European Medicines Agency

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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
MARCH 2006 PLENARY MEETING
MONTHLY REPORT

The Committee for Medicinal Products for Human Use (CHMP) held its March plenary meeting from 20-23 March 2006.

Centralised procedure

Initial applications for marketing authorisation

The CHMP adopted positive opinions on two initial marketing authorisation applications at this meeting:

- **Ganfort** (bimatoprost/timolol), Allergan Pharmaceuticals Ireland. Ganfort is an eye-drop solution, intended for reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to topical beta-blockers or prostaglandin analogues. EMEA review began on 18 May 2005 with an active review time of 196 days.
- **Zostavax** (herpes zoster vaccine), Aventis Pasteur MSD. Zostavax is a vaccine intended for the prevention of herpes zoster (shingles) and herpes zoster related postherpetic neuralgia (PHN). EMEA review began on 15 June 2005 with an active review time of 202 days.

Summaries of opinion for these medicinal products are available on the EMEA website: http://www.emea.eu.int. Further information will be included in the European Public Assessment Report (EPAR) once the European Commission has granted final approval.

Re-examination procedure concluded

Following the re-examination of the negative opinion adopted on 14 December 2005, the Committee confirmed its previous position, recommending not to grant a marketing authorisation for **Zelnorm** (tegaserod), from Novartis Europharm Limited for the repeated symptomatic short-term treatment of Irritable Bowel Syndrome in women whose predominant bowel habit is constipation.

A question and answer document explaining the grounds for the negative opinion has been published and can be found here.

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Extensions of indication and other recommendations

The Committee adopted positive opinions on the extension of indication of medicinal products that are already authorised in the European Union:

- **Emend** (aprepitant), from Merck Sharp & Dohme, to add prevention of post-operative nausea and vomiting. Emend was first authorised in the European Union on 11 November 2003. It is currently approved for prevention of nausea and vomiting in chemotherapy.
- **Keppra** (levetiracetam), from UCB S.A., to add treatment of myoclonic seizures in patients with juvenile myoclonic epilepsy. Keppra was first authorised in the European Union on 29 September 2000 and is currently approved for adjunctive therapy in the treatment of partial onset seizures in patients with epilepsy.
- **Taxotere** (docetaxel), from Aventis Pharma S.A., to add the treatment of metastatic gastric adeno-carcinoma in combination with cisplatin and 5-fluorouracil. Taxotere was first authorised in the European Union on 27 November 1995. It is currently approved for use in the treatment of breast cancer, non-small cell lung cancer and prostate cancer.

Summaries of opinions for all these products are available and can be found here. Further information will be included in the EPAR once the European Commission has granted final approval.

Lists of Questions

The Committee adopted two Lists of Questions on initial applications (one under the mandatory scope and one under the optional scope) and five Lists of Questions on "line extensions" applications (in accordance with Annex II of Commission Regulation (EC) No. 1085/2003).

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 European Commission has granted no marketing authorisations for medicinal products since the CHMP plenary meeting in February 2006.

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 February 2006 are provided in **Annex 3**.

Referral procedures

Finalised referral procedure

- The Committee finalised a referral procedure for **atorvastatin**-containing medicinal products (Sortis and other associated names) recommending granting an extension of indication to patients who have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors. The procedure was initiated by Spain under Article 6(12) of Commission Regulation (EC) No 1084/2003 following an application submitted by Parke-Davis GmbH to extend the indication to the prevention of cardiovascular events in patients with multiple risk factors. The CHMP was asked to look at the issue because Member States had different opinions with regard to the extent of the patient population likely to benefit from atorvastatin therapy in this clinical setting, especially in view of the lack of established benefit in women observed in the clinical trials.

Start of arbitration procedures

The Committee started an arbitration procedure for three generic **doxazosin**-containing medicines: Cardoreg from Pharmcom Oy, Doxagamma from Generics UK limited, Doxastad from Stada Arzneimittel. The procedure under Article 29 of the Community code on human medicinal products (Directive 83/2001/EC as amended) was initiated on the request of the United Kingdom because of potential differences in the release profile between the reference product and the generic versions. Doxazosin-containing medicines are approved in a number of EU Member States for the treatment of essential hypertension and symptomatic treatment of benign prostatic hyperplasia.

