The European Agency for the Evaluation of Medicinal Products
*Evaluation of Medicines for Human Use*

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EMEA/CPMP/6248/02

# COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
# DECEMBER 2002 PLENARY MEETING
# MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 88th plenary meeting from 17 – 18 December 2002.

**Product related issues**

*Centralised procedures*

The Agency's scientific committee, the CPMP, adopted 1 opinion for an initial marketing authorisation application at this meeting:

- A positive opinion for **Forsteo** (teriparatide) from Eli Lilly, which is intended for the treatment of established osteoporosis in postmenopausal women. EMEA review began on 19 June 2001 and the opinion was adopted on 19 December 2002, with an active review time of 207 days.

A summary of this opinion is available on the EMEA web site: http://www.emea.eu.int

The CPMP revised its opinions of 25 July 2002 for valdecoxib containing medicines **Bextra** (Pharmacia-Pfizer EEIG), **Valdyn** (Pharmacia Europe EEIG) and **Kudeq** (Pfizer Limited). The revision follows the EMEA public statement of 22 October 2002 on reports of serious hypersensivity reactions and serious skin reactions in some patients treated with valdecoxib, which is now reflected in the revised product literature. The opinions for **Valdecoxib Pfizer Ltd** (Pfizer Limited) and **Valdecoxib Pharmacia Europe EEIG** (Pharmacia Europe EEIG) were not revised since the applicants have withdrawn these applications.

The Committee also adopted 4 opinions by consensus on "line extension" applications (2 Part A and 2 Part B) (in accordance with Annex II of Commission Regulation (EC) No. 542/95, as amended) and 1 List of Questions (Part B) on an orphan designated medicinal product.

The Committee gave a positive opinion for an extension of indication for the already authorised medicinal product **Forcaltonin** (recombinant salmon calcitonin) from Unigene UK Ltd to include the product's use in the prevention of acute bone loss due to sudden immobilisation (such as in patients with recent bone fractures). Forcaltonin was first authorised in the European Union in January 1999.

Further information on this extension will be included in the European Public Assessment Report (EPAR) once the European Commission has granted final approval.

The CPMP noted the withdrawal for commercial reasons of the Marketing Authorisation for **Hepacare** (triple antigen hepatitis B recombinant vaccine), indicated for active immunisation against hepatitis B virus infection in non-immune adults (≥18 years). Hepacare was not marketed anywhere in the world. For further details please see the Public Statement (EMEA/32933/02) available on the EMEA web site: http://www.emea.eu.int.

An overview of centralised procedures since 1995 is given in **Annex 1**. The list of medicinal products for which marketing authorisations have been granted by the European Commission since the CPMP plenary meeting in November 2002 is provided in **Annex 2.** The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 3**.

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The Committee concluded its Community-wide review for:

The centrally authorised medicinal products containing desloratadine (**Azomyr**, **Opulis**, **Allex**, **Aerius** and **Neoclarityn**) from SP Europe. Desloratadine is the major metabolite of loratadine. The CPMP considered that the benefit/risk balance of desloratadine containing medicinal products remains favourable. The scientific assessment of the safety signal of hypospadias following use of loratadine during pregnancy concluded that, based on the available data, a causal relationship could neither be confirmed nor excluded. As a precautionary measure the product information for desloratadine will be revised to state that the use of desloratadine during pregnancy is not recommended. The separate referral procedure for loratadine containing medicinal products is still ongoing as the Committee is also assessing other aspects of the safety and efficacy of these nationally approved products.

*Scientific Advice procedures*

The CPMP was informed of the outcome of the discussions of the Scientific Advice Review Group (SciARG) meeting, which was held on Monday 16 December 2002. For further details, please see **Annex 4**.

**Non-product related issues**

*CPMP Working Parties and Ad Hoc Groups*

The **Working Parties Chairpersons' meeting**, chaired by Dr Daniel Brasseur, was held on 17 December 2002. Consolidated comments from CPMP Working Parties on Annex I of Directive 2001/83/EC were discussed. These comments will be forwarded to the Pharmaceutical Committee for discussion at their next meeting in January 2003.

