric indications were granted.
Timelines Q1-Q2 2014	The PDCO approved the proposed timelines.
Update on Enpr-EMA activities: Dates for the 2014 annual workshop	The committee was informed about the date of the annual Enpr-EMA workshop, scheduled for 26 and 27 June 2014.

Any other business

- Inter-committee SAG Oncology* A proposal was discussed, considering the opportunities for paediatric oncology.
- Horizon 2020 project and off-patent medicines for children. The PDCO has received questions by other stakeholders, including members of GRiP network and the Enpr-EMA network, regarding a lack of specific funding for the development of off-patent medicinal products for children in the current draft of the Horizon 2020 project. The PDCO has adopted a letter to the European Commission (DG research) asking for clarifications, in the light of the obligation to provide specific funding from the EU budget, for these developments, as mandated in art. 40 of the Paediatric Regulation.
- Joint Informal Meeting CAT and PDCO on 25-26 November 2013, Trieste, Italy. The draft agenda* was presented to the committee.

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 October 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 Declaration of Interests	Topics on the current Committee Agenda for which this restriction applies
Marina Dimov	Restriction level XR	EMEA-001094-PIP01-10-M01
Adriana Ceci	Restriction level DP	EMEA-001071-PIP02-12-M01
Tadej Avcin	Restriction level XP	EMEA-001071-PIP02-12-M01
Carine de Beaufort	Restriction level XR	EMEA-001489-PIP01-13
Michal Odermarsky	Restriction level XP	EMEA-001418-PIP01-13
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

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 October 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
Marianne ORHOLM	Denmark
Irja LUTSAR	Estonia
Pirjo LAITINEN-PARKONNEN	Finland
Sylvie BENCHETRIT	France
Birka LEHMANN	Germany
Agnes GYURASICS	Hungary
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
Stefan GROSEK	Slovenia
Fernando DE ANDRÉS TRELLES	Spain
Viveca Lena ODLIND	Sweden
Julia DUNNE	United Kingdom

Alternates appointed by Member States or CHMP

Christoph MALE	Austria

Jacqueline CARLEER	Belgium
Marta GRANSTRÖM	Denmark
Jana LASS	Estonia
Immanuel Barth	Germany
Brian AYLWARD	Ireland
Francesca ROCCHI	Italy
Herbert LENICKER	Malta
Jolanta WITKOWSKA-OZOGOWSKA	Poland
Hugo TAVARES	Portugal
Dana Gabriela MARIN	Romania
Ninna GULLBERG	Sweden
Angeliki SIAPKARA	United Kingdom

Members representing health care professionals

Adriana CECI

Anthony James NUNN

Alternates representing health care professionals

Paolo PAOLUCCI

Experts

Peter BAUER	Medical statistician

Observers

Nao TSUCHIDA	National Center for Child Health and Development, Japan
Aina Jannnicke OVREBUST	Norwegian Medicines Agency

European Medicines Agency

Zaide FRIAS	Head of Division, Human Medicines Research & Development Support (ad interim)
Jordi Llinares GARCIA	Head of Product Development Scientific Support
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 VESELY	Scientific Officer, Paediatric Medicines
Thorsten OLSKI	Scientific Officer, Paediatric Medicines
Cecile OLLIVIER	Scientific Officer, Paediatric Medicines
Alessandro JENKNER	National Expert on Secondment, Paediatric Medicines
Ramona ZEMACHE	Assistant, Paediatric Medicines
Aurelie HERVIEU	Assistant, Paediatric Medicines
Francesco PIGNATTI	Head of Oncology, Haematology and Diagnostics
Jean-Marc VIDAL	Scientific Officer, Specialised Scientific Disciplines Department