Review procedures

- The Committee finalised a safety review procedure for **tacrolimus**-containing dermatological medicinal products (Protopic/Protopy). In view of the potential risk of malignancies (including skin cancer and lymphoma), the European Commission initiated a review procedure under Article 18 of Council Regulation (EEC) No 2309/93 of 22 July 1993, that was finalised under Article 20 of Regulation (EC) No 726/2004 of 31 March 2004, to request the Opinion of the CHMP on the benefit/risk profile of Protopic/Protopy. Following this request, the CHMP reviewed the available data on this safety issue, including post-marketing reports, data from non-clinical studies, clinical trials and epidemiological studies. On the basis of the available data, the Committee considered the benefit/risk balance of dermatological medicinal products containing tacrolimus to be favourable in the treatment of patients aged 2 years and over with moderate to severe atopic dermatitis who are not adequately responsive to or are intolerant of conventional therapies such as topical corticosteroids. The Committee concluded that a potential association of the cases of malignancy with the use of tacrolimus ointment could not be ruled out and therefore further data are needed to ensure an acceptable long term safety profile. The Committee recommended changes to the current product information, which aim at raising awareness of patients and prescribers of the potential long-term risks associated with the use of these products.

- The Committee finalised a safety review procedure for **pimecrolimus**-containing dermatological medicinal products (Elidel and associated names). In view of the potential risk of malignancies (including skin cancer and lymphoma), Denmark initiated a referral procedure under Article 31 of Directive 2001/83/EC, as amended, to request the Opinion of the CHMP on the benefit/risk profile of Elidel. Following this request, the CHMP reviewed data on efficacy and the available data on the mentioned safety issue, including post-marketing reports, data from non-clinical studies, clinical trials and epidemiological studies. On the basis of the available data, the Committee considered the benefit/risk balance of medicinal products containing pimecrolimus cream to be favourable in the treatment of patients aged 2 years and over with mild or moderate atopic dermatitis where treatment with topical corticosteroids is either inadvisable or not possible. The Committee concluded that a potential association of the cases of malignancy with the use of pimecrolimus cream could not be ruled out and therefore further data are needed to ensure an acceptable long term safety profile. The Committee recommended changes to the current product information, which aim at raising awareness of patients and prescribers of the potential long-term risks associated with the use of these products.

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 27 February – 1 March 2006. For further details, please see **Annex 4**.

Documents prepared by the CHMP Working Parties adopted during the March 2006 CHMP meeting are listed in **Annex 5**.

Invented 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 6.**

Upcoming meetings following the March 2006 CHMP plenary meeting:

- The 21st meeting of the CHMP will be held at the EMEA on 24-27 April 2006.
- The next Invented Name Review Group meeting will be held at the EMEA on 24 April 2006.
- The sixth CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised Procedures-Human) will be held at the EMEA on 24-26 April 2006.

Organisational matters

The main topics addressed during the March 2006 CHMP meeting related to:

- Organisational activities aiming at improving the work of the Committee due to legislative requirements of the new legislation and ensuring a consistent working approach (for instance activities relating to reporting/requesting inspections, benefit/risk assessment, ethical issues).

EMEA Implementation of the New EU Pharmaceutical Legislation

The fifteenth CHMP/EMEA Implementation Task Force (CEITAF) meeting took place on Monday 20 March 2006.

The following documents were adopted by the CHMP and will be released on the EMEA website for consultation:

- Revised Guideline on Compassionate use and its Question and &Answer document. These documents will be released on the EMEA website for 3 months consultation

PROCEDURAL ANNOUNCEMENT

Reminder on the Submission of Follow-up Measures, Specific Obligations and Periodic Safety Update Reports

When submitting data relating to a Follow-up Measure or Specific Obligation for Centrally Authorised Medicinal Products, Marketing Authorisation Holders (MAHs) should review whether these data would require changes to the Product Information or to the Marketing Authorisation (e.g. changes to the Quality Module) of the Medicinal Product. If such changes are identified, the MAH should submit the FUM/ SO data within the framework of the appropriate variation/extension procedure(s). This will minimise the processing and review time and will allow quicker implementation of the required changes.

Similarly, should the MAH identify a need for changes to the Product Information further to a Periodic Safety Update Report (PSUR), he should submit a Type II variation in parallel to the PSUR.

When submitting a Follow-up Measure/ Specific Obligation /PSUR, MAHs are requested to confirm in the cover letter that they consider that there is no need for an update of the Product Information or of the Marketing Authorisation.

