25th February 2010
EMA/CHMP/108850/2010

Monthly Report

Committee for Medicinal Products for Human Use (CHMP)

15-19 February 2010

The CHMP welcomed Dr Milena Stain as the new CHMP Alternate from Austria, replacing Prof Hans Winkler in this role and Dr Roxana Mustata as the new CHMP Alternate from Romania, replacing Dr Raluca Cirstea in this role. Dr Mustata is also the CHMP representative (alternate) on the PDCO. The Chairman, on behalf of the Committee, thanked Prof Hans Winkler for his contributions to the CHMP during the past year, and Dr Cirstea for her alternate roles in the CHMP and PDCO.

CENTRALISED PROCEDURE

5th pandemic vaccine recommended for approval

The Agency's Committee for Medicinal Products for Human Use (CHMP) recommended by majority the granting of a conditional marketing authorisation for a fifth pandemic vaccine, **Humenza** (split virion, inactivated, AF03 adjuvanted influenza H1N1 pandemic vaccine), from Sanofi Pasteur SA, intended for the prophylaxis of influenza in an officially declared pandemic situation. This recommendation was made using an emergency procedure which fast-tracks evaluation of new vaccines developed during a pandemic.

More information on pandemic medicines is available in a separate press release.

Initial applications for marketing authorisation

New medicinal products

The CHMP adopted a positive opinion by majority on an initial marketing authorisation application recommending the granting of a conditional marketing authorisation for:

- **Votrient** (pazopanib), from Glaxo Group Ltd, intended for the treatment of patients with advanced renal cell carcinoma. The review for Votrient began on 25 March 2009 with an active review time of 210 days. Votrient is the **63rd orphan medicinal product** to receive a positive opinion by the CHMP. A marketing authorisation under conditional approval means that further evidence on the

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medicinal product is awaited. In the case of Votrient this relates to clinical data of pazopanib in comparison with sunitinib in the treatment of patients with advanced renal cell carcinoma. The European Medicines Agency will review new information within one year and update the product information as necessary.

- The Committee adopted a negative opinion by majority, recommending that **Zeftera** (ceftobiprole medocaril), from Janssen-Cilag International NV, should not be granted a marketing authorisation. Zeftera is an antibiotic, intended for the treatment of patients with complicated skin and soft tissue infections. *More information about Zeftera is available in a question-and answer-document.*

Generic medicinal products

The Committee adopted two positive opinions by consensus for the following generic medicines:

- **Docefrez** (docetaxel), from Sun Pharmaceutical Industries Europe B.V., a generic of Taxotere, which is authorised in the European Union for the treatment of breast cancer, non-small cell lung cancer, prostate cancer, gastric adenocarcinoma, and head and neck cancer.
- **Raloxifene Teva** (raloxifene hydrochloride), from Teva Pharma B.V., a generic of Evista, which is authorised in the European Union for treatment and prevention of osteoporosis in postmenopausal women.

Summaries of opinion for all above mentioned medicines, including their full indication, can be found here.

Further information will be included in the European Public Assessment Reports (EPARs) once the European Commission has granted final approval for the above mentioned positive opinions.

Positive opinion for the second 'compassionate use' application adopted

The Committee adopted the second positive opinion on compassionate use by consensus under the European rules on compassionate use. This application related to **IV Zanamivir**, a new intravenous formulation of zanamivir, from GlaxoSmithKline Research & Development Limited, to treat critically ill patients having a life-threatening condition due to pandemic or seasonal influenza.

A separate press release with more information about the compassionate use procedure is available here.

Withdrawals

The European Medicines Agency has been formally notified by United Therapeutics Europe Ltd of its decision to withdraw its application for a centralised marketing authorisation for the medicine Tyvaso (treprostinil sodium) 0.6 mg/ml nebuliser solution. This medicine was intended for use as adjuvant therapy in patients with pulmonary arterial hypertension who were also receiving either an endothelin receptor antagonist or a phosphodiesterase-5 inhibitor. A separate press release with more information is available. A question-and-answer document will be published following the March CHMP meeting.

Post-authorisation procedures

Extensions of indications and other recommendations

The Committee gave two positive opinions by consensus for applications for extension of indication, adding a new treatment option, for the following medicines:

- **Cholestagel** (colesevelam), from Genzyme Europe B.V., to extend the therapeutic indication, to include combination treatment of colesevelam with ezetimibe, with or without a statin, in adult patients with primary hypercholesterolaemia, including patients with familial hypercholesterolaemia.
- **Tyverb** (lapatinib), from Glaxo Group Ltd, to extend the therapeutic indication to include the treatment of patients with breast cancer whose tumours overexpress HER2 (ErbB2), in combination with an aromatase inhibitor in postmenopausal women with hormone receptor-positive metastatic disease, not currently intended for chemotherapy. The patients in the registration study were not previously treated with trastuzumab or an aromatase inhibitor.

