09 October 2013
EMA/PDCO/556160/2013
Human Medicines Development and Evaluation

Paediatric Committee (PDCO)

Minutes of the 11-13 September 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 September 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 September 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 September 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 95 procedures in total[1], of which:

- 33 paediatric investigation plan applications;
- 12 product-specific waiver applications;
- 8 compliance check procedures (interim and final);
- 42 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 November 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 September 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.

VI Discussion on the applicability of class waiver

Active substance	Proposed indication	Condition	Outcome	Potential paediatric interest of this medicine suggested by PDCO
Neratinib	Treatment	Treatment of	Confirmed	Yes, potential interest for

[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
	of HER2-Positive metastatic breast cancer	breast carcinoma		the treatment of paediatric oncology indications (e.g. neuroblastoma, glioma, PH+ ALL)
Neratinib	Treatment of HER2-Mutant non-small cell lung cancer	Treatment of lung carcinoma (non-small cell carcinoma)	Confirmed	Yes, potential interest for the treatment of paediatric oncology indications (e.g. neuroblastoma, glioma, PH+ ALL)
Trifuridine (FDA; a,a,a triflurothymidine) and tipiracil hydrochloride (TPI: 5-chloro-6[(2 iminopyrrolidin-1-yl)methyl]pyrimide-2,4-(1H,3H)-dione monohydrochloride	Treatment of patients with small cell lung cancer (SCLC) refractory or sensitive to first line platinum-based chemotherapy	Treatment of lung carcinoma (small cell and non-small cell)	Confirmed	Yes, potential interest for the treatment of paediatric oncology indications, to be investigated
Trifuridine (FDA; a,a,a triflurothymidine) and tipiracil hydrochloride (TPI: 5-chloro-6[(2 iminopyrrolidin-1-yl)methyl]pyrimide-2,4-(1H,3H)-dione monohydrochloride	Treatment of patients with metastatic colorectal cancer refractory to standard chemotherapies	Treatment of adenocarcinoma of the colon and rectum	Confirmed	Yes, potential interest for the treatment of paediatric oncology indications, to be investigated
RO5520985	Treatment of carcinoma of the colon or	Treatment of adenocarcinoma of the colon and rectum	Confirmed	Yes, potential interest for the treatment of paediatric oncology indications, to be investigated

Active substance	Proposed indication	Condition	Outcome	Potential paediatric interest of this medicine suggested by PDCO
	rectum			
RO5520985	Treatment of epithelial ovarian cancer, fallopian tube or primary peritoneal cancer	Treatment of ovarian carcinoma (excluding rhabdomyosarcoma and germ cell tumours)	Condition "Treatment of ovarian carcinoma (excluding rhabdomyosarcoma and germ cell tumours)" was confirmed for the indication "Treatment of epithelial ovarian cancer". The other 2 indications "Treatment of fallopian tube" and "Treatment of primary peritoneal cancer" were considered covered by 2 different class waiver conditions, "Treatment of Fallopian tube carcinoma (excluding rhabdomyosarcoma and germ cell tumours)" and "Treatment of peritoneal carcinoma (excluding blastomas and sarcomas)" respectively.	Yes, potential interest for the treatment of paediatric oncology indications, to be investigated
Enobosarm (GTx-024, ostarine)	Prevention and treatment of muscle wasting in patients with non-small cell lung cancer	Treatment of lung carcinoma (small cell and non-small cell carcinoma)	Not confirmed	No
estradiol	Hormone	Treatment of	Confirmed	No

Active substance	Proposed indication	Condition	Outcome	Potential paediatric interest of this medicine suggested by PDCO
(hemihydrates)	replacement therapy (HRT) for estrogen deficiency symptoms in postmenopausal women (natural or surgical menopause, with or without a uterus). The experience in treating women older than 65 years is limited.	climacteric symptoms associated with decreased oestrogen levels, as occurring at menopause		
MORAb-004	Treatment of metastatic colo-rectal cancer	Treatment of adenocarcinoma of the colon and rectum	Confirmed	Yes, potential interest for the treatment of melanoma in children above 12 years old and treatment of soft tissue sarcoma.
MORAb-004	Treatment of metastatic melanoma	Treatment of melanoma (from 0 to less than 12 years old).	Confirmed for the paediatric subset from birth to less than 12 years old.	Yes, potential interest for the treatment of melanoma in children above 12 years old and treatment of soft tissue sarcoma. A PIP or a product-specific waiver will be needed for the paediatric subset from 12 years old to less than 18 years old.
Fasitibant Chloride	Symptomatic treatment of hip and knee osteoarthritis	Treatment of primary and secondary osteoarthrosis	Confirmed	No