The **Herbal Medicinal Products Working Party,** chaired by Dr Konstantin Keller, held its meeting on 4–5 November 2002. The HMPWP proposals for Core data on Peppermint oil (http://www.emea.eu.int/pdfs/human/hmpwp/141702en.pdf), Core data on Peppermint leaf (http://www.emea.eu.int/pdfs/human/hmpwp/141802en.pdf) and Core data on Nettle leaf (http://www.emea.eu.int/pdfs/human/hmpwp/141602en.pdf) were released for three months consultation. For further details on the meeting, please see the published Press Release of the meeting http://www.emea.eu.int/htms/hotpress/he28546.htm.

The CPMP appointed Prof R. Bass as a new Chairperson for the **Ad Hoc Group of Experts on the revision of the Guideline on Excipients in the Package Leaflet** in replacement of Pharm. Geert de Greef.

The **Work programmes for the years 2003 and 2004** for the following CPMP Working Parties and CPMP Ad Hoc Working Groups are available on the EMEA Website (http://www.emea.eu.int):

- Biotech Working Party (BWP)
- Efficacy Working Party (EWP)
- Herbal Medicinal Products Working Party (HMPWP)
- Safety Working Party (SWP)
- Quality Working Party (QWP)
- Blood Products Working Group (BPWG)
- Ad Hoc Paediatric Expert Group (PEG)

Documents prepared by the CPMP Working Parties and the CPMP Ad Hoc Groups adopted during the December 2002 CPMP meeting can be seen in **Annex 5**.

 

*Upcoming meetings following the December 2002 CPMP plenary meeting:*

- The Joint QWP/Ad Hoc GMP Inspectors meeting on parametric release, enhanced quality monitoring and NIRS (Near-InfraRed Spectroscopy) will take place at the EMEA on 15 January 2003.
- The international symposium which is organised by the EDQM, European Pharmacopoeia will devote one session on "Standardisation and Quality Control Cell and Gene Therapy Products" in Strasbourg on 24 – 25 February 2003 and one session on "Microbiological Control Methods in the European Pharmacopoeia: Present and Future" in Copenhagen on 5 – 6 May 2003. For further information, visit the EDQM Internet site: http://www.pheur.org .

*Organisational Matters*

The CPMP noted a report from the Heads of Agencies on Establishing a European Risk Management Strategy. Following the ongoing discussions on the EMEA Risk Management Strategy, the CPMP had further discussions on the EMEA's proposals for the future handling of safety concerns by the Committee and agreed on proposals to further improve the handling of such concerns in the pre-authorisation phase.

The 18th CPMP Organisational Matters meeting (ORGAM) chaired by Dr D. Brasseur, took place on Monday 16 December 2002. During the meeting organisational issues were discussed on the:
- opportunities to increase IT use during the review process and
- EMEA's involvement in the consultation procedure for ancillary medicinal substances in medical devices.

The next CPMP Organisational Matters meeting is scheduled to take place on Monday 20 January 2003.

*Mutual Recognition procedure*

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 16 December 2002. For further details, please see **Annex 6.**

The 89th plenary meeting of the CPMP will be held on 21 – 23 January 2003.

The Executive Director, EMEA staff and CPMP Members wish you all a Happy New Year.

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

 

## EMEA CENTRALISED PROCEDURES

| | 1995-2001 | | | 2002 | | | Overall Total |
|---|---|---|---|---|---|---|---|
| | Part A | Part B | Total | Part A | Part B | Total | |
| **Scientific Advice** | 88 | 164 | 252 | 9 | 41 | 50 | 302 |
| **Follow-up to Scientific Advice** | 18 | 17 | 35 | 5 | 10 | 15 | 50 |
| **Protocol Assistance** | 0 | 2 | 2 | 5 | 6 | 11 | 13 |
| **Follow-up to Protocol Assistance** | 2 | 0 | 2 | 1 | 1 | 2 | 4 |

| | 1995-2001 | | | 2002 | | | |
|---|---|---|---|---|---|---|---|
| | Part A | Part B | Total | Part A | Part B | Total | |
| **Applications submitted** | 120 | 215 | 335 | 7 | 24 | 31 | 366 |
| **Consultation for Medical Device**[1] | NA | N/A | N/A | 0 | 1 | 1 | 1 |
| **Withdrawals** | 15 | 45 | 60 | 5 | 8 | 13 | 73 |
| **Positive CPMP opinions** | 77 | 131 | 208 | 15 | 24 | 39 | 247[2] |
| **Negative CPMP opinions**[3] | 1 | 4 | 5 | 0 | 0 | 0 | 5[4] |
| **Marketing authorisations granted by the Commission** | 71 | 123 | 194 | 17 | 23 | 40 | 234[5] |

| | 1995-2001 | | | 2002 | | | Overall Total |
|---|---|---|---|---|---|---|---|
| | Part A | Part B | Total | Part A | Part B | Total | |
| **Variations type I** | 448 | 806 | 1254 | 137 | 326 | 463 | 1717 |
| **Positive opinions, variations type II** | 285 | 362 | 647 | 120 | 149 | 269 | 916 |
| **Negative opinions, variations type II** | 1 | 6 | 7 | 0 | 0 | 0 | 7 |
| **Extensions (Annex II applications)** | 38 | 36 | 74 | 6 | 8 | 14 | 88 |