In case of doubt on how to proceed MAHs are encouraged to contact the PTL for the product concerned.

Mutual Recognition procedure and Decentralised procedures-Human

The CHMP noted the report from the fifth CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 20-21 March 2006. For further details, please see **Annex 7**.

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

PRE-AUTHORISATION: MARKETING AUTHORISATION APPLICATIONS

Activity	Dec 2005/2006[1]							1995 onwards
	Optional Scope			Mandatory scope			Total	Overall total
	NAS	Significant innovation	Interest of Patients	Biotech	Indications	Orphans		
Applications for MA submitted[2]	**5**	**4**	**0**	**10**	**3**	**3**	**25**	**515**
Positive opinions[3]	**5**	**1**	**0**	**3**	**0**	**2**	**11**	**337[4]**
Negative opinions[4]	**1**	**0**	**0**	**1**	**0**	**0**	**2**	**9[6]**
Withdrawals prior to opinion	**2**	**1**	**0**	**0**	**0**	**2**	**5**	**104**
Marketing authorisation granted by the Commission	**8**	**0**	**0**	**1**	**0**	**1**	**10**	**321**

PRE-AUTHORISATION: SCIENTIFIC SERVICES

Activity (submissions)	Dec 2005/2006	1995 onwards
Compassionate use applications	**0**	**0**
Art. 58 applications	**0**	**2**
Consultation for medical devices[5]	**0**	**4**
PMF	**2**	**10**
VAMF	**0**	**0**

[1] Starting point for operation of the new eligibility criteria to the centralised procedure
[2] Number of accelerated reviews requested and number of accelerated reviews granted (3/0)
[3] Subdivided by conditional and exceptional (0/0)
[4] In case of Re-examination under Art. 9(2) of Regulation (EC) No. 726/2004, the opinion will not be counted twice.
[5] 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 MARCH 2006 CHMP MEETING IN RELATION TO ACCELERATED ASSESSMENT PROCEDURES

Substance	Intended indications(s)	Accelerated Assessment Requests	
		Accepted	Rejected
N/A	N/A	N/A	N/A

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

Activity	2006	Overall total 1995 onwards
Type I Variations (positive notifications)	115	3555
Type II Variations (positive opinions)	140	2322
Type II Variations (negative opinions)	0	7
Annex II Applications (positive opinions)	6	133
Annual Re-assessment (positive opinions)	8	N/A
Opinion for renewals of conditional MA's (positive opinions)	0	0
5 Year Renewals (positive opinions)	17	N/A

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
3 Extensions of indication	3 Positive opinions
18 SPC changes	18 Positive opinions
35 Quality changes	35 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Onsenal (celecoxib) Pharmacia-Pfizer EEIG	Positive Opinion adopted	The Marketing Authorisation will remain under Exceptional circumstances
Xagrid (anagrelide) Shire Pharmaceutical Contracts Ltd	Positive Opinion adopted	The Marketing Authorisation will remain under Exceptional circumstances
Zevalin (ibritumomab tiuxetan) Schering AG	Positive Opinion adopted	The Marketing Authorisation will remain 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**
Aranesp (darbepoetin alfa) Amgen Europe B.V	Positive Opinion adopted	Unlimited validity
Nespo (darbepoetin alfa) Dompé Biotec S.p.A	Positive Opinion adopted	Unlimited validity
Caelyx (doxorubicin) SP Europe	Positive Opinion adopted	Unlimited validity
Puregon (follitropin beta) N.V. Organon,	Positive Opinion adopted	Unlimited validity
Osigraft (eptotermin alfa) Howmedica International S. de R.L,	Positive Opinion adopted	Additional 5-year renewal

OVERVIEW OF DESIGNATED ORPHAN MEDICINAL PRODUCTS THAT HAVE BEEN THE SUBJECT OF A CENTRALISED APPLICATION FOR MARKETING AUTHORISATION: UPDATE SINCE THE FEBRUARY 2006 CHMP MEETING

Active substance	**Sponsor/applicant**	**EU Designation Number & Date of Orphan Designation**	**Designated Orphan Indication**
Imatinib mesylate (Glivec)	Novartis Europharm Limited	EU/3/05/306 26/08/2005	Treatment of mastocytosis

OUTCOME OF THE MARCH 2006 CHMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

EMEA CENTRALISED PROCEDURES

	1995 - 2005	2006	Overall Total
Scientific Advice	558	40	598
Follow-up to Scientific Advice	94	6	100
Protocol Assistance	107	15	122
Follow-up to Protocol Assistance	26	2	28
	785	63	848

