European Medicines Agency
Evaluation of Medicines for Human Use

London, October 30th 2009
EMEA/CHMP/674356/2009

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
OCTOBER 2009 PLENARY MEETING
MONTHLY REPORT

The Committee for Medicinal Products for Human Use (CHMP) held its October plenary meeting on 19-22 October 2009.

The CHMP welcomed Dr Kolbeinn Gudmundsson as the new CHMP Alternate from Iceland, replacing Dr Magnús Jóhannsson in this role.

The CHMP elected Dr Hubert G.M. Leufkens from the Netherlands as the 5th Co-opted member replacing Prof. Ingemar Persson.

The CHMP also noted that this was the last meeting for Dr. Steffen Thirstrup and Dr. Antonio Addis and thanked them for their efforts and contributions during their time on the Committee.

CENTRALISED PROCEDURE

Initial applications for marketing authorisation

The CHMP adopted two positive opinions by consensus on initial marketing authorisation applications.

New medicinal products

- **Scintimun** (besilesomab), from CIS bio international, a radiopharmaceutical intended for use in scintigraphic imaging, in conjunction with other appropriate imaging modalities, for determining the location of inflammation/infection in peripheral bone in adults with suspected osteomyelitis. The review of Scintimun began on 23 July 2008, with an active review time of 203 days.
- **Zenas** (amifampridine), from EUSA Pharma SAS, intended for the symptomatic treatment of Lambert-Eaton Myasthenic Syndrome (LEMS) in adults, a rare disorder of neuromuscular transmission caused by impaired presynaptic release of acetylcholine (Ach). The review of Zenas began on 25 June 2008, with an active review time of 196 days. Zenas is the **60th orphan medicinal product** to receive a positive opinion by the CHMP. The Committee recommended that it be granted a marketing authorisation under 'exceptional circumstances'.

Positive opinions for 'informed consent' applications

The Committee adopted a positive opinion by consensus for **Leflunomide Winthrop** (leflunomide), from Sanofi-Aventis Deutschland GmbH, intended for the treatment of adult patients with active rheumatoid arthritis and with active psoriatic arthritis. The application was made as an 'informed consent' application. This type of application requires that reference is made to an authorised medicinal product and that the marketing authorisation holder of the reference product has given consent to the use of their dossier in the application procedure. The reference medicine for Leflunomide Winthrop is Arava.

Generic medicinal products

The Committee adopted a positive opinion by consensus for the following generic medicine, for which a reference medicine is already authorised in the EU. The medicine concerned is **Sildenafil ratiopharm** (sildenafil), from ratiopharm GmbH, a generic of Viagra, indicated for the treatment of erectile dysfunction.

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Summaries of opinion for these medicinal products are available here. Further information will be included in the European Public Assessment Reports (EPARs) once the European Commission has granted final approval.

Post-authorisation procedures

Extensions of indication and other recommendations

The Committee gave seven positive opinions by consensus for applications for extensions of indication, adding new treatment options, for the following medicines:

- **Adcirca** (tadalafil), from Eli Lilly Nederland B.V., to change the indication to pulmonary arterial hypertension. Adcirca was previously authorised as Tadalafil Lilly for the treatment of erectile dysfunction. However, this indication is being withdrawn by the marketing authorisation holder and will be replaced by the new indication related to pulmonary arterial hypertension.
- **Angiox** (bivalirudin), from The Medicines Company UK Ltd, to extend the indication to include patients with ST-segment myocardial infarction undergoing primary percutaneous coronary intervention (PCI). Angiox is currently authorised for treatment of adult patients with acute coronary syndromes (unstable angina/non-ST segment elevation myocardial infarction (UA/NSTEMI)) planned for urgent or early surgical intervention.
- **Cymbalta** (duloxetine), from Eli Lilly Nederland B. V., and **Xeristar** (duloxetine), from Boehringer Ingelheim International GmbH, to extend the indication of these medicines to include treatment of major depressive disorder. Both products are currently authorised for the treatment of major depressive episodes, of diabetic peripheral neuropathic pain in adults and of generalised anxiety disorder.
- **Micardis** (telmisartan), from Boehringer Ingelheim International GmbH, **Pritor** (telmisartan), from Bayer Schering Pharma AG, and **Kinzalmono** (telmisartan), from Bayer Schering Pharma AG, to extend the indication to include the reduction of cardiovascular morbidity in patients with manifest atherothrombotic cardiovascular disease (history of coronary heart disease, stroke, or peripheral arterial disease), or type 2 diabetes mellitus with documented target organ damage. These medicines are currently authorised for the treatment of essential hypertension in adults.

Summaries of opinion for these extensions of indication are available here. Further information will be included in the EPARs once the European Commission has granted final approval.

