EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 March 2014
EMA/PDCO/60343/2014
Human Medicines Research & Development Support Division

# Paediatric Committee (PDCO)

## Minutes of the 12-14 February 2014 meeting

Chair: Dirk Mentzer

## I Introduction

### *I.1 Adoption of the minutes from previous meeting*

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.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 February 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

### *I.5 Leaving/New Members and Alternates*

Please refer to the February 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

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

# 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 February 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 96 procedures in total[1], of which:

- 44 paediatric investigation plan applications;
- 4 product-specific waiver applications;
- 8 compliance check procedures (interim and final);
- 39 requests for modifications of an agreed paediatric investigation plan;
- 1 re-examination request.

# IV Nomination of Rapporteurs and Peer reviewers

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| • List of letters of intent received for submission of applications with start of procedure April 2014[1] for Nomination of Rapporteur and Peer reviewer<br>• 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 February 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.

[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 |
|---|---|---|---|---|
| TV-45070 | Treatment of pain in patients with osteoarthritis | Treatment of primary and secondary osteoarthrosis | Not confirmed | Treatment of pain in chronic paediatric diseases. |
| vemurafenib | Treatment of adult patients with metastatic colorectal cancer positive for the $BRAF^{V600}$ mutation in combination with an anti-EGFR agent | Treatment of adenocarcinoma of the colon and rectum | Confirmed | Leukaemia, low and high grade gliomas, papillary thyroid carcinoma, Langerhans histiocytosis, neurofibromatosis-related malignancies, Juvenile myelomonocytic leukaemia (JMML) and rhabdomyosarcoma. |

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

No requests were received for the month of February.

## VIII Annual reports on deferrals

| Annual report based on PIP decision for | Substances (abbrev.) | Product Name | Orphan | Difficulties progressing the PIP? | Outcome |
|---|---|---|---|---|---|
| EMEA-000978-PIP01-10 | (propane-1-sulfonic acid {3-[5-(4-chlorophenyl)-1H-pyrrolo[2,3-b]pyridine-3-carb... | Zelboraf | No | Yes | The applicant is facing recruitment difficulties with the adolescent trial and plans to submit a PIP Modification request. |
| EMEA-000052-PIP01-07 | vandetanib | Caprelsa | Yes | No | The PDCO noted the report. |
| EMEA-000653-PIP01-09 | romiplostim | Nplate | Yes | Yes | The applicant reports recruitment difficulties. A procedure of modification of the agreed PIP is currently on-going. |

| Annual report based on PIP decision for | Substances (abbrev.) | Product Name | Orphan | Difficulties progressing the PIP? | Outcome |
|---|---|---|---|---|---|
| EMEA-000469-PIP01-08 | anidulafungin | Ecalta | No | Yes | The PDCO is informed of potential safety concerns with the use of the product in neonates. The concerns will be discussed with the committee through a planned modification procedure. |
| EMEA-000994-PIP01-10 | gadobutrol | Gadovist | No | No | The PDCO noted the report. |
| EMEA-000816-PIP02-10 | potassium sulphate / Magnesium sulphate, heptahydrate / Sodium sulphate, anhydro... | Izinova | No | No | The PDCO noted the report. |
| EMEA-000306-PIP01-08 | corifollitropin alfa | Elonva | No | No | The PDCO noted the report. |
| EMEA-001115-PIP01-10 | loxapine | Adasuve | No | No | The PDCO noted the report. |
| EMEA-000533-PIP01-08 | tenofovir disoproxil (as fumarate) | Viread | No | No | The safety issues with Tenofovir have been subject to CHMP discussion with PDCO input. The PIP has been modified. |
| EMEA-000553-PIP01-09 | lisdexamfetamine dimesylate | Venvanse | No | No | The PDCO noted the report. |

## IX Other topics

| Guidelines | |
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| Draft guideline on the clinical development of medicinal products for the treatment of human-immunodeficiency-virus (HIV) infection (under public consultation until 31/03/2014) | The PDCO discussed the draft guideline and agreed to contact PENTA for their view on the required duration of paediatric studies. |