VIII Annual reports on deferrals

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan	Difficulties progressing the PIP?	Outcome
EMEA-000228-PIP01-08	asenapine maleate		No	No	Clinical trials initiated earlier than planned.
EMEA-000366-PIP01-08	Adalimumab	Humira	No	No	The PDCO noted the report.
EMEA-000366-PIP02-09	Adalimumab	Humira	No	No	The PDCO noted the report.
EMEA-000555-PIP01-09	decitabine	DACOGEN	Yes	No	The PDCO noted the report.
EMEA-000020-PIP01-07	maraviroc	CELSENTRI	No	Yes	Recruitment difficulties due to a low MTC transmission and to the availability of effective therapies enabling fewer children to fail therapy.
EMEA-000018-PIP01-07	Tapentadol Hydrochloride	Palexia, Yantil, Tapentadol	No	No	The PDCO noted the report.
EMEA-000325-PIP01-08	Tapentadol hydrochloride	Palexia, Yantil, Tapentadol	No	Yes	Difficulties with the development of the prolonged release formulation – modification planned
EMEA-000482-PIP01-08	Teduglutide ([gly2] recombinant human glucagon-like peptide)	Revestive	Yes	Yes	Applicant changed its strategy with regards to the PIP. Follow-up scientific advice procedure has been recommended
EMEA-000485-PIP01-08	Tapentadol hydrochloride	Palexia, Yantil, Tapentadol	No	Yes	Difficulties with the development of the prolonged release formulation –

Annual report based on PIP decision for	Substances (abbrev.)	Product Name	Orphan	Difficulties progressing the PIP?	Outcome
					modification planned
EMEA-000486-PIP01-08	Tapentadol hydrochloride	Palexia, Yantil, Tapentadol	No	Yes	Difficulties with the development of the prolonged release formulation – modification planned
EMEA-000494-PIP01-08	Tapentadol hydrochloride	Palexia, Yantil, Tapentadol	No	No	The PDCO noted the report.
EMEA-000495-PIP01-08	Tapentadol hydrochloride	Palexia, Yantil, Tapentadol	No	No	The PDCO noted the report.
EMEA-000196-PIP01-08	Telaprevir		No	Yes	Difficulties with recruitment. Modification procedure is planned.

IX Other topics

Guidelines	
Guideline on the evaluation of Medicinal Products for the treatment of Chronic Constipation*	The PDCO discussed the paediatric part of the guideline.
Revised draft guideline on clinical evaluation of medicinal products for the treatment of chronic hepatitis C*	When available, the revised draft guideline for chronic hepatitis C will be discussed by the PDCO, before public consultation.
Revision - Addendum on Paediatric Oncology to anti-cancer guideline*	The PDCO noted the current draft revision of the addendum, which will be discussed at the Oncology Working Party meeting.
Working groups	
Paediatric inventory	The draft inventory for the therapeutic area 'neurology' was finalised.
Paediatric oncology	Recent publications on early-phase trials with children with cancer were discussed. Product-specific discussions were prepared. A draft plan for a project on results of juvenile animal studies of anti-cancer medicine was discussed.
Extrapolation	The topic for discussion was extrapolation in type II diabetes.

Vaccine schedules in PIPs - Preparation of expert meeting	Preliminary discussion occurred on the agenda for an expert meeting to be held by the end of the year. Further discussion will be needed next month.
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	
Election of PDCO Chair and Vice-Chair	At the beginning of the September meeting, the PDCO elected as new Chair Dirk Mentzer, with 23 votes in favour and one blank ballot. The PDCO then elected as new vice-chair Hendrik van den Berg, with 21 votes in favour and 3 blank ballots. The PDCO thanked its former chair, Daniel Brasseur, for his outstanding work as Chair of the Committee from its beginning 6 years ago.
PDCO rules of procedures: Inputs of the European Commission	The PDCO approved the improvements to the rules of procedure proposed by the European Commission.
New call for PDCO members from Academia / Health Care / Patient Representatives	The PDCO was informed that the European Commission has published the call of interest for nomination of new PDCO members from Academia / Health Care / Patient Representatives in 2014: http://ec.europa.eu/health/human-use/paediatric-medicines/developments/index_en.htm http://ec.europa.eu/health/files/paediatrics/2013-09_ped.zip
Application and Opinion synopses for extrapolation and for modelling / simulation studies (measures 4 and 5 in scientific document)* - (Comments until 3 October 2013)	The PDCO noted that some comments had been provided on the draft synopses and awaits further comments from concerned EMA working groups.
Draft agenda PCWP/HCPWP joint meeting 25 September 2013	The document was presented to the Committee for information.
Draft agenda workshop on patient's voice in the evaluation of medicines 26 September 2013	The document was presented to the Committee for information.
How to find Opinions, Summary Reports, and Presentations in MMD?	A presentation was given to the PDCO members to help them locate these documents in the external filing system.
CHMP update on paediatric topics	There were no CHMP final opinions on products with paediatric relevance.
PDCO/COMP workshop on the determination of the condition in rare	The PDCO agreed to have a 2-hours slot in the agenda of the October plenary meeting. Two PDCO members volunteered to prepare a presentation on the PDCO

diseases on 9th October 2013	position.