Update on H1N1 pandemic vaccines

The CHMP reviewed early data from clinical studies for the three authorised pandemic vaccines, **Celvapan**, **Focetria** and **Pandemrix**. The Committee concluded to maintain the recommendation it adopted in September, namely that the three vaccines be preferably given as two doses, at least three weeks apart. The data currently available for Pandemrix and for Focetria indicate that one dose may be sufficient in adults, but are too limited to allow the Committee to recommend the general use of a single-dose vaccination schedule.

More information is available in a question and answer document.
The updated product information showing the changes is also available for Focetria and Pandemrix. The EPAR Summaries for Focetria and Pandemrix have also been updated and can be found on the Agency's pandemic influenza H1N1 website http://www.emea.europa.eu/influenza/vaccines/home.htm

Within the context of the pandemic situation, the National Agency for Medicines (NAM - Finnish Agency) notified the EMEA under Article 83(1) of Regulation (EC) 726/2004 of its intention to initiate a compassionate use at National level for the intravenous use of **Tamiflu** (oseltamivir) from Roche Registration Ltd to treat severe influenza in critically ill patients in hospitals. The CHMP agreed to prepare an opinion on the condition for use, distribution and the patients targeted.

Updated safety information

Following assessment of information related to levothyroxine, antiepileptics interactions and adverse events related to pancreatitis and oxalate nephropathy associated with **alli** (orlistat), from Glaxo Group Ltd, the CHMP recommended updating the product information to reflect that patients taking medicines such as levothyroxine and antiepileptic drugs or patients with kidney disease should consult a doctor before starting treatment and that oxalate nephropathy and pancreatitis have been reported in a number of patients taking orlistat. The CHMP and the MAH (Glaxo Group Ltd) agreed on a Direct Healthcare Professional Communication concerning this updated information.

The CHMP adopted amendments to sections 4.4 and 4.8 of the Summary of Product Characteristics (SPC) of **Nexavar** (sorafenib) from Bayer Schering Pharma AG. Section 4.4 of the SPC was amended regarding an observed higher mortality in the subset of patients with squamous cell carcinoma of the lung treated with sorafenib and carboplatin and paclitaxel versus those treated with carboplatin and paclitaxel alone. No definitive cause was identified for this finding. The concerned subset of patients was part of a randomized controlled trial comparing safety and efficacy of carboplatin and paclitaxel plus or minus sorafenib in chemonaive patients with Stage IIIB-IV Non-Small Lung Cell Cancer (NSCLC) which was stopped early, when the independent Data Monitoring Committee concluded that the study would not meet its primary endpoint of improved overall survival. Safety events were generally consistent with those previously reported. In addition, in section 4.8 of the SPC, the frequency of the term "congestive heart failure" was changed to "common" and further information on this adverse drug reaction was added. Furthermore, the term "interstitial lung disease-like events" was added with the frequency "uncommon". The Package Leaflet was updated accordingly.

The CHMP agreed to further update the temporary treatment recommendations for **Cerezyme** (imiglucerase) from Genzyme B.V., to deal with the supply shortage of the medicine. The new temporary recommendations aim to ensure that patients at greatest need continue to receive Cerezyme. The medicine is used in the treatment of patients with Gaucher disease, a disease in which patients do not have enough of an enzyme called glucocerebrosidase. The updated recommendations are available here.

The CHMP finalised a review of a number of reports of deaths with **Exjade (**deferasirox) from Novartis Europharm Ltd. in the USA coming from a prescribing system called the Exjade Patient Assistance and Support Services Program (EPASS). The EPASS is a closed drug distribution system that was established in November 2005 at the time of marketing approval in the USA. Approximately 85% of Exjade sales in the USA are controlled via this system. There is currently no issue with reports of death in Europe. The MAH identified 1,935 cases (out of a total of 16,514 patients) in the EPASS system for which majority of these cases had not been included in the ARGUS database, and had not yet been reported to regulatory authorities.
The CHMP concluded that most of the deaths reported occurred in elderly patients with underlying myelodysplastic syndromes (MDS). A warning for patients with advanced malignancies and limited life expectancy not to use Exjade (patients with MDS) was therefore included in section 4.4 of the SPC. In addition, the CHMP highlighted that a strict respect of the European Risk Management Plan should be maintained and that efforts concerning renal follow-up is of the utmost importance. A request to conduct a Pharmacovigilance (PV) inspection of the Novartis PV system was also issued.
In parallel, the product information is being revised with the following statements:
- on higher frequency of adverse drug reactions in elderly patients.
- on the occurrence of renal tubulopathy in young thalassemia patients.
- on reports of fatal gastrointestinal haemorrhages in elderly patients with haematologic malignancies and/or low platelet counts together with a caution in patients with low platelet counts.
- on updated information on a longer observation period for the absence of effects on paediatric growth and development.
Furthermore, following extension of the recommended dose range for maintenance therapy to 40 mg/kg/day for patients not adequately controlled, a warning that increased risk of renal adverse events with Exjade dose above 30 mg/kg cannot be excluded was introduced in section 4.4 of the SPC.

