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PRESS RELEASE
Meeting highlights from the Paediatric Committee, 27-29 August 2008

Opinions on paediatric investigation plans adopted
The Paediatric Committee (PDCO) adopted positive opinions on paediatric investigation plans (PIPs) for the following medicines:

- **Abatacept,** from Bristol-Myers Squibb Pharma EEIG, in the therapeutic area of immunology and rheumatology;
- **Alanine, arginine, aspartic acid, cysteine/cystine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine monohydrate, methionine, ornithine hydrochloride, phenylalanine, proline, serine, taurine, threonine, tryptophan, tyrosine, valine, sodium chloride, potassium acetate, magnesium acetate, tetrahydrate, calcium chloride, sodium glycerophosphate, glucose, olive oil refined, soya-bean oil refined**, from Baxter World Trade SA/NV, in the therapeutic area of nutrition;
- **Catridecacog,** from Novo Nordisk A/S, in the therapeutic area of haematology;
- **Denosumab,** from Amgen Europe B.V., in the therapeutic areas of oncology and immunology and rheumatology;
- **Diphtheria, tetanus, acellular pertussis, haemophilus B, and poliomyelitis vaccine,** from Sanofi Pasteur MSD SNC, in the therapeutic area of vaccines;
- **Influenza virus surface antigens,** from Novartis Vaccines & Diagnostics GmbH & Co. KG, in the therapeutic area of vaccines;
- **Liraglutide,** from Novo Nordisk A/S, in the therapeutic area of endocrinology, gynaecology, fertility and metabolism;
- **Mometasone furoate - formoterol fumarate dihydrate,** from Novartis Europharm Limited, in the therapeutic area of pneumology;
- **Peginterferon alfa-2b,** from Schering-Plough Europe, in the therapeutic area of gastroenterology;
- **Valsartan,** from Novartis Europharm Limited, in the therapeutic area of cardiovascular diseases;
- **Vicriviroc maleate,** from Schering-Plough Europe, in the therapeutic area of infectious diseases.

A paediatric investigation plan sets out a programme for the development of a medicine in the paediatric population. The PIP aims to generate the necessary quality, safety and efficacy data through studies to support the authorisation of the medicine for use in children of all ages. These data have to be submitted to the EMEA as part of an application for a marketing authorisation for new medicinal products or products covered by a patent. In some cases, a PIP may include a waiver to study one or more age groups of children, or a deferral when it is appropriate to conduct studies in adults prior to initiating studies in the paediatric population, or when studies in the paediatric population would take longer to conduct than studies in adults.

* The information concerning the therapeutic areas of denosumab has been corrected.

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Opinions on product-specific waivers
The PDCO adopted a product-specific waiver, recommending that the obligation to submit data obtained through clinical studies with children be waived in all subsets of the paediatric population, for the following medicines:

- **Chimeric murine-human anti interleukin 6 monoclonal antibody,** from Centocor, BV, in the therapeutic area of oncology;
- **Lidocaine - prilocaine,** from Plethora Solutions Limited, in the therapeutic area of uro-nephrology;
- **Naproxen - esomeprazole magnesium trihydrate,** from AstraZeneca AB, in the therapeutic area of immunology and rheumatology.

Waivers to the obligation to submit clinical-trials data in children at the time of an application for a marketing authorisation can be issued if there is evidence showing that the medicinal product concerned is likely to be ineffective or unsafe in the paediatric population, or that the disease or condition targeted occurs only in adult populations, or that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

Re-examination of opinion
Following a request for re-examination of the opinion adopted for a product-specific waiver in July 2008, the PDCO confirmed its previous position and adopted a product-specific waiver for **pioglitazone (as hydrochloride) - metformin hydrochloride,** from Takeda Global Research and Development (Europe) Limited, in the therapeutic area of endocrinology and metabolism.

A re-examination of an opinion can be requested by the applicant within 30 days following receipt of the opinion of the PDCO. The grounds for the re-examination should be based only on the original information and scientific data provided in the application which were previously available to the PDCO and on which the initial opinion was based. This may include new analysis of the same data or minor protocol amendments to a previously proposed study. Significant changes to the previous plan cannot be part of the re-examination process.

Adoption of a class waiver
The PDCO adopted an opinion on a class waiver for a class of medicinal products called PPAR-gamma modulators, including dual and multiple PPAR modulators (e.g. thiazolidinediones, glitazars, triple modulators), used in the treatment of type II diabetes mellitus. The Committee recommended that, for medicines belonging to this class and developed in this condition, the requirement to submit clinical trials data in all subsets of the paediatric population in compliance with an agreed PIP be waived, because the class of medicinal products is likely to be unsafe in all of the paediatric population in the condition specified. The opinion will be forwarded to the EMEA for a decision.