Summaries of opinion for all mentioned medicines, including their full indication, can be found here.

Additional safety information

The CHMP agreed on a Direct Healthcare Professional Communication for **Aclasta** (zoledronic acid) 5mg solution for infusion from Novartis Europharm Limited informing healthcare professionals that renal impairment and renal failure have been observed following administration of Aclasta, especially in patients with pre-existing renal dysfunction or other risks, including advanced age, concomitant use of nephrotoxic medicinal products, diuretic therapy, or dehydration. In order to minimize the risk of adverse reactions, the following advice is given to health care professionals: *creatinine clearance should be measured before each Aclasta dose; Aclasta should not be used in patients with creatinine clearance < 35 ml/min; monitoring of serum creatinine should be considered in patients at risk. Patients, especially elderly patients and those receiving diuretic therapy, should be appropriately hydrated prior to administration of Aclasta*. Furthermore the CHMP agreed, on the basis of these findings, to update section 4.2, 4.4, 4.5 and 4.8 of the Summary of Product Characteristics. The Package Leaflet has been updated accordingly.

Following the assessment of the 4th Periodic Safety Update Report (PSUR), the CHMP adopted amendments to sections 4.4 and 4.8 of the Summary of Product Characteristics (SPC) of **Revlimid** (lenalidomide) from Celgene Europe Limited, to add a warning indicating that myocardial infarction has been reported in patients receiving lenalidomide, particularly in those with known risk factors. Consequently, patients with known risk factors should be closely monitored, and action should be taken to try to minimize all modifiable risk factors (e.g. smoking, hypertension, and hyperlipidaemia). Myocardial infarction has been added to section 4.8 of the SPC as a common adverse reaction of Revlimid. The Package Leaflet has been updated accordingly.

The CHMP adopted amendments to section 4.4 of the Summary of Product Characteristics (SPC) of **Arava** (leflunomide) from Sanofi-Aventis Deutschland GmbH. Section 4.4 of the SPC was amended to include a warning that rare cases of Progressive Multifocal Leukoencephalopathy (PML) have been reported in patients receiving leflunomide among other immunosuppressants. This variation application was submitted further to a request from CHMP, following the assessment of a follow-up measure discussing the occurrence of PML in two patients treated with leflunomide.

The CHMP adopted several amendments to sections 4.4 and 4.8 of the Summary of Product Characteristics (SPC) of **Thalidomide Celgene** (thalidomide) from Celgene Europe Limited, with

information regarding the risk of tumour lysis syndrome and addition of the adverse drug reactions febrile neutropenia and gastrointestinal perforations reported in the post-marketing experience, as requested by the CHMP further to the assessment of the 2nd Periodic Safety Update Report. The Package Leaflet has been updated accordingly.

The CHMP adopted amendments to sections 4.4 and 4.8 of the Summary of Product Characteristics (SPC) of **InductOs** (dibotermin alfa) from Wyeth Europa Ltd. Section 4.4 of the SPC was amended to inform that a device migration (movement of the metal cage from the initial surgical placement) could occur after the use of dibotermin alfa in spinal fusion surgery and that this may necessitate surgical revision. In addition section 4.8 of the SPC was amended to report that in some cases, the device migration was reported in association with bone resorption and formation of fluid collections.

The CHMP adopted amendments to sections 4.4 and 4.8 of the Summary of Product Characteristics (SPC) of **Ivemend** (fosaprepitant dimeglumine) from Merck Sharp & Dohme Ltd. Section 4.4 of the SPC was amended to add a warning of immediate hypersensitivity reactions such as flushing, erythema, and dyspnea that have rarely occurred during fosaprepitant infusion.

Sanofi-Aventis Deutschland GmbH, MAH for **Lantus/Optisulin** (insulin glargine) submitted to the Agency final study protocols of epidemiological studies regarding the conduct of clinical trials investigating the possible association between insulin glargine and cancer. The assessment of these study protocols by the CHMP is currently ongoing. Further communication on this aspect will follow once the review of these study protocols is completed. The Committee had concluded in July 2009 that the available data did not provide a cause for concern and that changes to the prescribing advice were therefore not necessary.