Withdrawals

The EMEA has been formally notified by Arpida Ltd of its decision to withdraw its application for a centralised marketing authorisation for the medicine **Mersarex** (iclaprim), 12.8 mg/ml concentrate for solution for infusion. Mersarex was expected to be used for the treatment of complicated skin and soft tissue infection. A separate press release document with more information is available. An additional question-and-answer document will be available following the November CHMP meeting.

The EMEA was formally notified by CTI Life Sciences Ltd. in September 2009 of its decision to withdraw its application for a centralised marketing authorisation for **Opaxio** (paclitaxel poliglumex) 269 mg powder for concentrate for solution for infusion. Opaxio was expected to be used for first line monotherapy treatment of PS2 patients with advanced Non Small Cell Lung Cancer. An additional question-and-answer document is now available.

The EMEA was formally notified by Glaxo Group Ltd in September 2009 of its decision to withdraw its application for a centralised marketing authorisation for **Zunrisa** (casopitant). Zunrisa was expected to be used for the prevention of nausea and vomiting in patients undergoing surgery or receiving chemotherapy. A separate press release document with more information and a question-and-answer document are available.

OTHER INFORMATION ON THE CENTRALISED PROCEDURE

Lists of Questions

The Committee adopted three Lists of Questions on initial applications under the optional scope.

Detailed information on the centralised procedure

An overview of centralised procedures since 1995 is given in **Annex 1**. The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 2**. The list of medicinal products for which marketing authorisations have been granted by the European Commission since the CHMP plenary meeting in September 2009 is provided in **Annex 3.**

Applications for marketing authorisation for orphan medicinal products

Details of those orphan medicinal products that have been subject of a centralised application for marketing authorisation since the September 2009 CHMP plenary meeting are provided in **Annex 4**.

REFERRAL PROCEDURES

Referral procedures concluded

The CHMP concluded a referral procedure under Article 29 of Directive 2001/83/EC for **Myderison** (tolperison hydrochloride), 50 mg and 150 mg film coated tablets from Meditop Pharmaceutical Ltd, indicated for the spasticity of the skeletal muscles. This procedure was initiated because of concerns raised by some Member States over efficacy and safety. The CHMP concluded that the benefit/risk ratio of Myderison is not considered to be favourable. The CHMP recommended by consensus the refusal of the marketing authorisation in the Concerned Member States and the revocation of the Marketing Authorisation in the Member States where the product is currently authorised.

This type of procedure is initiated by one or more Member States in cases where an agreement cannot be reached in the context of the mutual recognition procedure or the decentralised procedure.

The CHMP concluded a referral for **Extraneal** (icodextrin) 7.5% solution for peritoneal dialysis from Baxter Healthcare Limited, recommending approval of the type II variation updating the finished product specification by including the peptidoglycan (PG) test. Extraneal is authorised in a number of Member States as solution for peritoneal dialysis. It is recommended as a once daily replacement for a single glucose exchange as part of a continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal

dialysis (APD) regimen for the treatment of chronic renal failure, particularly for patients who have lost ultrafiltration on glucose solutions, because it can extend time on CAPD therapy in such patients.
The referral procedure was initiated under Article 6(12) of Commission Regulation (EC) No 1084/2003. This type of procedure is triggered in the mutual recognition or decentralised procedure when there is a disagreement between Member States on a type II variation (change to a marketing authorisation) that is then referred to the CHMP for arbitration. A question-and-answer document with further information is now available.

The CHMP concluded a referral review procedure under Article 107 of directive 2001/83/EC, as amended for **iodocasein/thiamine-containing medicines** approved for the treatment of obesity, recommending the revocation of the marketing authorisations of these medicines because of the risks of hyperthyroidism and thyrotoxicosis.

This type of procedure is initiated in cases where a Member State intends to withdraw, suspend or change the marketing authorisation of a decentralised authorised medicine as a result of the evaluation of safety data. It provides for a harmonised European approach because the CHMP is asked to prepare an opinion on whether or not the regulatory actions should be implemented throughout the European Union.

Referral procedures started

The CHMP started a referral procedure under Article 29 of Directive 2001/83/EC, as amended for **Levact and associated names** (bendamustine), 2.5 mg/ml powder for concentrate for infusion from Astellas Pharma GmbH, used in chemotherapy. The procedure was initiated because of disagreements regarding the efficacy of some of the proposed indications.

The CHMP started two referral procedures under Article 31 of Directive 2001/83/EC as amended. This type of procedure is initiated when an interest at Community level is raised. The medicinal products concerned are:

- **Modified release oral opioid medicinal products** (containing morphine, fentanyl, oxycodone and hydromorphone) used for management of pain due to concerns on the dissolution of the prolonged-release oral products and their sensitivity and interaction with alcohol, which may cause dose dumping and potential overdose. The procedure was initiated on the request of the European Commission.
- **Fibrate medicines** (fenofibrate, bezafibrate, ciprofibrate and gemfibrozil) because of concerns over their long-term clinical benefit in the primary and secondary prevention of cardiovascular disease. This procedure was initiated on the request of the UK.