[1] 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 derivatives of human blood or plasma and Directive 2001/104/EC.
[2] 247 positive opinions corresponding to 185 substances
[3] In case of appeal, the opinion will not be counted twice
[4] 5 negative opinions corresponding to 4 substances
[5] 234 marketing authorisations corresponding to 175 substances

 

**ANNEX 2 to CPMP Monthly Report December 2002**

**MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE NOVEMBER 2002 CPMP MONTHLY REPORT**

| | |
|---|---|
| **Invented Name** | Somavert |
| **INN** | pegvisomant |
| **Marketing Authorisation Holder** | Pharmacia Enterprise |
| **ATC code** | H01AX (proposed) |
| **Indication** | Treatment of patients with acromegaly who had an inadequte response to surgery and/or radiation therapy and who did not respond to treatment with somatostatin analogues. |
| **CPMP Opinion date** | 25.7.2002 |

 

## OUTCOME OF THE NOVEMBER CPMP MEETING IN RELATION TO CENTRALISED APPLICATIONS IN THE POST-AUTHORISATION PHASE

| **Opinions for Type II Variation applications** | |
|---|---|
| **Number of Opinions** | **Outcome** |
| 1 Extensions of indication | 1 Positive opinion by consensus |
| 17 SPC changes | 17 Positive opinions by consensus |
| 6 Quality changes | 6 Positive opinions by consensus |

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

| **Opinions for Renewal applications** | | |
|---|---|---|
| **Name of Medicinal Product (INN) MAH** | **Outcome** | **Comments** |
| **Quadramet** (samarium [153SM] lexidronam),<br>CIS bio International | Positive opinion by consensus | --- |

 

## OUTCOME OF THE DECEMBER 2002 CPMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

| Substance | Intended indications(s) | Topic | | | | |
|---|---|---|---|---|---|---|
| | | Type of Request | | Pharma-ceutical | Pre-Clinical | Clinical |
| | | New | Follow-up | | | |
| Biological | Diabetes | **X** | | **X** | **X** | **X** |
| Chemical | Sjögren's Syndrome | **X** | | | | **X** |
| Biological | Acute Intermittent Porphyria | **X** (Protocol Assistance/ Significant benefit) | | | | **X** |
| Chemical | Head lice | **X** | | | | **X** |

In December 2002, the above-mentioned 3 final Scientific Advice letters and 1 Protocol Assistance letter were adopted. The Committee accepted 5 new Scientific Advice requests, 1 Follow-up Scientific Advice request, 2 new Protocol Assistance requests and 1 Follow-up Protocol Assistance requests.

 

## DOCUMENTS PREPARED BY THE CPMP WORKING PARTIES AND AD-HOC GROUPS ADOPTED DURING THE DECEMBER 2002 CPMP MEETING

### BIOTECH WORKING PARTY

| Reference number | Document | Status |
|---|---|---|
| CPMP/BWP/2879/02 | Revised CPMP Position Statement on CJD and Plasma-derived and Urine-derived medicinal products | Adopted |
| CPMP/BWP/17372/02 | Report from the EMEA Workshop on the Plasma Master File | Adopted |

### EFFICACY WORKING PARTY

| Reference number | Document | Status |
|---|---|---|
| CPMP/EWP/18/01 | Note for Guidance on the clinical investigation of medicinal products for the treatment of urinary incontinence | Adopted |

### SAFETY WORKING PARTY

| Reference number | Document | Status |
|---|---|---|
| CPMP/SWP/5199/02 draft 2 | Position Paper on the limits of genotoxic impurities | Released for 3 months consultation |

### QUALITY WORKING PARTY

| Reference number | Document | Status |
|---|---|---|
| CPMP/QWP/122/02 | Note for Guidance on Stability testing of existing active substances and related finished products (revision of CPMP/QWP/556/96) | Adopted |
| CPMP/QWP/297/97 rev. 1 | Revised Note for Guidance on Summary of requirements for active substances in the quality part of the dossier | Released for 6 months consultation |