The CHMP finalised three type II variations procedures for **Volibris** (ambrisentan) from Glaxo Group Limited. Further to data submitted on drug-drug interactions with warfarin added in section 4.5 of the Summary of Product Characteristics (SPC), a warning in section 4.4 was also introduced to ensure close monitoring of patients when co-administered with rifampicin. The SPC was also updated to introduce a warning in section 4.4 on possibility of pulmonary veno-occlusive disease in patients treated with endothelin receptor antagonists. Furthermore, following the assessment of the 3rd PSUR, section 4.8 of the SPC was amended to add hypotension, syncope, nausea, vomiting, and diarrhoea as undesirable effects of unknown frequency.

The CHMP recommended amendments to sections 4.4, 4.8 and 5.1 of the Summaries of Product Characteristics (SPCs) of the rosiglitazone-containing medicines **Avandia, Avandamet** and **Avaglim** from SmithKline Beecham Ltd. This followed the finalisation of the review of a recently completed long-term cardiovascular outcome study with Avandia (the 'RECORD' study) and an update of the meta-analysis of 42 short-term studies investigating cardiac ischaemia. The Committee recommended updating the information on myocardial ischaemia in sections 4.4 and 4.8 of the SPC and including the RECORD study's results in section 5.1. In addition the Committee recommended updating the information on bone disorders in sections 4.4 and 4.8 of the SPC to reflect the additional experience from the RECORD study. The Committee concluded that no additional changes are necessary to the already existing warnings and contraindications concerning the cardiovascular safety of these medicines.

Update on supply shortage for Cerezyme and Fabrazyme

The Committee was informed that the supply shortages for Cerezyme and Fabrazyme are continuing for longer than expected and that Genzyme has not resumed full production.

Therefore, patients and prescribers of Cerezyme and Fabrazyme are advised to continue to follow the interim recommendations made by the Committee on 22 October 2009 for Cerezyme and 25 September 2009 for Fabrazyme.

All patients, especially those with adjusted dose regimens, should be closely monitored by their doctor. These recommendations remain valid until further notice.

Because the manufacturing difficulties have been on-going since June 2009, the CHMP is closely monitoring the GMP compliance status of the manufacturing site and has requested a further inspection.

OTHER INFORMATION ON THE CENTRALISED PROCEDURE

Lists of Questions

The Committee adopted one List of Questions on initial applications under the optional scope together with one List of Questions on a "line extension" application (in accordance with Annex II of Commission Regulation (EC) No. 1085/2003).

Detailed information on the centralised procedure

Since January 2010 the monthly figures related to the centralised procedure activities are published independently on the Agency's website within two weeks following the end of the CHMP meeting and can be found here. The overview of opinions for annual re-assessments and renewals is provided in **Annex 1**. The list of medicinal products for which marketing authorisations have been granted by the European Commission since the CHMP plenary meeting in January 2010 is provided in **Annex 2.**

Applications for marketing authorisations for orphan medicinal products

Details of those orphan medicinal products that have been subject of a centralised application for marketing authorisation since the January 2010 CHMP plenary meeting are provided in **Annex 3**.

Name Review Group (NRG)

Statistical information on the outcome of the checking of acceptability of proposed invented names for medicinal products processed through the centralised procedure is provided in **Annex 4** *(corrections to figures provided in the December 2009 CHMP report regarding the Name Review Group statistical outcome are provided in* ***Annex 4 bis****)*.

REFERRAL PROCEDURES

Review of Regranex concluded

Finalising a review of **Regranex** (bercaplermin), from Janssen-Cilag International NV, and the possible risk of cancer, the Committee concluded that the benefits of this medicine continue to outweigh its risks for diabetic patients with long-term skin ulcers, but recommended to contraindicate Regranex, as a precautionary measure, in patients who have any pre-existing cancer. The review was carried out under Article 20 of Regulation (EC) No 726/2004.

More information about this review is available in a separate press release and a question-and-answer document.

Arbitrations concluded

The Committee completed arbitration procedures initiated because of disagreement among EU Member States regarding the authorisation of **Clopidogrel Teva 75 mg Film coated Tablets** (clopidogrel), from Teva Pharma, and **Clopidogrel Orion 75 mg Film coated Tablets** (clopidogrel), from Orion Corporation. These medicines are generics of Plavix and are indicated for patients suffering from myocardial infarction, ischaemic stroke, established peripheral arterial disease or acute coronary syndrome. The procedures were initiated because of concerns regarding the use of a clopidogrel base as the active substance, which had to be stabilised using the antioxidant butylated hydroxyanisole. The Committee concluded that the antioxidant used to stabilise the clopidogrel base did not pose a serious risk to patients and that the benefit-risk profile of these medicines was positive and recommended that marketing authorisations should be granted.