Benefit-risk review for Tysabri started

The Committee started a review of the benefits and risks of **Tysabri** (natalizumab) from Elan Pharma International Ltd in view of reports of 24 cases (the last of which was reported after publication of the October CHMP press release) of progressive multifocal leukoencephalopathy (PML) worldwide since Tysabri has been on the market. The review was initiated at the request of the European Commission under Article 20 of Regulation (EC) No 726/2004 to discuss any additional measures necessary to ensure the safe use of Tysabri and how to balance the risks to the patients against the benefits of the treatment. Tysabri is indicated for patients suffering from highly active relapsing remitting multiple sclerosis with high disease activity despite treatment with a beta-interferon and for patients with rapidly evolving severe relapsing-remitting multiple sclerosis.

Re-examination procedures concluded under Article 32(4) of the Directive 2001/83/EC, as amended

Following re-examination of its negative opinion adopted in June 2009 recommending the refusal of the granting of the Marketing Authorisation in the Concerned Member States for **Teicoplanin Hospira and associated names** (teicoplanin), 200 mg and 400 mg powder and solvent for injection for infusion the CHMP adopted a final negative opinion by consensus re-confirming its previous recommendation. This procedure was initiated because of disagreements regarding the demonstration of bioequivalence to the

reference medicinal product. The CHMP had concluded in June 2009 that sufficient evidence had not been presented to demonstrate that Teicoplanin Hospira was a generic of the reference product.

Following re-examination of its opinion adopted in June 2009 recommending the withdrawal of the Marketing Authorisations for **Dextropropoxyphene containing medicinal products** used in the treatment of acute and chronic pain, the CHMP adopted a final opinion by majority re-confirming its previous recommendation to withdraw the marketing authorisation for all non-parenteral forms of these medicines (tablets, capsules and suppositories), because their risks, particularly the risk of potentially fatal overdose, are greater than their benefits.
However, for the parenteral forms, the Committee concluded by majority that the marketing authorisations should not be withdrawn but suspended until further clinical data are available which may support the re-introduction of this formulation onto the market.

Dextropropoxyphene is a painkiller used to treat acute and chronic pain. It has been available as a prescription-only medicine for about 40 years, either on its own or in combination primarily with paracetamol, as tablets, capsules, suppositories and solutions for injection.

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

Withdrawal

The EMEA has been formally notified by Arrow Generics Limited of its decision to cancel its decentralised Marketing Authorisations for **Escitalopram Arrow and associated names** 5, 10 and 20 mg tablets (escitalopram oxalate), in the Netherlands and the UK. In September 2009, the CHMP had initiated a referral procedure under Article 30 of Directive 2001/83/EC as amended, for Escitalopram Arrow 5 mg/10 mg/20 mg (escitalopram oxalate), indicated in the treatment of major depressive disorder episodes.

MUTUAL-RECOGNITION AND DECENTRALISED PROCEDURES - HUMAN

The CHMP noted the report from the 44th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 19-21 October 2009. 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 28 September-1 October 2009. For further details, please see **Annex 5**.

Documents prepared by the CHMP Working Parties adopted during the October 2009 CHMP meeting are listed in **Annex 6**.

UPCOMING MEETINGS FOLLOWING THE OCTOBER 2009 CHMP PLENARY MEETING

- The 60th meeting of the CHMP will be held at the Agency on 16-19 November 2009.
- The next Name Review Group meeting will be held at the Agency on 24 November 2009.
- The 44th CMD(h) will be held at the Agency on 16-17 November 2009.

ORGANISATIONAL MATTERS

The main topics addressed during the October 2009 CHMP meeting related to:

- A discussion on the list of priorities for safety topics to be taken into consideration for the 5th Call within the project on the Important Public Health Issues for Drug Safety Research conducted by DG Research within the Scope for Health Themes in the 7th Framework Programme. The list of topics will be finalised taking into account the feedback from the Committee and sent to DG Research in the near future.

- A presentation by the European Commission on the Pharmaceutical package focusing on Pharmacovigilance aspects.
- An update on the Agency's interaction with Health Technology Assessment bodies focusing on the improvement of EPARs.
- An update on the EMEA road map to 2015 which will now be presented to the Management Board at their next meeting for agreement on the launch of the public consultation.
- Follow-on discussion regarding the appointment of Rapporteurs and Co-Rapporteurs in the context of Work Sharing variations.
- A presentation on the new EMEA structure that should be fully in place by December 2009. All stakeholders will be informed in due course of any changes to the teams handling their procedures.
- A brief update and roll out project for the Product Shared Mailboxes which was announced in the September CHMP Monthly Report.
- The adoption of the Overview of Comments (EMEA/CHMP/663087/2009) received on the Draft revision 2 of the SmPC guideline.