Substance	**Intended indications(s)**	**Type of Request**				**Topic**			
		New		**Follow-up**		**Pharma ceutical**	**Pre-clinical**	**Clinical**	**Significant Benefit**
		SA	**PA**	**SA**	**PA**				
Biological	Alzheimer's disease	X						X	
Chemical	Alzheimer's disease	X					X	X	
Chemical	Alzheimer's disease	X						X	
Chemical	Epilepsy	X						X	
Chemical	Amyotrophic Lateral Sclerosis	X						X	
Chemical	Cervical cancer due to HPV infection	X					X		
Chemical	Cerebral and cardiac angiography; computer tomography contrast agent	X				X	X	X	
Chemical	Thrombocytopenias	X						X	
Biological	Hypovolemia	X						X	
Biological	Emphysema secondary to congenital alpha-1-antitrypsin deficiency (AATD)	X						X	
Chemical	Allergic rhinitis	X						X	
Chemical	Fibromyalgia	X						X	
Chemical	Constipation-predominant irritable bowel syndrome (IBS-c)	X					X	X	
Biological	Hypereosinophilic Syndrome (HES)		X			X		X	

Biological	Promotion of interbody fusion lumbar degenerative disc disease	X					X	X	
Chemical	Steroid sensitive Nephrotic Syndrome		X			X	X	X	X
Biological	Malabsorption due to exocrine pancreatic enzyme insufficiency				X			X	
Chemical	Diarrhoea-predominant Irritable Bowel Syndrome (d-IBS)	X					X	X	
Chemical	HIV/AIDS	X					X	X	
	Total	**16**	**2**		**1**				

SA: Scientific Advice
PA: Protocol Assistance

The above-mentioned 16 Scientific Advice letters, 2 Protocol Assistance letters, 0 Follow-up Scientific Advice letters and 1 Follow-up Protocol Assistance letters were adopted at the March 2006 CHMP meeting.

The Committee accepted 8 Initial Scientific Advice Requests, 0 Follow-up Scientific Advice Request, 5 Initial Protocol Assistance Requests and 1 Follow-up Protocol Assistance Request started at the meeting that took place on 20-23 March 2006.

DOCUMENTS PREPARED BY THE CHMP WORKING PARTIES ADOPTED DURING THE MARCH 2006 CHMP MEETING

BIOLOGICS WORKING PARTY

Reference number	Document	Status
CHMP/BWP/91765/ 2006	Interim EU Recommendations for the influenza vaccine composition for the season 2006/2007	Adopted

QUALITY WORKING PARTY (QWP)

Reference number	Document	Status
CPMP/QWP/227/02 Rev 2 draft EMEA/CVMP/134/ 02 Rev 2 draft	Revised Guideline on Active Substance Master File in relation to Herbal Medicinal Products (introducing a specific annex)	Adopted by the CHMP. Publication subject to adoption by the CVMP
CPMP/QWP/2820/00 rev. 1 CVMP/815/00 rev. 1	Guideline on specifications: Test procedures and acceptance criteria for Herbal substances, Herbal preparations and Herbal medicinal products / traditional Herbal medicinal products	Adopted
CPMP/QWP/2819/00 rev. 1 CVMP/814/00 rev. 1	Guideline on quality for Herbal medicinal products and traditional Herbal medicinal products	Adopted
CHMP/QWP/92877/ 2005	Concept paper on the revision of note for guidance on radiopharmaceuticals	Released for 3 months consultation
CHMP/QWP/49313/ 2005	Guideline on the pharmaceutical quality of inhalation and nasal product	Adopted

EFFICACY WORKING PARTY (EWP)

Reference number	Document	Status
CHMP/EWP/2459/02	Reflection paper on methodological issues in confirmatory clinical trials with flexible design and analysis plan	Released for 6 months external consultation

PAEDIATRIC WORKING PARTY (PEG)

Reference number	Document	Status
EMEA/127047/2006	Concept paper on the impact of Lung and Heart Immaturity when investigating Medicinal Products intended for Neonatal Use	Released for 6 months consultation
CHMP/189220/2005	Assessment of the Paediatric Needs – Pain	Adopted

SAFETY WORKING PARTY (SWP)