Question-and-answer documents with more information about these referrals can be found here.

Harmonisation referrals concluded

The Committee recommended that the marketing authorisations of generic **escitalopram-**containing medicinal products from Alfred E. Tiefenbacher GmbH & Co KG and associated companies should be suspended in Member States where these medicines are currently authorised. These medicines are used to treat major depressive episodes. The review was initiated because of disagreements on whether to maintain or suspend the marketing authorisations in the countries where they were authorised. The Committee noted that some of the data to support the applications for the generic medicines were still protected under the data exclusivity rules and could not be used in the assessment of the application. The CHMP was of the opinion that the rest of the submitted data provided insufficient evidence to show that the generic medicines were comparable to the reference medicine and recommended that marketing authorisations should be suspended.

A question-and-answer document with more information about these referrals can be found here.

Review of Diflucan started

The Committee started a harmonisation exercise for **Diflucan** (fluconazole) an antifungal medicinal product from Pfizer group of companies and associated companies. The review was triggered by the European Commission under Article 30 of Directive 2001/83/EC, as amended, due to the need of harmonisation of the Summary of Product Characteristics across various Members States.

Review of nimesulide started

The Committee started a full assessment of the benefits and risks of **nimesulide-containing medicinal products** for systemic use, because of ongoing concerns over their gastrointestinal and hepatic safety. Nimesulide is a non-steroidal anti-inflammatory drug (NSAID) used to treat acute pain, the symptoms of painful osteoarthritis and primary dysmenorrhoea.
The review was started at the request of the European Commission under Article 31 of Directive 2001/83/EC. The CHMP will make a recommendation on whether marketing authorisations of nimesulide-containing medicinal products should be maintained, changed, suspended or revoked.

MUTUAL-RECOGNITION AND DECENTRALISED PROCEDURES - HUMAN

The CHMP noted the report from the 48th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 15-16 February 2010. For further details, please see the relevant press release on the CMD(h) website under the heading 'Press Releases': http://www.hma.eu/

CHMP WORKING PARTIES

The CHMP was informed of the outcome of the discussions of the Scientific Advice Working Party (SAWP) meeting, which was held on 25-27 January 2010. For further details, please see **Annex 5**.

Documents prepared by the CHMP Working Parties adopted during the February 2010 CHMP meeting are listed in **Annex 6**.

UPCOMING MEETINGS FOLLOWING THE DECEMBER 2009 CHMP PLENARY MEETING

- The 64th meeting of the CHMP will be held at the Agency on 15-19 March 2010.
- The next Name Review Group meeting will be held at the Agency on 23 March 2010.
- The 49th CMD(h) will be held at the Agency on 15-16 March 2010.
- The workshop on Nanomedicines will be held at the Agency on 26th-27th April 2010.

ORGANISATIONAL MATTERS

The main topics addressed during the February 2010 CHMP meeting related to:

- The re-election of Dr Raine as Chair of the Pharmacovigilance Working Party.
- The endorsement of the Pharmacovigilance Working Party recommendation regarding the proposal to appoint Dr Torbjørn Callreus, Dr Giampiero Mazzaglia and Dr Eugene van Puijenbroek as Co-opted PhVWP members.
- The re-appointment of Dr Gale as Chair of the SAG Diabetes and Endocrinology and Dr Kiess as Vice-Chair.
- The adoption of Rapporteurs and CHMP assessment report templates for conditional renewals.
- A presentation of an overview of the peer review process since its implementation in April 2005. The Committee acknowledged the overall benefit of such process. An SOP setting out the actions and responsibilities of the peer reviewers is publicly available. Comments were raised with regard to extending the scope of the peer review to other procedures such as extension of indications, Article 31 referrals, and generics. It was agreed that further reflections on such points were needed and follow-up discussion will take place at future ORGAM meetings.
- Follow-up discussions regarding Working Parties (WP) restructure. The complexity and workload of the system have increased considerably over the years. This fact, together with the creation of new Committees has created a need to review, in-depth, the structure, composition and mandate of

CHMP WPs with the aim of improving their efficiency and avoiding overlapping tasks and priorities amongst them, while stating clearly the role that each WP is expected to play. Once proposals are at a final stage these will be published on the Agency's website.