PROCEDURAL ANNOUNCEMENTS

- **Submission of Type IA and Type IB variations in December 2009**

Please note that the EMEA will be closed between 24 December 2009 and 1 January 2010 (inclusive).

Marketing Authorisation Holders (MAHs) are therefore requested not to submit Type IA variation applications to the EMEA between 14 and 23 December 2009 (inclusive) because the 14-day timeframe for the Agency to acknowledge the validity of the submitted Type IA variation(s) (see article 4 of Commission Regulation (EC) No 1085/2003) would coincide with the official closure of the EMEA.

Type IA variation applications submitted no later than 11 December 2009 will be finalised before the EMEA Christmas break. Any Type IA variation application submitted to the EMEA between 14 December 2009 and 1 January of 2010 will be finalized in January 2010, under the current Variation Regulation (Commission Regulation (EC) No 1085/2003).

Marketing Authorisation Holders intending to apply for Type IB variations in December 2009 are encouraged to liaise with the EMEA prior to their submission.

Further information on transitional arrangements in view of the upcoming implementation of the new Variation Regulation (Commission Regulation (EC) No 1234/2008) will be provided separately.

- **Application of article 28(2) of Paediatric Regulation (EC) No 1901/2006**

MAHs and Applicants are reminded that Article 28(2) of Regulation (EC) No 1901/2006 as amended created the obligation to record in the Summary of Product Characteristics (SPC) and, if appropriate in the Package Leaflet, any waiver or deferral which has been granted where a marketing authorisation is granted or varied.

The requirement concerns applications submitted under Articles 7, 8 or 30 of Regulation (EC) No 1901/2006.

MAHs and Applicants should refer to the statements provided in Section 5.1 of the Guideline on Summary of Product Characteristics (Revision 2) published on the European Commission website in September 2009, to update their SPC in compliance with this requirement.
See also QRD templates: http://www.emea.europa.eu/htms/human/qrd/docs/Hannotatedtemplate.pdf

- **"Droit de regard" - Important notice to stakeholders**

The Commission DG ENTR has published on their website the following statement which is a follow-up to the notice published on 29th July 2009.

"*Following an agreement with the responsible Committee in the European Parliament and in accordance with the interinstitutional agreement of 3 June 2008, the period of the "droit de regard" for the Commission Decisions taken as part of the "Decision making process" is shortened on a permanent basis to 7 days. This applies also in the recess periods of European Parliament.*

The shortened period of the "droit de regard" does, however, not apply in the following cases:

- *the draft Commission Decision is not in accordance with the scientific opinion of the EMEA;*
- *Member States, during the vote, request that the draft Decision is discussed in a plenary meeting of the Standing Committee; or*
- *the opinion of the Standing Committee is unfavourable.*

The "Notice to applicants", Chapter VII, is going to be updated to this effect.

This arrangement applies with immediate effect, i.e.:

- *Procedures in the Comitology phase which have been in the "droit de regard" stage for more than 7 days are going to be moved into the adoption phase (15 calendar days);*
- *Procedures in the Comitology phase which are still in the voting phase of Member States will be*

subject to a shortened period of "droit de regard" of 7 days.

In practice, the additional 7 days of the droit de regard following the vote by Member States will be used to prepare the final Decision for adoption once the 7 days have expired. Therefore, in practice, the timelines will not be much affected by the droit de regard.

Companies are kindly requested to refrain from ringing up the Commission staff to urge a faster processing of the draft Decision of their products."

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

ANNEX 1 TO CHMP MONTHLY REPORT OCTOBER 2009

PRE-AUTHORISATION: MARKETING AUTHORISATION APPLICATIONS

Activity	2009								1995 onwards
	Optional Scope				Mandatory scope			Total	Overall total
	NAS	Significant innovation	Interest of Patients	Generics	Biotech	Indications	Orphans		
Applications for MA submitted	19	4	0	38	7	4	5	77	875
Positive opinions	19	10	0	45	12	3	6	95	588
Negative opinions[1]	0	2	0	0	2	0	1	5	26
Withdrawals prior to opinion	4	0	0	1	3	2	2	12	151
Marketing authorisation granted by the Commission	15	10	0	26	10	4	8	73	558

PRE-AUTHORISATION: SCIENTIFIC SERVICES

Activity (submissions)	2009	1995 onwards
Compassionate use applications	0	0
Art. 58 applications	0	4
Consultation for medical devices[2]	1	6
PMF (Click here for a list of PMF certifications)	1	14
VAMF	0	0

[1] In case of Re-examination under Art. 9(2) of Regulation (EC) No. 726/2004, the opinion will not be counted twice.
[2] Consultation in accordance with Council Directive 93/42/EEC concerning medical devices as amended by Directive 2000/70/EC as regards medical devices incorporating stable derivates of human blood or plasma and Directive 2001/104/EC

