11 September 2013
EMA/PDCO/485847/2013
Human Medicines Development and Evaluation

Paediatric Committee (PDCO)

Minutes of the 07-09 August 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 August 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 August 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

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

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 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 90 procedures in total[1], of which:

- 38 paediatric investigation plan applications;
- 11 product-specific waiver applications;
- 6 compliance check procedures (interim and final);
- 35 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 October 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 August 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	Proposed indication	Condition	Outcome
EMEA-33-2012	TH-302	Treatment of locally advanced unresectable or metastatic pancreatic adenocarcinoma	Treatment of adenocarcinoma of the pancreas	Confirmed
EMEA-34-2013	Neratinib	Treatment of HER2-Positive metastatic breast cancer	Treatment of breast carcinoma	Postponed
EMEA-35-2013	Neratinib	Treatment of HER2-Mutant non-small cell lung cancer	Treatment of lung carcinoma (non-small cell carcinoma)	Postponed
EMEA-36-2013	Tiotropium + Olodaterol	Maintenance bronchodilator treatment in patients with chronic obstructive pulmonary disease (COPD)	Chronic obstructive pulmonary disease (COPD)	Confirmed
EMEA-37-2013	ODM-201	Treatment of patients with non-metastatic castration resistant prostate cancer with a high risk of developing metastases	Treatment of prostate carcinoma (excluding rhabdomyosarcoma)	Confirmed
EMEA-38-2013	Lu AE58054	Treatment of mild to moderate dementia of the Alzheimer's Type as adjunctive therapy to Acetylcholinesterase Inhibitors	Treatment of Alzheimer's Disease	Confirmed
EMEA-39-2013	Buparlisib (BKM120)	Treatment of breast cancer	Treatment of breast carcinoma	Confirmed
EMEA-40-2013	Buparlisib (BKM120)	Treatment of castration resistant prostate cancer	Treatment of prostate carcinoma (excluding rhabdomyosarcoma)	Confirmed
EMEA-41-2013	Buparlisib (BKM120)	Treatment of non-small cell lung cancer	Treatment of lung carcinoma (small cell and non-small cell carcinoma)	Confirmed

Class waiver number	Active substance	Proposed indication	Condition	Outcome
EMEA-42-2013	Ticagrelor (Brilique)	Prevention of atherothrombotic events in patients with established lower extremity arterial disease	Treatment of peripheral atherosclerosis	Confirmed
EMEA-43-2013	Ticagrelor (Brilique)	Prevention of atherothrombotic events in adult patients with a history of myocardial infarction and a high risk of developing an atherothrombotic event	Treatment of coronary atherosclerosis	Confirmed
EMEA-44-2013	AZD5363	Treatment of patients with hormone-receptor positive advanced breast cancer receiving their first exposure to chemotherapy, as a combination with paclitaxel	Treatment of breast carcinoma	Confirmed
EMEA-45-2013	AZD5363	Treatment of patients with metastatic castration resistant prostate cancer (CRPC) in whom maximum androgen blockade has failed	Treatment of prostate carcinoma	Confirmed
EMEA-46-2013	BAY 80-6946	Treatment of relapsed/refractory follicular lymphoma alone or in combination with rituximab	Treatment of follicular lymphoma	Confirmed
EMEA-47-2013	rilimogene galvacirepvec / rilimogene glafolivec	Treatment of metastatic, castrate-resistant prostate cancer	Treatment of prostate carcinoma (excluding shabdomyosarcoma)	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-000019-PIP02-07	Everolimus	Votubia	Yes	Yes	The PDCO noted that no difficulties were reported on progressing the paediatric trials.
EMEA-000019-PIP08-12	Everolimus	Votubia	Yes	No	The PDCO noted the report.
EMEA-000498-PIP01-08	linagliptin	Ondero	No	Yes	The applicant informed the EMA/PDCO of the slow recruitment into their PK/PD study. The reasons for the slow recruitment are too restrictive inclusion/exclusion criteria (HbA1c and previous insulin use) as well as presence of ICA and GAD antibodies. It is noted that compared to the applicants last AR the recruitment rate has been faster. The applicant plans to come for a modification.
EMEA-000222-PIP01-08	Etravirine	Intelence	No	Yes	The applicant informed the EMA/PDCO that one clinical trial is currently on hold for screening additional subjects in cohort I until a new protocol amendment will be finalized. This protocol amendment will contain new dose escalation rules for individual subjects and in addition the cohort pass/fail rules will be amended. The impact on the PIP completion date of this screening holds in cohort I will be evaluated and if necessary, a PIP modification will be submitted.
EMEA-000174-PIP01-07	Plerixafor	Mozobil	Yes	No	The PDCO noted the report.