- The adoption of CHMP meeting dates foreseen for 2013, 2014 and 2015. These will be published shortly.
- Follow-up discussion on selection of control arms for confirmatory trials. Due to the complexity of the topic, further discussion is foreseen at future ORGAM meetings.
- Preliminary discussion to address the heavy workload during monthly CHMP meetings. Proposals for improvement of efficiency during meetings will be investigated.
- Preliminary discussion regarding the working definition of nanomedicines.
- An oral report outlining the main conclusions of the workshop on Radiopharmaceuticals labelled with Radionuclides produced in Reactors that was held on 4th-5th February 2010.

PROCEDURAL ANNOUNCEMENT

Notification of Cessation of marketing activity

The Agency has been made aware that a number of Marketing Authorisation Holders have failed to inform the Agency about the cessation of marketing of presentations for centrally authorised medicinal products in accordance with the post-authorisation guidance (http://www.ema.europa.eu/htms/human/postguidance/18007805en.pdf). The Agency reminds Marketing Authorisation Holders of their legal obligation to inform the Agency (Product Team Leader) as early as possible, at least two months in advance of the planned cessation of the marketing activity of any presentation of an authorised product per Member State, so that ways can be sought to lessen the impact on patients. Marketing Authorisation Holders are encouraged to proactively discuss with the Agency and Rapporteurs well in advance of any cessation and covering different aspects such as grounds, length of cessation period, Member States concerned and company's intentions to provide information to prescribers and patients etc. The Agency reserves the right to make breaches of this legal obligation by Marketing Authorisation Holders public.

Dossier submission requirements - Number of electronic copies and cover letter

From the date of the publication of this monthly report, only one copy (on CD-ROM or DVD) of applications in electronic format should be submitted to the Agency.
Applicants are reminded that the electronic application should always be accompanied by a cover letter providing information as to the origin and nature of the application, preferably in the 'subject' line

- Product name (or proposed name)
- Product number ("EMEA/…" number; not EU number) - where applicable
- Type of submission (Type IA/ IB/ II / Renewal, Annual re-assessment, PSURs , FUMs, SOBs)
- Brief description of submission (e.g. scope of variation, responses to Request for Supplementary Information, responses to Day 120 List of Questions etc…)
- eCTD sequence number
- Customer account number if applicable
- Purchase number if applicable
- Contact person and Technical contact at MAA with telephone number and email address

Replacement sequences of a previously submitted eCTD application (e.g. following corrections) are not acceptable. Instead corrected eCTD applications should always be submitted as a new eCTD sequence.

Applicants are also reminded that since 1st January 2010, eCTD is the only acceptable electronic format for all applications and all submission types. Non-eCTD electronic applications are no longer a valid format for submissions.

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This CHMP Monthly Report and other documents are available on the Internet at the following address: http://www.ema.europa.eu

ANNEX 1 TO CHMP MONTHLY REPORT FEBRUARY 2010

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Benefix (nonacog alfa), Wyeth Europe Ltd	Positive opinion	No remaining grounds for the Marketing Authorisation to remain under exceptional circumstances
Atryn (recombinant antithrombin alfa), LEO Pharma A/S	Positive opinion	Marketing Authorisation remains under exceptional circumstances
Yondelis (trabectedin), PharmaMar S.A.	Positive opinion	Marketing Authorisation remains under exceptional circumstances
Xagrid (anagrelide), Shire Pharmaceutical Contracts Ltd	Positive opinion	Marketing Authorisation remains under exceptional circumstances
Ceplene (Histamine dihydochloride), EpiCept GmbH	Positive opinion	Marketing Authorisation remains under exceptional circumstances

Opinion for renewals of conditional MA's		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
N/A	N/A	N/A

Opinions for 5-Year Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Optisulin (insulin glargine), Sanofi-Aventis Deutschland GmbH	Positive opinion	Recommending additional renewal
Lantus (insulin glargine), Sanofi-Aventis Deutschland GmbH	Positive opinion	Recommending additional renewal
Orgalutran (ganirelix), N.V. Organon	Positive opinion	Unlimited validity
PegIntron (peginterferon alfa-2b), Schering-Plough Europe	Positive opinion	Unlimited validity
ViraferonPeg (peginterferon alfa-2b), Schering-Plough Europe	Positive opinion	Unlimited validity
Visudyne (verteporfin), Novartis Europharm Ltd	Positive opinion	Unlimited validity

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE THE JANUARY 2010 CHMP MONTHLY REPORT