Reference number	Document	Status
CHMP/SWP/203927/2005	Guideline on Risk Assessment of Medicinal Products on Human Reproduction and Lactation: From Data to Labelling	Released for 6 months consultation
CHMP/SWP/94227/2004	Guideline on the Non-Clinical Investigation of Dependence Potential of Medicinal Products	Adopted
CHMP/SWP/91850/2006	Concept Paper on the Development of a CHMP Guideline on the Non-Clinical Requirements to Support early Phase I Clinical Trials with Pharmaceutical Compounds	Released for 3 months consultation

WORKING PARTY ON SIMILAR BIOLOGICAL (BIOSIMILAR) MEDICINAL PRODUCTS (BMWP)

Reference number	Document	Status
CHMP/BMWP/94526/2005	Annex to Guideline on Similar Biological Medicinal Products containing Biotechnology-Derived Proteins as active substance: Non-Clinical and Clinical Issues Guidance on Similar Medicinal Products containing Recombinant Erythropoietins	Adopted

INVENTED NAME REVIEW GROUP (NRG)

	March 2006			2006	
	Accepted	Rejected	Pending	Accepted	Rejected
Proposed invented names	7	15	19	23	34
Justification for retention of invented name *	0	4	5[1]	1	11

*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.

[1] One Justification request has been postponed from the March NRG meeting

Co-ordination Group for Mutual Recognition and Decentralised Procedures - Human

Report from the CMD(h) meeting held from 20th to 22nd March 2006

General Issues

Meeting on Harmonisation of SPCs with Interested Parties

The Sub-Group on Harmonisation of SPCs met with Interested Parties to hear their views on future harmonisation of authorisations for medicinal products authorised in the Community.
The CMD(h) Sub-Group on Harmonisation of SPCs will continue its work, with a view to laying down a list of medicinal products for which a harmonised SPC should be drawn up, taking into account the proposals from all Member States, in accordance with Article 30(2) of Directive 2001/83/EC, as amended.

New Questions and Answers on CMD(h) SOP – Disagreement in Procedures – Referral to CMD(h)

The CMD(h) has agreed 2 new Q&A to address submission of 'new data' and format of the response document for applications referred to the CMD(h) for the 60 days referral procedure.
The updated Q&A document will be published on the website.

Best Practice Guide on Break-out Sessions

The CMD(h) has agreed an updated Best Practice Guide on Break-out Sessions, mainly to consider the new decentralised procedure and to take account of initial comments received from Interested Parties.

Any comments on the updated Best Practice Guide on Break-out Sessions should be sent by 20 April 2006, coordinated where possible by trade associations, to the CMD(h) secretariat (sonia.ribeiro@emea.eu.int).

Consultation with target patients groups for the package leaflet

Applicants are reminded that the submission of the results of consultation with target patient groups, in accordance with Article 59(3) of Directive 2001/83/EC, as amended, or justification for its absence is required with the submission of applications for marketing authorisation via the mutual recognition procedure.

For applications submitted via the decentralised procedure this is also a requirement; however, applicants should consider the need and timing of consultation with target patients groups within the procedural timeframe.
For further information on the timing of user consultation, submission and assessment within the evaluation procedure in the mutual recognition or decentralised procedure, please refer, respectively, to the Best Practice Guide for the Mutual Recognition Procedure and to the Decentralised procedure – Member States SOP, available on the Heads of Medicines Agencies website.

Submission of Detailed description of the Pharmacovigilance and Risk Management Systems

Applicants are reminded that the submission of a detailed description of the pharmacovigilance and, where appropriate, of the risk-management system which the applicant will introduce is required with the submission of applications for marketing authorisation via the mutual recognition or decentralised procedures, in accordance with Article 8.3(ia) of Directive 2001/83/EC, as amended.

Applicants, which have already a national marketing authorisation and have planned to start a mutual recognition procedure soon, are advised to contact the RMS to discuss the possibility of a transitional period. The transitional period is limited to a maximum of 6 months.

For further information, please refer to the Guideline on Risk Management Systems for medicinal products for human use, published on the EMEA website.

Notifications to the EMEA/CHMP in the Mutual Recognition/Decentralised Procedures

The above mentioned document has been updated to take account of Directive 2004/27/EC.
Applicants are no longer requested to inform the EMEA of the submission of applications for marketing authorisation via the mutual recognition or the new decentralised procedure.
Only in the event of arbitration for applications for marketing authorisation or variations to marketing authorisation, the EMEA should receive the dossier for the respective procedure.