OUTCOME OF THE OCTOBER 2009 CHMP MEETING IN RELATION TO ACCELERATED ASSESSMENT PROCEDURES

Substance	Intended indications(s)	Accelerated Assessment Requests	
		Accepted	Rejected
Chemical	Treatment of cystic fibrosis		X
Biological	Treatment of Type I Gaucher disease	X	

ANNEX 2 TO CHMP MONTHLY REPORT OCTOBER 2009

POST-AUTHORISATION: TYPE I AND II VARIATIONS, ANNEX II, RENEWALS AND ANNUAL RE-ASSESSMENT APPLICATIONS

Activity	2009	Overall total 1995 onwards
Type I Variations (positive notifications)	876	72458
Type II Variations (positive opinions)	920	5463
Type II Variations (negative opinions)	2	18
Annex II Applications (positive opinions)	47	230
Annual Re-assessments (positive opinions)	14	-
Opinions for renewals of conditional MA's (positive opinions)	3	9
5-year Renewals (positive opinions)	53	-

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
7 Extension of indication	7 Positive opinions
42 SPC changes	42 Positive opinions
33 Quality changes	33 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
N/A	N/A	N/A

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**
Avastin (bevacizumab) Roche Registration Ltd	Positive Opinion adopted	Recommending additional renewal
Prialt (ziconotide) Eisai Ltd	Positive Opinion adopted	Recommending additional renewal
Thyrogen (thyrotropin alfa) Genzyme Europe B.V	Positive Opinion adopted	Unlimited validity
Tractocile (atosiban) Ferring Pharmaceuticals A/S	Positive Opinion adopted	Unlimited validity
Zonegran (zonisamide) Eisai Ltd	Positive Opinion adopted	Unlimited validity

ANNEX 3 TO CHMP MONTHLY REPORT OCTOBER 2009

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE THE SEPTEMBER 2009 CHMP MONTHLY REPORT

Invented Name	ChondroCelect
INN	Characterised viable autologous cartilage cells expanded ex vivo expressing specific marker proteins.
Marketing Authorisation Holder	Tigenix nv
Proposed ATC code	Not yet assigned
Indication	Repair of single symptomatic cartilage defects of the femoral condyle of the knee (International Cartilage Repair Society [ICRS] grade III or IV) in adults. Concomitant asymptomatic cartilage lesions (ICRS grade I or II) might be present. Demonstration of efficacy is based on a randomised controlled trial evaluating the efficacy of Chondrocelect in patients with lesions between 1-5cm².
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	05.10.2009

Invented Name	Simponi
INN	golimumab
Marketing Authorisation Holder	Centocor B.V.
Proposed ATC code	L04AB06
Indication	Rheumatoid arthritis (RA) Simponi, in combination with methotrexate (MTX), is indicated for the treatment of moderate to severe, active rheumatoid arthritis in adult patients when the response to disease-modifying anti-rheumatic drug (DMARD) therapy including MTX has been inadequate. Simponi has also been shown to improve physical function in this patient population. Psoriatic arthritis (PsA) Simponi, alone or in combination with MTX, is indicated for the treatment of active and progressive psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate. Simponi has also been shown to improve physical function in this patient population. Ankylosing spondylitis (AS) Simponi is indicated for the treatment of severe, active ankylosing spondylitis in adult patients who have responded inadequately to conventional therapy.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	01.10.2009

Invented Name	Resolor
INN	prucalopride
Marketing Authorisation Holder	Movetis NV
Proposed ATC code	A03AE04
Indication	Resolor is indicated for symptomatic treatment of chronic constipation in women in whom laxatives fail to provide adequate relief.
CHMP Opinion date	23.07.2009
Marketing Authorisation Date	15.10.2009

Invented Name	Cimzia
INN	certolizumab pegol
Marketing Authorisation Holder	UCB Pharma SA
Proposed ATC code	L04AB05
Indication	Cimzia, in combination with methotrexate (MTX), is indicated for the treatment of moderate to severe, active rheumatoid arthritis (RA) in adult patients when the response to disease-modifying antirheumatic drugs (DMARDs) including methotrexate, has been inadequate. Cimzia can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate. Cimzia has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function, when given in combination with methotrexate.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	01.10.2009

Invented Name	Onglyza
INN	saxagliptin
Marketing Authorisation Holder	Bristol-Myers Squibb/AstraZeneca EEIG
Proposed ATC code	A10BH03
Indication	Onglyza is indicated in adult patients with type 2 diabetes mellitus to improve glycaemic control: • in combination with metformin, when metformin alone, with diet and exercise, does not provide adequate glycaemic control; • in combination with a sulphonylurea, when the sulphonylurea alone, with diet and exercise, does not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate. • in combination with a thiazolidinedione, when the thiazolidinedione alone with diet and exercise, does not provide adequate glycaemic control in patients for whom use of a thiazolidinedione is considered appropriate.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	01.10.2009