Invented Name	Elonva
INN	corifollitropin alfa
Marketing Authorisation Holder	N.V. Organon
Proposed ATC code	G03GA09
Indication	Controlled Ovarian Stimulation (COS) in combination with a GnRH antagonist for the development of multiple follicles in women participating in an Assisted Reproductive Technology (ART) program.
CHMP Opinion date	19.11.2009
Marketing Authorisation Date	25.01.2010

Invented Name	Temomedac
INN	temozolomide
Marketing Authorisation Holder	Alfred E. Tiefenbacher GmbH & Co. KG
Proposed ATC code	L01A X03
Indication	Treatment of: - adult patients with newly-diagnosed glioblastoma multiforme concomitantly with radiotherapy (RT) and subsequently as monotherapy treatment. - children from the age of three years, adolescents and adult patients with malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma, showing recurrence or progression after standard therapy.
CHMP Opinion date	19.11.2009
Marketing Authorisation Date	25.01.2010

Invented Name	Docetaxel TEVA
INN	docetaxel
Marketing Authorisation Holder	Teva Pharma B.V.
Proposed ATC code	L01CD 02
Indication	Breast cancer, Non-small cell lung cancer, Prostate cancer, Gastric adenocarcinoma, Head and neck cancer
CHMP Opinion date	19.11.2009
Marketing Authorisation Date	26.01.2010

Invented Name	Telmisartan Teva
INN	telmisartan
Marketing Authorisation Holder	Teva Pharma B.V.
Proposed ATC code	C09CA07
Indication	Treatment of essential hypertension in adults
CHMP Opinion date	19.11.2009
Marketing Authorisation Date	26.01.2010

Invented Name	Temozolomide Teva
INN	temozolomide
Marketing Authorisation Holder	Teva Pharma B.V.
Proposed ATC code	L01A X03
Indication	Treatment of: - adult patients with newly-diagnosed glioblastoma multiforme concomitantly with radiotherapy (RT) and subsequently as monotherapy treatment. - children from the age of three years, adolescents and adult patients with malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma, showing recurrence or progression after standard therapy.
CHMP Opinion date	19.11.2009
Marketing Authorisation Date	28.01.2010

Invented Name	Urorec
INN	silodosin
Marketing Authorisation Holder	Recordati Ireland Ltd.
Proposed ATC code	G04CA04
Indication	Treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).
CHMP Opinion date	19.11.2009
Marketing Authorisation Date	29.01.2010

Invented Name	Silodyx
INN	silodosin
Marketing Authorisation Holder	Recordati Ireland Ltd.
Proposed ATC code	G04CA04
Indication	Treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).
CHMP Opinion date	19.11.2009
Marketing Authorisation Date	29.01.2010

OVERVIEW OF DESIGNATED ORPHAN MEDICINAL PRODUCTS THAT HAVE BEEN THE SUBJECT OF A CENTRALISED APPLICATION FOR MARKETING AUTHORISATION: UPDATE SINCE THE JANUARY 2010 CHMP MEETING

Active substance	Sponsor/applicant	EU Designation Number and Date of Orphan Designation	Designated Orphan Indication
Tobramycin (inhalation powder)	Novartis Europharm Limited-UK	EU/3/03/140	Treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis

ANNEX 4 TO CHMP MONTHLY REPORT FEBRUARY 2010

NAME REVIEW GROUP (NRG)

	NRG meeting 26 Jan 2010		NRG meeting 23 Mar 2010		NRG meeting 26 May 2010		NRG meeting 27 Jul 2010		NRG meeting 6 Sep 2010		NRG meeting 23 Nov 2010		2010	
	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected
Proposed invented names	25	35											**25**	**35**
Justification for retention of invented name *	1	6											**1**	**6**

*In case of objections to the proposed invented name(s), the applicant may justify the retention of the proposed invented name using the relevant justification form available on the EMEA website.

	NRG meeting 26 Jan 2010		NRG meeting 23 Mar 2010		NRG meeting 25 May 2010		NRG meeting 27 Jul 2009		NRG meeting 6 Sep 2009		NRG meeting 23 Nov 2009		2010	
Objections	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected
Total number of objections raised	83	32											**83**	**32**
Criterion - Safety concerns														
Similarity with other Invented name	73	21											**73**	**21**
Conveys misleading therapeutic/pharmaceutical connotations	1	0											**1**	**0**
Misleading with respect to composition	0	0											**0**	**0**
Criterion - INN concerns														
Similarity with INN	5	3											**5**	**3**
Inclusion of INN stem	3	6											**3**	**6**
Criterion - Other public health concerns														
Unacceptable qualifiers	0	1											**0**	**1**
Conveys a promotional message	0	1											**0**	**1**
Appears offensive or has a bad connotation	0	0											**0**	**0**
Similarity between name of individual active substance and fixed combinations and/or between fixed combinations	1	0											**1**	**0**
Similarity between name of prodrug and related active substance	0	0											**0**	**0**

See *Guideline on the Acceptability of Names for Human Medicinal Products Processed through the Centralised Procedure (CPMP/328/98 Rev. 5)* for detailed explanations of criteria used.