 

# Report from the meeting held on 16 December 2002

**General issues:**

The following new document will be published on the MRFG website:

- MRFG Position on changing the Reference Member State

The following updated documents will be published on the MRFG website:

- List of MRFG Contact Points
- Notifications to the EMEA/CPMP in the Mutual Recognition Procedure
- Mutual Recognition Assessment Report Update
- Core SPC on Hormone Replacement Therapy HRT
  (Marketing Authorisation Holders are recommended to contact their RMS not later than 30 January 2003 to discuss implementation of the amended core SPC.)

It is mentioned that in cases where a simplified handling of variations in MRP has been agreed, the fees still remain under national consideration. Reference is made to the respective MRFG publications below:

- When is simplified handling of variations in MRP after a merger acceptable? (press release 9/00)
- When is simplified handling of variations in MRP not related to a merger acceptable? (press release 11/00)

Implementation of the Commission Decision after a referral procedure
The SPC of the recently finalised referral for clozapine has been published on the EMEA website (www.emea.eu.int/htms/human/referral/referral.htm).

The MAH may choose the RMS for the Mutual Recognition Procedure if there is no RMS already in place:
Once a medicinal product has been through an Article 30 or 31 referral all future variations and renewals have to go through the mutual recognition procedure. Reference is made to the MRFG recommendation paper on MRP after finalisation of an arbitration procedure with a positive opinion by the CPMP and a positive decision by the EU-Commission.

Change in the EU-Presidency
The December MRFG meeting was the last one under the Danish presidency. Greece will take over the presidency in January 2003. Julia Yotaki will be the next MRFG chairperson and she should be contacted in future in case of any questions regarding the MRP.

Meeting schedule
The next MRFG meeting will be held on 20 January 2003.

 

## Annex 1

Joint CPMP/ MRFG working Group on harmonisation of SPC's:
No meeting of the working group was held in December.

*Merry Christmas and a Happy New Year!*
*Feliz Navidad y Próspero Año Nuevo!*
*Glædelig Jul and godt Nytår!*

The MRFG noted that 28 new mutual recognition procedures were finalised during the month of November 2002, as well 193 type I and 28 type II variations.

The status as of 30th November 2002 of procedures under mutual recognition is as follows:

| Year | Procedures from New applications finalised | Procedures from New applications in process | Procedures from Type I variations finalised | Procedures from Type I variations pending | Procedures from Type II variations finalised | Procedures from Type II variations pending | Arbitrations referred to CPMP |
|---|---|---|---|---|---|---|---|
| 2002 | 374 | 95 | 1906 | 282 | 474 | 245 | 2 N.A.<br>7 Var. |

**21** new procedures (regarding 51 products) started in November 2002. The categories of these procedures are as follows:

**1** new active substance (first authorisation in the European Community after RMS approval).

**1** known active substances (already authorised in at least one member state).

**16** abridged applications including **2** multiple applications and **1** repeat use .

**3** Line extension including **1** multiple application.

The new procedures started last month relate to 3 full dossiers, 16 generics, 1 bibliographic application and 1 for different use, route or dose.

The procedures consisted of 21 chemical substances.

20 of these procedures were prescription-only medicinal products in the reference Member State and 1 was 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 procedures started in November 2002

| Reference Member State (number of products involved in the procedure) | Number of CMSs involved in the procedure |
|---|---|
| DK (3) | 2 |
| DK (3) | 3 |
| DK (3) | 2 |
| DK (3) | 5 |
| DK (3) | 3 |
| DK (2) | 3 |
| DK (3) | 7 |
| DK (3) | 2 |
| DK (3) | 1 |
| DK (3) | 1 |
| DK (3) | 1 |

 

| Reference Member State (number of products involved in the procedure) | Number of CMSs involved in the procedure |
|---|---|
| DK (4) | 1 |
| FR (1) | 16 |
| NL (1) | 3 |
| SE (1) | 1 |
| SE (1) | 1 |
| UK (2) | 2 |
| UK (1) | 11 |
| UK (4) | 9 |
| UK (4) | 6 |

**All documents mentioned in this press release can be found at the MRFG website at the European Medicines Authorities Windows under the heading SOP.**

*Information on the above mentioned issues can be obtained by the presiding chair of the MRFG:*


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