Invented Name	Clopidogrel Krka
INN	clopidogrel
Marketing Authorisation Holder	Krka, d.d., Novo mesto
Proposed ATC code	B01AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	23.09.2009

Invented Name	Zyllt
INN	clopidogrel
Marketing Authorisation Holder	Krka, d.d., Novo mesto
Proposed ATC code	B01AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease. • Patients suffering from acute coronary syndrome: - Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA). - ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	28.09.2009

Invented Name	Enyglid
INN	repaglinide
Marketing Authorisation Holder	Krka, d.d., Novo mesto
Proposed ATC code	A10BX02
Indication	Repaglinide is indicated in patients with Type 2 diabetes (Non Insulin-Dependent Diabetes Mellitus (NIDDM)) whose hyperglycaemia can no longer be controlled satisfactorily by diet, weight reduction and exercise. Repaglinide is also indicated in combination with metformin in Type 2 diabetes patients who are not satisfactorily controlled on metformin alone. Treatment should be initiated as an adjunct to diet and exercise to lower the blood glucose in relation to meals.
CHMP Opinion date	23.07.2009
Marketing Authorisation Date	14.10.2009

Invented Name	Clopidogrel Qualimed
INN	clopidogrel
Marketing Authorisation Holder	Qualimed
Proposed ATC code	B01AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	23.09.2009

Invented Name	Clopidogrel TAD
INN	clopidogrel
Marketing Authorisation Holder	Tad Pharma GmbH
Proposed ATC code	B01AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	23.09.2009

ANNEX 4 TO CHMP MONTHLY REPORT OCTOBER 2009

OVERVIEW OF DESIGNATED ORPHAN MEDICINAL PRODUCTS THAT HAVE BEEN THE SUBJECT OF A CENTRALISED APPLICATION FOR MARKETING AUTHORISATION:
UPDATE SINCE THE SEPTEMBER 2009 CHMP MEETING

Active substance	**Sponsor/applicant**	**EU Designation Number & Date of Orphan Designation**	**Designated Orphan Indication**
Recombinant human C1-inhibitor	Pharming Group N.V.	EU/3/01/036	Treatment of angioedema caused by C1 inhibitor deficiency

ANNEX 5 TO CHMP MONTHLY REPORT OCTOBER 2009

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

	1995 - 2008	2009	Overall Total
Scientific Advice	887	**197**	**1084**
Follow-up to Scientific Advice	171	**41**	**212**
Protocol Assistance	198	**35**	**233**
Follow-up to Protocol Assistance	90	**15**	**105**
	1346	**288**	**1634**

OUTCOME OF THE OCTOBER 2009 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				
Chemical	Treatment of type 2 diabetes mellitus.			x				x	
Chemical	Treatment of type 2 diabetes mellitus.	x				x		x	
Biological	Treatment of Chronic Inflammatory Demyelinating poly(radiculo)-neuropathy.	x						x	
Biological	Treatment of non-infectious uveitis.	x						x	
Chemical	Treatment of non-invasive bladder cancer.			x			x	x	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharma ceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Chemical	Treatment of advanced or metastatic HER2-overexpressing breast cancer.	x						x	
Biological	Treatment and prevention of recurrent flares in chronic gouty arthritis patients.	x				x	x	x	
Chemical	Treatment of relapsing-remitting multiple sclerosis.	x					x	x	
Chemical	Treatment of epithelial neoplasias of the vulva positive for human papilloma virus.		x			x	x	x	
Chemical	Treatment of metastatic endometrial cancer.	x						x	
Chemical	Treatment of HER2 negative metastatic breast cancer.	x						x	
Chemical	Treatment of high grade resectable non metastatic osteosarcoma.				x			x	
Biological	Treatment of chronic lymphocytic leukaemia.				x			x	
Chemical	Treatment of pancreatic cancer.		x					x	
Chemical	Treatment of non small cell lung cancer.	x						x	
Biological	Prevention of secondary bleeding.	x						x	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharma ceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Treatment of haemophilia B.				x			x	x
Biological	Treatment of haemophilia B.		x			x	x		
Biological	Prevention and/or reduction of post-operative adhesions in gynaecology surgeries.	x					x	x	
Biological	Improvement of haemostasis where standard surgical techniques are ineffective or impractical.	x				x	x	x	
Biological	Treatment of congenital haemophilia A.	x				x			
Chemical	Treatment of essential hypertension.			x				x	
Biological	Treatment of severe Peripheral Arterial Disease.	x					x	x	
Chemical	Treatment of erythropoietic protoporphyria.		x			x	x	x	
Chemical	Prevention of Chronic Pulmonary Bronchodysplasia	x				x	x	x	
Biological	Active immunisation of pregnant/non-pregnant women for the prevention of invasive disease in infants caused by Group B streptococci.			x			x		