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan drug	Difficulties progressing the PIP?	Outcome
EMEA-000556-PIP01-09	velaglucerase alfa	N/A	No	Yes	The applicant experiences enrolment difficulties. Additional sites have been opened to solve the issue.
EMEA-000362-PIP01-08	Aliskiren	Rasilez	No	Yes	The PDCO noted the report.
EMEA000-769-PIP01-09-M03	Ceftaroline fosamil	Zinforo	No	No	The PDCO noted the report.

IX Other topics

Working groups	
Paediatric inventory	No meeting in August.
Paediatric oncology	The working group discussed upcoming public meetings, draft standard PIPs and product-specific issues.
Extrapolation	No meeting in August.
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	
Involvement from Children and Young people – feedback from EMPATHY	The EU Patient forum invited EMA to be part of a 4 day seminar, held in Brussels 8-11 July to allow young patients the opportunity to explore challenges that young patients face in relation to healthcare services, discrimination, policies and the use of the media to convey health messages. The project was funded with support from The Youth in Action Programme of the EC. The EMA was given a 2-hour slot to discuss how EMA may involve children and young people in the work of the PDCO. A 15-minute presentation was given to explain the work of the PDCO; this was followed with a discussion about a DRAFT video that had been produced to ask young people to consider getting involved. Participants provided valuable feedback on how to amend the proposed video. A questionnaire devised at the PDCO was distributed. Participants were asked to complete it and then a discussion was held on the clarity and content of the questionnaire. The findings will be reported in the next month, and a revision of the questionnaire done in line with the comments received.
A Standard PIP for Gaucher disease*	The PDCO was informed that during follow-up discussion with the FDA some amendments to the non-clinical and extrapolation part of the PIP had been proposed. This is currently under review and will be presented back to the PDCO in September.

Paediatric inflammatory bowel disease (IBD) – update on ongoing activities	The PDCO was updated on the ongoing activities in this area. Two papers on outcome measures for ulcerative colitis (UC) from iIBD (international IBD working group) are going to be published. ECCO (European Crohn's and Colitis Organisation) submitted a draft of their article on outcome measures for IBD in children. Members of the PDCO can comment on this draft. Guidelines for UC and CD (Crohn's disease) in children are being prepared by the gastroenterology drafting group.
CHMP update on paediatric topics	An update on CHMP procedures of products with a Paediatric Investigation plan was presented to the PDCO. There were no CHMP final opinions on products with paediatric relevance.
Connectra keys and PedRA access – information for new members	The new members of the PDCO were reminded of the possibility to access PedRA (the Paediatric database) from their offices; if situated outside of the EudraNet network (i.e. outside of a national competent authority), PDCO members need a security device, obtainable from the EMA IT Service Desk. To obtain a password, PDCO members should contact PDCO Secretariat.
Update on Pancreatic Risks of incretin based therapies: CHMP conclusion	The PDCO was informed that the CHMP concluded during their July 2013 plenary meeting that no new concerns for GLP-1 therapies have been identified on the basis of available evidence. The review of available clinical and nonclinical data did not give raise to additional pancreatic safety risks. The PDCO concluded that for the time being no action on own motion will be taken regarding the existing 11 PIPs with GLP-1 therapies. However, PDCO will closely follow the upcoming future long-term safety results as they become available. The PDCO confirmed that a medical need for novel medicines for type 2 diabetes in children in Europe exists, even if greater interest may exist in the US, Asia and Africa. It was concluded that the short-term risks associated with GLP-1 therapies is not likely to be different in adolescents and adults. However, children are likely to be treated with these novel medications for (much) longer than adults are. The PDCO concluded that thorough pre-clinical studies with specific pancreatic histopathology and biomarker endpoints could be of value, as routine toxicology studies do not usually include such specific endpoints.
Synopses for extrapolation and modelling / simulation studies	In addition to non-clinical studies and clinical trials, extrapolation exercises and modelling and simulation studies can be part of agreed paediatric investigation plans, in the PDCO Opinion. The PDCO discussed that they should be submitted by applicants using specific templates, because these exercises and studies need to be specially described. The EMA will update the electronic PDF form "Key elements form: Applicant's proposal for a paediatric-investigation-plan opinion.pdf".
Single summary report, from initial to last modification	The PDCO discussed opportunities to simplify the handling of summary reports and to collect information evolving during the conduct of a paediatric investigation plan in a core document.
PRAC request of PDCO opinion on Numeta and	The Paediatric Committee adopted an Opinion on a request from the Pharmacovigilance Risk Assessment Committee on the quality, efficacy and safety of the medicinal product Numeta (Numeta G13%E and Numeta