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 September 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-001454-PIP01-13
Adriana Ceci	Restriction level XR	EMEA-000362-PIP01-08-M03
Adriana Ceci	Restriction level XR	EMEA-001333-PIP02-13
Adriana Ceci	Restriction level XR	EMEA-000527-PIP03-13
Adriana Ceci	Restriction level XR	EMEA-000527-PIP04-13
Adriana Ceci	Restriction level DP	EMEA-001071-PIP02-12-M01
Alexandra Compagnucci	Restriction level XR	EMEA-001454-PIP01-13
Alexandra Compagnucci	Restriction level XR	EMEA-000527-PIP03-13
Alexandra Compagnucci	Restriction level XR	EMEA-000527-PIP04-13
Carine de Beaufort	Restriction level XR	EMEA-001395-PIP01-12
Carine de Beaufort	Restriction level XR	EMEA-001053-PIP01-10-M02
Christoph Male	Restriction level DP	EMEA-001382-PIP01-12
Christoph Male	Restriction level DP	EMEA-001064-PIP01-10-M01
Jean-Pierre Aboulker	Restriction level XR	EMEA-001454-PIP01-13
Jean-Pierre Aboulker	Restriction level XR	EMEA-000527-PIP03-13
Jean-Pierre Aboulker	Restriction level XR	EMEA-000527-PIP04-13
Marek Migdal	Restriction level DP	EMEA-001455-PIP01-13
Marina Dimov Di Gusti	Restriction level XR	EMEA-001094-PIP01-10-M01
Romaldas Mačiulaitis	Restriction level XR	EMEA-001395-PIP01-12
Romaldas Mačiulaitis	Restriction level XR	EMEA-50-2013

Member, alternate, expert name	Outcome restriction following evaluation of electronic evaluation form	Topics on the current Committee Agenda for which this restriction applies
Romaldas Mačiulaitis	Restriction level XR	EMEA-51-2013
Tadej Avcin	Restriction level XP	EMEA-001071-PIP02-12-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 September 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
Jaroslav STERBA	Czech Republic
Marianne ORHOLM	Denmark
Irja LUTSAR	Estonia
Pirjo LAITINEN-PARKONNEN	Finland
Sylvie BENCHETRIT	France
Dirk MENTZER	Germany
Stefanos MANTAGOS	Greece
Agnes GYURASICS	Hungary
Gylfi OLKARSSON	Iceland
Kevin CONNOLLY	Ireland
Dina APELE-FREMIANE	Latvia
Romaldas MACIULAITIS	Lithuania
Carine de BEAUFORT	Luxembourg
Siri WANG	Norway
Marek MIGDAL	Poland
Helena FONSECA	Portugal
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
Ann Marie KAUKONEN	Finland
Birka LEHMANN	Germany
Melinda SOBOR	Hungary
Brian AYLWARD	Ireland
Francesca ROCCHI	Italy
Maaike van DARTEL	The Netherlands
Jolanta WITKOWSKA-OZOGOWSKA	Poland
Hugo TAVARES	Portugal
Dana Gabriela MARIN	Romania
Maria Jesus FERNANDEZ CORTIZO	Spain
Ninna GULLBERG	Sweden
Angeliki SIAPKARA	United Kingdom

Members representing patients' organisations

Tsveta SCHYNS-LIHARSKA

Members representing health care professionals

Adriana CECI

Anthony James NUNN

Alternates representing health care professionals

Paolo PAOLUCCI

Experts

Peter BAUER	Medical statistician

Observers

Immanuel BARTH

Aina OVERBUST

Tove Lill STENDAL

European Medicines Agency

Paolo TOMASI	Head of Paediatric Medicines

Sophie OLIVIER	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
Emilie DESFONTAINE	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
Cecile OLLIVIER	Scientific Administrator, Paediatric Medicines
Alessandro JENKNER	National Expert on Secondment, Paediatric Medicines
Aurelie HERVIEU	Assistant, Paediatric Medicines
Ramona ZEMACHE	Assistant, Paediatric Medicines