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharma ceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Broader advice on general issues concerning transfer of production of several authorised drug products containing biotech active substance.	x				x			
Chemical	Treatment of HIV-1 infections.			x			x	x	
Chemical	Treatment of Peyronie's Disease.	x						x	
Chemical	Differential diagnosis of Essential Tremor and Parkinsonian Syndromes related to idiopathic Parkinson's disease, Multiple System Atrophy and Progressive Supranuclear Palsy.	x					x	x	
Chemical	Treatment of mild to moderately severe Alzheimer’s dementia.	x						x	
Chemical	Treatment of mild to moderate Alzheimer's disease.			x				x	
Chemical	Treatment of signs and symptoms of Keratoconjunc-tivitis sicca.	x				x	x	x	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharma ceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Treatment of non-infectious intermediate, posterior and panuveitis.	x						x	
Chemical	Treatment of open angle glaucoma and ocular hypertension.	x				x	x	x	
Chemical	Diagnostic positron emission topografy to identify bone metastasis in prostate cancer.	x					x	x	

SA: Scientific Advice
PA: Protocol Assistance

The above-mentioned 23 Scientific Advice letters, 4 Protocol Assistance letters, 6 Follow-up Scientific Advice and 3 Follow-up Protocol Assistance letters were adopted at the 19-22 October 2009 CHMP meeting.

New requests for Scientific Advice Procedures

The Committee accepted 40 new Requests for which the procedure started at the SAWP meeting held on 28 September-1 October 2009. The new requests are divided as follows: 20 Initial Scientific Advice, 10 Follow-up Scientific Advice, 8 Initial Protocol Assistance and 2 Follow-up Protocol Assistance.

DOCUMENTS PREPARED BY THE CHMP WORKING PARTIES ADOPTED DURING THE OCTOBER 2009 CHMP MEETING

BIOLOGICS WORKING PARTY (BWP)

Reference number	Document	Status[3]
EMEA/CHMP/BWP/ 233408/2009	Report of the Epidemiology Workshop held at the EMEA on 30th-31st March 2009	Adopted
EMEA/CHMP/BWP/38 4556/2009	BWP Work Programme for 2010	Adopted

BLOOD PRODUCTS WORKING PARTY (BPWP)

Reference number	Document	Status
EMEA/CHMP/BPWP/ 194455/2009	BPWP Work Programme for 2010	Adopted

VACCINE WORKING PARTY (VWP)

Reference number	Document	Status
EMEA/CHMP/VWP/ 642639/2009	VWP Work Programme for 2010	Adopted

GENE THERAPY WORKING PARTY (GTWP)

Reference number	Document	Status
EMEA/CHMP/GTWP/ 60436/2007 ▪ EMEA/CHMP/ GTWP/570240/2009	Guideline on Follow-up of Patients Administered with Gene Therapy Medicinal Products ▪ Overview of Comments received	Adopted
EMEA/CHMP/GTWP/ 607698/2008	ICH Considerations on Oncolytic Viruses	Noted

SIMILAR BIOLOGICAL MEDICINAL PRODUCTS WORKING PARTY (BMWP)

Reference number	Document	Status
EMEA/CHMP/BMWP/ 528785/2009	BMWP Work Plan for 2010	Adopted
EMEA/CHMP/BMWP/ 632613/2009	Concept Paper on Monoclonal Antibodies	Adopted

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

PHARMACOGENOMICS WORKING PARTY (PgWP)

Reference number	Document	Status
EMEA/637553/2009	PGWP Report to PhVWP regarding Phenytoin and Risk of Stevens-Johnson Syndrome	Adopted

CELL-BASED PRODUCTS WORKING PARTY (EWP)

Reference number	Document	Status
EMEA/CHMP/CPWP/ 570905/2009 ▪ EMEA/CHMP/CPWP/ 83508/2009	Guideline on Xenogeneic Cell Based Medicinal Products ▪ Overview of Comments received	Adopted

EFFICACY WORKING PARTY (EWP)

Reference number	Document	Status
EMEA/CHMP/EWP/ 10797/2009	Paper on the need for revision of the CHMP Note for Guidance on the Clinical Investigation of Medicinal Products in the Treatment of Asthma (CPMP/EWP/2922/01)	Adopted for 3-month public consultation
EMEA/CHMP/EWP/ 9147/2008	Guideline on the Clinical Development of Medicinal Products for the Treatment of Cystic Fibrosis	Adopted
EMEA/CHMP/EWP/ 692702/2008	Reflection Paper on the on extrapolation results in clinical studies to the EU population	Adopted
EMEA/CHMP/EWP/ 356954/2008 ▪ EMEA/CHMP/EWP/ 582423/2009	Guideline on the Clinical Investigations of Medicinal Products for the Treatment of Pulmonary Arterial Hypertension ▪ Overview of Comments received	Adopted
EMEA/16274/2009	Guideline on Medicinal Products for the Treatment of Insomnia (former Guideline on Clinical Investigation of Hypnotic Medicinal Products 3CC27A)	Adopted for 6-month public consultation