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| Draft guideline on the clinical development of medicinal products for the treatment of Autism Spectrum Disorder (ASD)* | The PDCO has been informed about an expected delay of the review of the autism guideline. |
| Draft Guideline on clinical investigation of medicinal products for the treatment of Multiple Sclerosis* | The PDCO was informed about the status of the guideline and will provide further comments. |
| Draft Guideline on clinical investigation of medicinal products for the treatment of Duchenne and Becker muscular dystrophy* | The PDCO was informed about the status of the guideline. |
| **Working groups** | |
| Paediatric inventory | The group discussed the therapeutic areas of ophthalmology and oncology. |
| Paediatric oncology | The participants discussed contributions to the inventory concerning anti-cancer medicines and informed each other on ongoing activities concerning guidelines and projects. |
| Extrapolation | The meeting was cancelled. |
| 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** | |
| CHMP update on paediatric topics | An update on CHMP procedures of products with a Paediatric Investigation plan was presented to the PDCO members. |
| Debriefing on meetings related to the draft guideline on format and content of PIP applications* | A meeting was conducted at the Agency with the participation of staff from the European Commission, to agree on the provision of comments and suggestions from the Agency and its Paediatric Committee to the EC, regarding the proposed revised EC Guideline on the Format and Content of PIP applications. The PDCO will discuss the comments received by the EC in the March meeting. |
| Proposal for communicating on measures to prevent medication errors* | A presentation was given by colleagues in the Stakeholder and Communication Division to update the PDCO on initiatives regarding measures to prevent medication errors. |

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| Update on Enpr-EMA activities | Representatives of projects funded through the EC FP7 on off-patent medicines in children were invited to a meeting organised by the Enpr-EMA chair and hosted by the European Medicines Agency with the objectives:<br>1. To share experience with other international networks funded by FP7<br>2. To identify best practice for evaluating off-patent medicines in Europe<br>3. To identify key learning points for investigators, sponsors and regulators<br>4. To summarise the progress so far of the FP7 projects<br>5. To develop strategies that optimises the development and evaluation of off-patent medicines in Europe in order to avoid "reinventing the wheel" in future projects.<br>The minutes of the meeting will be circulated in the post-mail.<br>A meeting with the PDCO committee is planned within the next 2 months to discuss the proposals with the PDCO members. A representative from the EC will also be invited. |
| Project 2014 - Move to Churchill Place | Postponed |
| Election/designation of the new FWG Chair | The Committee was informed that the Formulation Working Group is in need of a Chair. Interested members were invited to apply. |
| Opening Managing Meeting Documents (MMD) access to members across committees | The Committee was informed that members and alternates of EMA committees can now access MMD areas with documents tabled for other committees (and the SAWP). |
| Draft standard PIP for DTP-Polio-Hib*: next steps | Following PDCO's last month comment on the risk of interference with maternal antibodies at 2 months, it was considered important to discuss this new element with the Expert working group (TC to organise). The draft standard PIP will also be presented to the experts after review by a subgroup of PDCO members.<br>Conclusions from the TC will then be rediscussed with the PDCO, who could adopt a letter to the CHMP/VWP. |

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| Extrapolation Group – working program for 2014* | The PDCO was informed that Gerard Pons is now Chair of the group and D. Brasseur (CHMP) Vice-Chair. The drafting of the reflection paper shall start end of February. There was a call for volunteers to review extrapolation in PIP applications and Guidance for extrapolation in PIP application will be published in March. |
| Propylene glycol in IV formulations for children under 4 years of age (EMEA/H/A-5(3)/1317) | The PDCO discussed and commented the draft version of this paper with the goal of preparing a document expressing the PDCO opinion on how certain sections of the paper could be improved. |
| Draft - Minutes of PDCO-COMP Working Group* | The PDCO discussed the draft minutes and acknowledged that the working group started its work. |
| Gaucher PIP – status update | The FDA has reviewed the last version of the document following SAWP comments. The document is now with SAWP/CHMP for finalisation |

### Any other business

- Inclusion of PDCO in the standard group of recipients for the early notification system:
  The Committee requested to be included in the early notification system mailing list of the Agency; the request will be forwarded to the relevant Division.
- Press activity on development of anticancer medicines for children:
  Several articles, which have appeared recently in the lay and specialised press on the lack of sufficient paediatric development for cancer medicines, were presented and discussed by the PDCO. The Committed agreed that while development of potentially useful paediatric oncology drugs has increased thanks to the Paediatric Regulation, more could still be done to address this acknowledged problem. Potential approaches are currently being discussed with the Agency and the EC, also in view of the on-going review of the EC Guideline on the Format and Content of PIP Applications. The Committee also decided to add to the Agenda of the next meeting the review of the class waiver list.
- Selection of Applications for routine inspections to be adopted during February CHMP:
  The PDCO was informed of the applications proposed for routine GCP inspections to be adopted at the February 2014 CHMP meeting.
- Agenda of the PCWP meeting: Document tabled for information
- Agenda of the PCWP/HCPWP joint meeting: Document tabled for information
- Agenda of the PCWP/HCPWP Workshop on benefit-risk: Document tabled for information