hypermagnesemia	G16%E) for its use in the paediatric population. Numeta is used for parenteral nutrition in neonatal and paediatric patients.

Any other business

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 August 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 DoI	Topics on the current Committee Agenda for which this restriction applies
Christoph Male	XP	EMEA-000778-PIP02-12
Adriana Ceci	XR	EMEA-000880-PIP02-11-M02
Paolo Rossi	XR	EMEA-000731-PIP01-09-M01
Carine de Beaufort	XR	EMEA-000731-PIP01-09-M01
Adriana Ceci	XR	EMEA-000527-PIP03-13
Jean-Pierre Aboulker	XR	EMEA-000527-PIP03-13
Alexandra Compagnucci	XR	EMEA-000527-PIP03-13
Adriana Ceci	XR	EMEA-000527-PIP04-13
Jean-Pierre Aboulker	XR	EMEA-000527-PIP04-13
Alexandra Compagnucci	XR	EMEA-000527-PIP04-13
Adriana Ceci	XR	EMEA-001454-PIP01-13
Jean-Pierre Aboulker	XR	EMEA-001454-PIP01-13
Alexandra Compagnucci	XR	EMEA-001454-PIP01-13
Marek Migdal	XR	EMEA-001455-PIP01-13
Michal Odermanski	XP	EMEA-001465-PIP01-13
Jean-Pierre Aboulker	XR	EMEA-001465-PIP01-13
Alexandra Compagnucci	XR	EMEA-001465-PIP01-13
Adriana Ceci	XR	EMEA-001333-PIP02-13
Paolo Rossi	XR	EMEA-001458-PIP01-13
Christoph Male	DP	EMEA-001382-PIP01-12
Carine de Beaufort	XR	EMEA-001395-PIP01-12
Romaldas Mačiulaitis	XR	EMEA-001395-PIP01-12
Carine de Beaufort	XR	EMEA-001053-PIP01-10-M02

Adriana Ceci	XR	EMEA-000362-PIP01-08-M03
Christoph Male	DP	EMEA-001064-PIP01-10-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 August 2013

List of Participants

Chair

Daniel BRASSEUR

Vice-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
Dirk MENTZER	Germany
Agnes GYURASICS	Hungary
Dina APELE-FREMIANE	Latvia
Carine de BEAUFORT	Luxembourg
John Joseph BORG	Malta
Hendrik van den BERG	The Netherlands
Siri WANG	Norway
Marek MIGDAL	Poland
Helena FONSECA	Portugal
Fernando DE ANDRÉS TRELLES	Spain
Viveca Lena ODLIND	Sweden

Alternates appointed by Member States or CHMP

Jacqueline CARLEER	Belgium
Peter SZITANYI	Czech Republic

Marta GRANSTRÖM	Denmark
Jana LASS	Estonia
Ann Marie KAUKONEN	Finland
Birka LEHMANN	Germany
Brian AYLWARD	Ireland
Jolanta WITKOWSKA-OZOGOWSKA	Poland
Dana Gabriela MARIN	Romania
Maria Jesus FERNANDEZ CORTIZO	Spain
Ninna GULLBERG	Sweden

Alternates representing patients' organisations

Gerlind BODE

Members representing health care professionals

Adriana CECI

Anthony James NUNN

Experts

Peter BAUER	Medical statistician
Martina RIEGL	Medicines and Healthcare products Regulatory Agency

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
Benjamin PELLE	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
Aneta KRZYSCIAK	Assistant, Paediatric Medicines
Aurelie HERVIEU	Assistant, Paediatric Medicines