Information on applications referred to the CMD(h) in accordance with Article 29(1) of Directive 2001/83/EC, as amended

Please find below information on the Name of the products in the RMS, active substances, pharmaceutical forms, procedure numbers, CMS, legal basis, grounds for referral to CMD(h), Day 60 and outcome of the procedures, for the referrals to the CMD(h) finalised on 3 March 2006.

Name of the product in the RMS	Epratenzide Plus 600/12.5 mg
Active substance	eprosartan, hydrochlorothiazide
Pharmaceutical form	Film-coated tablet
Procedure number	DE/H/538/01
CMS	FR, PT, SE
Legal basis	Article 10.1(b), Directive 2001/83/EC – Fixed combination
Grounds for referral to CMD(h)	Efficacy of the combination product in comparison with eprosartan as monotherapy. Inconsistent information in SPC section 4.6 (Pregnancy and lactation) in comparison to other medicinal products with angiotensin-II antagonists in combination with hydrochlorothiazide.
Day 60	03.03.2006
Outcome	Agreement reached

Name of the product in the RMS	Cardoreg	Doxagamma
Active substance	doxazosin mesylate	
Pharmaceutical form	Prolonged release tablet	
Procedure number	DK/H/429/01/E01	DK/H/624/01/E01
CMS	CZ, HU, PL, SK, UK (wave 2) DE, ES, NO, SE (wave 1)	UK (wave 2) DE, NO, SE (wave 1)
Legal basis	Article 10.1(a)(iii), Directive 2001/83/EC - Generic	
Grounds for referral to CMD(h)	Different views on the clinical consequences of deviation from the existing bioequivalence guideline.	
Day 60	03.03.2006	
Outcome	Referred to CHMP for arbitration	

Name of the product in the RMS	Doxastad
Active substance	doxazosin mesylate
Pharmaceutical form	Prolonged release tablet
Procedure number	SE/H/469/01
CMS	DE, EE, ES, LT, LV, NL, UK
Legal basis	Article 10.1(a)(iii), Directive 2001/83/EC - Generic
Grounds for referral to CMD(h)	Different views on the clinical consequences of deviation from the existing bioequivalence guideline.
Day 60	03.03.2006
Outcome	Referred to CHMP for arbitration

Name of the product in the RMS	Formoterol Novolizer 6 µg, 12 µg
Active substance	formoterol
Pharmaceutical form	Inhalation powder
Procedure number	DE/H/571/01-02
CMS	AT, BE, ES, FR, IE, IT, LU, NL, PT, UK
Legal basis	Article 10.1(a)(iii), Directive 2001/83/EC - Last paragraph
Grounds for referral to CMD(h)	Different interpretation of the submitted data concerning safety and efficacy of the medicinal product.
Day 60	03.03.2006
Outcome	Agreement reached

Name of the product in the RMS	Lansoprazole Vetiquima 15 mg, 30mg	Lansoprazole Suprazol 15 mg, 30mg
Active substance	lansoprazole	
Pharmaceutical form	Gastro-resistant capsule, hard	
Procedure number	PT/H/113/01-02	PT/H/114/01-02
CMS	DE, IE, IT, NL, SE, UK	BE, DE, DK, FI, IT, NL, NO, SE, UK
Legal basis	Article 10.1 (a)(iii), Directive 2001/83/EC - Generic	
Grounds for referral to CMD(h)	Choice and composition of meal content used in the fed bioequivalence study and risk of dose dumping related to food intake. Discussion on clinical relevance of a lower C_{max} for the test product.	
Day 60	03.03.2006	
Outcome	Agreement reached	

Name of the product in the RMS	Nurofen Junior Zäpfchen 60 mg
Active substance	ibuprofen
Pharmaceutical form	Suppository
Procedure number	DE/H/0433/01
CMS	AT, BE, CZ, ES, EL, FR, LU, PL, PT, SK
Legal basis	Article 10.1(a)(ii) - Bibliographic
Grounds for referral to CMD(h)	Different interpretation of the existing bibliographic data.
Day 60	03.03.2006
Outcome	Agreement reached

Name of the product in the RMS	Alfuzosin Stada
Active substance	alfuzosin
Pharmaceutical form	Prolonged release tablet
Procedure number	SE/H/559/01
CMS	AT, CZ, DE, DK, ES, HU, IE, IT, NO, PL, SK, UK
Legal basis	Article 10.1(a)(iii), Directive 2001/83/EC - Generic
Grounds for referral to CMD(h)	Deficiencies in the study design to fully evaluate the influence of food on the formulation.
Day 60	03.03.2006
Outcome	Agreement reached

Meeting schedule

The next CMD(h) meeting will be held on 24th , 25th and 26th April 2006.