ANNEX 4 bis TO CHMP MONTHLY REPORT FEBRUARY 2010

NAME REVIEW GROUP (NRG)

(previously published in the December CHMP 2009 Monthly report with incorrect information now being amended)

	NRG meeting 27 Jan 2009		**NRG meeting 17 Mar 2009**		**NRG meeting 12 May 2009**		**NRG meeting 28 Jul 2009**		**NRG meeting 15 Sep 2009**		**NRG meeting 24 Nov 2009**		**2009**	
	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected
Proposed invented names	47	52	30	36	27	28	43	47	39	38	53	43	**239**	**244**
Justification for retention of invented name *	5	1	3	1	2	1	2	6	2	1	1	8	**15**	**18**

	NRG meeting 27 Jan 2009		**NRG meeting 17 Mar 2009**		**NRG meeting 12 May 2009**		**NRG meeting 28 Jul 2009**		**NRG meeting 15 Sep 2009**		**NRG meeting 24 Nov 2009**		**2009**	
Objections	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected
Total number of objections raised	120	65	79	40	56	46	75	45	63	45	87	49	**480**	**290**
Criterion - Safety concerns														
Similarity with other Invented name	100	56	67	36	51	39	68	39	56	32	65	29	**407**	**231**
Conveys misleading therapeutic/pharmaceutical connotations	6	0	1	1	0	0	0	1	0	0	3	7	**10**	**9**
Misleading with respect to composition	0	0	3	0	0	2	0	2	0	1	3	2	**6**	**7**
Criterion - INN concerns														
Similarity with INN	2	3	1	1	1	4	2	2	2	2	5	0	**13**	**12**
Inclusion of INN stem	3	0	0	1	0	1	1	0	0	0	3	2	**7**	**4**
Criterion - Other public health concerns														
Unacceptable qualifiers	4	1	0	1	0	0	1	0	3	4	2	0	**10**	**6**
Conveys a promotional message	1	0	5	0	0	0	3	1	0	4	0	5	**9**	**10**
Appears offensive or has a bad connotation	1	1	0	0	1	0	0	0	1	0	1	1	**4**	**2**
Similarity between name of individual active substance and fixed combinations and/or between fixed combinations	3	4	2	0	3	0	0	0	1	2	5	3	**14**	**9**
Similarity between name of prodrug and related active substance	0	0	0	0	0	0	0	0	0	0	0	0	**0**	**0**

ANNEX 5 TO CHMP MONTHLY REPORT FEBRUARY 2010

PRE-AUTHORISATION: SCIENTIFIC ADVICE AND PROTOCOL ASSISTANCE
EMEA CENTRALISED PROCEDURES

	1995 - 2009	2010	Overall Total
Scientific Advice	1134	**34**	**1168**
Follow-up to Scientific Advice	232	**19**	**251**
Protocol Assistance	245	**12**	**257**
Follow-up to Protocol Assistance	109	**5**	**114**
	1720	**70**	**1790**

OUTCOME OF THE FEBRUARY 2010
CHMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