## 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 February 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 |
|---|---|---|
| Marek Migdal | Restriction level DP | EMEA-001581-PIP01-13 |
| Marek Migdal | Restriction level DP | EMEA-000486-PIP01-08-M03 |
| Marek Migdal | Restriction level DP | EMEA-000485-PIP01-08-M03 |
| Marek Migdal | Restriction level DP | EMEA-000325-PIP01-08-M03 |
| Marina Dimov Di Giusti | Restriction level DC | EMEA-001545-PIP01-13 |
| Michal Odermarsky | Restriction level XP | EMEA-000775-PIP01-09-M01 |
| Michal Odermarsky | Restriction level XP | EMEA-001577-PIP01-13 |
| Michal Odermarsky | Restriction level XP | EMEA-000804-PIP01-09-M02 |
| Michal Odermarsky | Restriction level XP | EMEA-001465-PIP01-13 |
| Paolo Rossi | Restriction level XR | EMEA-001458-PIP01-13 |
| Paolo Rossi | Restriction level XR | EMEA-001430-PIP01-13 |
| Violeta Iotova | Restriction level XP | EMEA-001030-PIP01-10-M02 |

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:<br>- 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.<br>- Cannot act as Rapporteur for these products<br>- [Cannot act as Rapporteur for development of guidelines in concerned therapeutic area]. |
| XC | Where cross product / general involvement is declared - COMPANY:<br>- No involvement (as outlined above) with respect to products from the specified company.<br>- Cannot act as Rapporteur for products from the relevant company(ies). |
| DP | Where Individual product involvement is declared - PRODUCT INDICATION:<br>- Involvement in discussions only with respect to procedures involving the relevant product or a competitor product<br>i.e. no part in final deliberations and voting as appropriate as regards these medicinal products.<br>- Cannot act as Rapporteur for these products. |
| DC | Where cross product / general involvement is declared - COMPANY:<br>- Involvement in discussions only with respect to products from the specified company.<br>- 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 February 2014

List of Participants

**Chair**

Dirk MENTZER

**Members appointed by Member States or CHMP**

| | |
|---|---|
| Karl Heinz HUEMER | Austria |
| Koenraad NORGA | Belgium |
| Violeta IOTOVA | Bulgaria |
| Marina DIMOV DI GUSTI | Croatia |
| Jaroslav STERBA | Czech Republic |
| Marianne ORHOLM | Denmark |
| Pirjo LAITINEN-PARKONNEN | Finland |
| Sylvie BENCHETRIT | France |
| Birka LEHMANN | Germany |
| Agnes GYURASICS | Hungary |
| Kevin CONNOLLY | Ireland |
| Paolo ROSSI | Italy |
| Carine de BEAUFORT | Luxembourg |
| John Joseph BORG | Malta |
| Siri WANG | Norway |
| Marek MIGDAL | Poland |
| 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**

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|---|---|
| Jacqueline CARLEER | Belgium |
| Bernard KAIC | Croatia |

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| Marta GRANSTRÖM | Denmark |
| Jana LASS | Estonia |
| Immanuel BARTH | Germany |
| Brian AYLWARD | Ireland |
| Herbert LENICKER | Malta |
| Maaike van DARTEL | The Netherlands |
| Jolanta WITKOWSKA-OZOGOWSKA | Poland |
| Hugo TAVARES | Portugal |
| Maria Jesus FERNANDEZ CORTIZO | Spain |
| Ninna GULLBERG | Sweden |
| Martina RIEGL | United Kingdom |

**Members representing patients' organisations**

Michal ODERMARSKY

**Members representing health care professionals**

Anthony James NUNN

**Alternates representing health care professionals**

Paolo PAOLUCCI

**Experts**

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| Mikael ANDERSSON | Medical Products Agency, Sweden |

**Observers**

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| Eleni GAKI | Medicines and Healthcare Products Regulatory Agency, United Kingdom |

**European Commission**

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| Florian SCHMIDT | European Commission, Directorate General for Health |

**European Medicines Agency**

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| Agnes SAINT RAYMOND | Head of Programme Design Board |
| Jordi LLINARES GARCIA | Head of Product Development Scientific Support Department |
| Paolo TOMASI | Head of Paediatric Medicines |
| Sophie OLIVIER | Scientific Officer, Paediatric Medicines |
| Andrea ECKER | Scientific Officer, Paediatric Medicines |
| Benjamin PELLE | Scientific Officer, Paediatric Medicines |

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| Cecile OLIVIER | Scientific Officer, Paediatric Medicines |
| Chrissi PALLIDIS | Scientific Officer, Paediatric Medicines |
| Dobromir PENKOV | Scientific Officer, Paediatric Medicines |
| Emilie DESFONTAINE | 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 |
| Ramona ZEMACHE | Assistant, Paediatric Medicines |
| Aurelie HERVIEU | Assistant, Paediatric Medicines |