NEW APPLICATIONS

Mutual Recognition Procedure

The CMD(h) noted that **24** new Mutual Recognition Procedures were finalised during the month of February 2006. **17** Mutual Recognition Procedures for new applications were referred to CMD(h) in this period.

The status as of 28th February of procedures under Mutual Recognition is as follows:

Year	Procedures from New applications finalised	Procedures from New applications in process	Procedures referred to CMD(h)	Arbitrations referred to CHMP
2006	70	89	25 N.A.	- -

27 Mutual Recognition Procedures (regarding **61** products) started in February 2006. The categories of these procedures are as follows:

6 known active substances (already authorised in at least one member state), including **1** repeat use.

20 abridged applications including **3** multiple applications and **3** repeat use.

1 line extension application.

The new procedures started related to **3** full dossiers, **18** generics, **2** generics-other and **4** bibliographic applications.

The procedures consisted of **27** chemical substances.

26 of these procedures were prescription-only medicinal products in the reference Member State and **1** procedure was classified as Non-prescription (including OTC) medicinal product[2].

1. As considered by RMS.
2. In this category products are classified as prescription-only or Non-prescription (OTC) products when the RMS has approved them accordingly, although the legal status is not part of the Mutual Recognition Procedure.

Number of countries involved in the new applications in Mutual Recognition procedure started in February 2006.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (1)	25
DE (1)	16
DK (4)	14
DK (1)	5
FI (1)	6
FI (2)	6
FI (2)	9
FI (5)	14
FI (5)	1
FI (5)	1
FR (3)	21
HU (1)	11
IT (1)	4
NL (2)	5
NL (2)	11
NL (2)	5
PT (2)	5
SE (2)	13
SE (1)	18
SE (5)	21

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
SE (1)	7
SE (3)	1
SE (1)	15
SE (3)	1
UK (1)	13
UK (1)	6
UK (2)	7

I Decentralised Procedure

The CMD(h) noted that **31** new Decentralised Procedures (regarding **39** products) started in February 2006. The categories of these procedures are as follows:

22 abridged applications including **4** multiple applications.

2 known active substances (already authorised in at least one member state), including **1** multiple application.

7 line extension applications, including **5** multiple applications.

The new Decentralised procedures started related to **5** full dossiers, **25** generics and **1** generic-other.

The procedures consisted of **31** chemical substances[3].

30 of these procedures were prescription-only medicinal products in the reference Member State and **1** procedure was classified as Non-prescription (including OTC) medicinal product[4].

3. As considered by RMS.
4. In this category products are classified as prescription-only or Non-prescription (OTC) products as applied for in the RMS, although the legal status is not part of the Decentralised Procedure.

Number of countries involved in the new applications in Decentralised procedures started in February 2006.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (4)	3
DK (1)	1
DK (1)	2
DK (1)	6
DK (1)	1
DK (1)	4
DK (1)	1
DK (1)	1
DK (1)	4
DK (1)	2
DK (1)	1
DK (3)	5
NL (1)	1
NL (1)	1
NL (1)	1
NL (1)	1
NL (4)	14
NL (1)	14
NL (1)	1
NL (1)	21
NL (1)	1
NL (1)	1
SE (1)	2
SE (1)	1

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
SE (1)	2
SE (1)	4
SE (1)	1
UK (1)	10
UK (1)	7
UK (1)	8
UK (1)	1

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **299** type IA variations, **135** type IB variations and **160** type II variations were finalised during the month of February 2006. **29** renewals were finalised in this period.

The status as of 28th February of variations and renewals under Mutual Recognition is as follows:

Year	Procedures from Type IA variations finalised	Procedures from Type IB variations finalised	Procedures from Type II variations finalised	Renewals finalised	Arbitrations referred to CHMP
2006	615	298	253	45	- -

All documents mentioned in this press release can be found at the CMD(h) website at the European Medicines Authorities Windows under the heading *Press Releases*.

Information on the above mentioned issues can be obtained from the chair of the CMD(h):

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http://heads.medagencies.org/