The EMEA already adopted decisions on a list of waivers in July 2008 for conditions that do not occur in children. The list of waivers will be regularly updated in light of the advance in knowledge and science in the paediatric field.

Opinion on a modification of an agreed PIP
The PDCO adopted an opinion on a modification of an agreed PIP for **13 valent pneumococcal conjugate vaccine**, from Wyeth Lederle Vaccines S.A., in the therapeutic area of vaccines. This opinion follows the adoption of the PDCO opinion in May 2008.

Modifications to an agreed PIP can be requested by the applicant when the plan is no longer appropriate or there are difficulties rendering the plan unworkable.

Update of the priority list for off-patent medicines

The PDCO finalised, after a public consultation phase, the second update of the priority list for studies into off-patent medicines (not covered by a patent in Europe). Companies applying for funding from the European Community through the Seventh Framework Programme can refer to this list. This will eventually result in the submission of applications for paediatric-use marketing authorisations. The updated list will be published shortly in the 'Medicines for children' section of the EMEA website, in advance of the next call from the European Commission in September 2008.

Following analysis of comments received from the National Institutes of Health and the US Food and Drug Administration, and following the discussions with these two bodies, the updated list comprises approximately 50 medicines relating to the therapeutic areas of cardiology, child and adolescent psychiatry, dermatology, endocrinology, gastroenterology, immunology, infections, intensive care/anaesthesiology, metabolism, neonatology, nephrology/urology, neurology, oncology, pain and rheumatology.

Data to be collected by Member States

The PDCO heard a progress report from its Austrian member on the work by Austrian authorities to collect data on all existing uses of medicinal products in the paediatric population, including their experience on the methodology used, for the benefit of other Member States, who will have to carry out similar exercises, in accordance with the Paediatric Regulation. To ensure consistency, the PDCO adopted guidance in October 2007 on the content and the format of data to be collected by Member States on all existing uses of medicinal products in the paediatric population. This exercise should be completed by the end of 2008, and the results have to be communicated to the Agency.

The data will be used by the PDCO to establish an inventory of paediatric needs, to be published by the EMEA by January 2010 at the latest.

The next meeting of the PDCO will be held on 17-19 September 2008.

-- ENDS --

Notes:

1. PDCO opinions on PIPs and waivers are transformed into EMEA decisions within the timeframe laid down by the Paediatric Regulation (Regulation (EC) No 1901/2006, as amended). The decisions can be found on the EMEA website: http://www.emea.europa.eu/htms/human/paediatrics/decisions.htm
2. More information about the PDCO and the Paediatric Regulation is available in the 'Medicines for children' section of the EMEA website.
3. This press release, together with other information on the work of the EMEA, can be found on the EMEA website: http://www.emea.europa.eu

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OVERVIEW OF PAEDIATRIC INVESTIGATION PLAN/WAIVER APPLICATIONS

	2007 (August to December)	**2008** (January to August)	**Cumulative Total**
Total number of validated PIP / waiver applications	**85**	**190**[1]	**275**[2]
Applications submitted for a product not yet authorised *(Article 7)*[3]	39	133	172 *(63%)*
Applications submitted for a product already authorised still under patent in view of a submission of a variation/extension for a new indication, pharmaceutical form or route of administration *(Article 8)*	45	52	97 (*35%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30)*	1	5	6 *(2%)*
PIPs and full waiver indications covered by these applications	**202**	**284**	**486**

Number of Paediatric Committee opinions	**2007**	**2008**	**Cumulative Total**
Positive on full waiver	10	28	38
Positive on PIPs including potential deferral	2	54	56
Negative opinions adopted	0	1	1
Positive opinions adopted on modification of the PIP	0	2	2
Positive opinion on compliance with PIP	0	1	1

[1] Figures including 27 August 2008 start of procedure; the figure does not include products that are currently under validation.
[2] Of which 58 are requests for full waiver.
[3] Applications submitted in accordance with Regulation (EC) No 1901/2006, as amended.

Areas covered by PIPs/waiver applications:	**2007 %**	**2008 %**
Neurology	12	3
Uro-nephrology	-	4
Gastroenterology-hepatology	9	3
Pneumology-allergology	8	6
Infectious diseases	12	8
Cardiovascular diseases	12	11
Diagnostics	-	2
Endocrinology-gynaecology-fertility-metabolism	19	18
Neonatology-paediatric intensive care	-	-
Immunology-rheumatology-transplantation	5	6
Psychiatry	5	3
Pain	1	3
Haematology-haemostaseology	1	6
Otorhinolaryngology	-	-
Oncology	11	13
Dermatology	1	2
Vaccines	2	8
Ophthalmology	1	2
Anaesthesiology	-	1
Nutrition	1	1