Final Scientific Advice Procedures

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Treatment of type 1 and type 2 diabetes mellitus	x					x	x	
Chemical	Treatment of type 2 diabetes mellitus			x				x	
Chemical	Treatment of type 2 diabetes mellitus	x					x	x	
Chemical	Treatment of castrate-resistant prostate cancer			x				x	
Biological	Treatment of ovarian cancer	x					x	x	
Chemical	Treatment of castrate-resistant prostate cancer	x					x	x	
Biological	Treatment of colorectal cancer			x		x		x	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Chemical	Treatment of relapsing-remitting multiple sclerosis			x				x	
Other innovative	Treatment of chronic Graft-versus-Host disease				x			x	x
Biological	Treatment of acute lymphoblastic leukaemia		x			x	x	x	x
Biological	Treatment of advanced hepatocellular carcinoma	x						x	
Biological	Treatment of non-Hodgkin's lymphoma and rheumatoid arthritis	x				x	x	x	
Biological	Treatment of B-cell non-Hodgkin's lymphoma	x				x	x	x	
Biological/ Other innovative	Treatment of ulcerative colitis or Chron's disease			x		x			
Chemical	Treatment of anaemia in patients with chronic renal failure	x				x	x		
Biological	Treatment of acute episodes of bleeding in haemophilia A or B patients		x					x	
Biological	Treatment of acute episodes of bleeding in haemophilia A or B patients		x					x	
Biological/ Other innovative	Treatment of children with Paroxysmal Nocturnal Hemoglobinuria		x					x	
Biological	Treatment and prophylaxis of haemorrhagic episodes in patients with haemophilia B	x				x	x	x	
Chemical	Treatment of heterozygous familial hypercholeste-rolemia	x					x	x	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Other innovative	Prevention of H1N1 influenza	x				x	x	x	
Chemical	Treatment of HIV-1 infection	x						x	
Biological	Replacement therapy in primary immunodefi-ciency syndromes, myeloma or chronic lymphocytic leukaemia with severe secondary hypogamma-globulinaemia and recurrent infections, children with congenital AIDS and recurrent infections, idiopathic thrombocytopenic purpura, in children or adults at high risk of bleeding or prior to surgery to correct the platelet count, Guillain Barré syndrome, Kawasaki disease and allogeneic bone marrow transplantation	x				x	x	x	
Biological	Prevention of Japanese encephalitis			x				x	
Biological	Prevention of influenza	x				x	x	x	
Chemical	Relief of signs and symptoms or rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis	x				x		x	
Biological	Treatment of Alzheimer's disease			x				x	
Biological	Treatment of chronic inflammatory demyelinating polyneuropathy	x						x	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Chemical	Treatment of insomnia	x					x	x	
Chemical	Treatment of schizophrenia, manic episodes associated with bipolar disorder and major depressive episodes in bipolar disorder	x				x		x	
Chemical	Treatment of cystic fibrosis		x			x			
Biological	Treatment of cystic fibrosis	x				x	x	x	
Chemical	Reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension	x				x	x	x	
Biological	Treatment of growth hormone deficiency in children and adults			x		x	x		

SA: Scientific Advice
PA: Protocol Assistance

The above-mentioned 20 Scientific Advice letters, 5 Protocol Assistance letters, 8 Follow-up Scientific Advice and 1 Follow-up Protocol Assistance letters were adopted at the 15 - 18 February 2010 CHMP meeting.

New requests for Scientific Advice Procedures

The Committee accepted 24 new Requests for which the procedure started at the SAWP meeting held on 25 - 27 January 2010. The new requests are divided as follows: 16 Initial Scientific Advice, 7 Follow-up Scientific Advice, 1 Initial Protocol Assistance and no Follow-up Protocol Assistance.

ANNEX 6 TO CHMP MONTHLY REPORT FEBRUARY 2010

DOCUMENTS PREPARED BY THE CHMP WORKING PARTIES ADOPTED DURING THE FEBRUARY 2010 CHMP MEETING

BIOLOGICS WORKING PARTY (BWP)

Reference number	Document	Status[1]
EMA/CHMP/BWP/ 534898/2008	Guideline on the Requirements for Quality Documentation concerning Biological Investigational Medicinal Products in Clinical Trials	6-month public consultation

QUALITY WORKING PARTY (QWP)

Reference number	Document	Status[1]
EMA/63033/2010	Concept Paper for the Revision of the Guideline on Stability Testing for Applications for Variations to a Marketing Authorisation	Adopted
EMA/CHMP/CVMP/QWP 136094/2008	Question-and-answer document on Stability Issues of Pharmaceutical Bulk Products for use in manufacture of drug product (Human and Veterinary)	Adopted

EFFICACY WORKING PARTY (EWP)

Reference number	Document	Status[1]
EMA/CHMP/EWP/ 520088/2008 *(previously EMEA/CHMP/EWP/ 520088/2008)*	Appendix 2 to the Guideline on the Evaluation of Anticancer Medicinal Products in Man (CPMP/EWP/205/95 Rev. 3) on Confirmatory Studies in Haematological Malignancies	Adopted
EMA/CHMP/EWP/20097/ 2008 *(previously EMEA/CHMP/EWP/20097/ 2008)*	Guideline on the Development of Medicinal Products for the treatment of Alcohol Dependence	Adopted
CPMP/EWP/558/95 Rev.2	Guideline on Evaluation of Medicinal Products Indicated for Treatment of Bacterial Infections	6-month public consultation

[1] Adopted or release for consultation documents can be found at the European Medicines Agency website (under "What's new-recent publications" or under Human Medicines-Guidance documents").