

Report from the CMD(h) meeting held on 18th, 19th and 20th February 2008

CMD(h)/EMA Sub-Group on Paediatric Regulation

The CMD(h) noticed that line listings have not been received for all authorised medicinal products. Marketing Authorisation Holders are requested to submit immediately the line listing for all their authorised medicinal products, together with a declaration (Annex I) to each Competent Authority(ies) where the medicinal products are authorised in electronic format only and a copy to the EMA (paedstudies@emea.europa.eu).

The excel templates for the line listings (in editable versions) and a list of addresses for the submission of paediatric information to each Competent Authority are published on the CMD(h) website.

The CMD(h) and the EMA have agreed on additional Q&As to address the submission of paediatric investigation plans (PIPs) in accordance with Articles 7 and 8 of the Paediatric Regulation in the framework of the mutual recognition procedure.

EU Work sharing Project – Assessment of paediatric data

The Marketing Authorisation Holder for the medicinal product Exocin (ofloxacin), involved in the EU work sharing project – assessment of paediatric data, is requested to submit, within 60 days of the finalisation of the procedure, i.e. by 13th April 2008, a national Type II variation to implement the agreed text for inclusion in the SPC.

Request for Marketing Authorisation Holders to assess the risk of occurrence of mesilate esters and related compounds in pharmaceuticals

Marketing Authorisation Holders are requested to undertake a risk assessment on the occurrence of mesilate esters impurities in their medicinal products. This risk assessment should also include the cleaning procedures and the used solvents.

If the outcome of the risk assessment is that the risk is not satisfactorily controlled taking into account the requirements of the Guideline on the limits of genotoxicity impurities (EMA/CHMP/QWP/251334/2006), a variation to the marketing authorisation should be submitted with the appropriate amendments to the manufacturing process/control of active substance and/or finished product.

A letter detailing this request, including additional information for the risk assessment will be published on the CMD(h) website under ‘Contacts with Representative Organisations.’

Best Practice Guide on the compilation of the dossier for new applications submitted in MRP and DCP

Further to the work carried out by the Working Group on Validation issues/National requirements, the CMD(h) has agreed a Best Practice Guide, which provides a summary overview of points to consider at validation, together with a list of references as to where to find advice.

The Best Practice Guide is aimed at emphasising the importance of taking care in the compilation of the dossier for a marketing authorisation application, to minimise delays in validation, to avoid invalidation of applications and to enhance the efficiency of the regulatory process.

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 product in the RMS, active substance, pharmaceutical forms, procedure number, CMS, legal basis, grounds for referral to CMD(h), Day 60 and outcome of the procedure, for the referral to the CMD(h) finalised on 01.02.2008.

Name of the product in the RMS	Lisonorm
Active substance	amlodipine besylate/lisinopril dihydrate
Pharmaceutical form	Tablet
Procedure number	HU/H/0133/001/MR
CMS	CZ, EE, LT, LV, PL, RO, SK
Legal basis	Art. 10b Dir. 2001/83/EC – Fixed combination
Grounds for referral to CMD(h)	This referral procedure concerned the justification of the new calcium antagonist - ACE inhibitor combination of Lisonorm (amlodipine – lisinopril). Additional concerns were raised due the choice of the reference tablets in the submitted bioequivalence trial.
Day 60	01/02/2008
Outcome	At the CMD(h) meeting, the RMS, CMS and the applicant presented their view on the outstanding issues. It was discussed what kind of clinical studies would be required to prove the efficacy and safety of this new fixed combination antihypertensive product but consensus was not reached. Referred to CHMP for arbitration.

Name of the product in the RMS	Ridal 0.25/ 0.5 / 1 / 2 / 3 / 4 / 6 mg Filmtabletten
Active substance	risperidone
Pharmaceutical form	film coated tablet
Procedure number	DE/H/0900/001-007/MR
CMS	AT, BE, EL, IT, PL, SI, UK
Legal basis	Art. 10(3) Dir. 2001/83/EC – Hybrid Application
Grounds for referral to CMD(h)	The marketing authorisation in Germany was based on a bioequivalence study, which was part of a GCP/GLP inspection carried out by the inspectorate of a MS in 2007. During this inspection several critical and major findings have been detected with regard to the GCP/GLP compliance of the trial. Following the invalidation of the bioequivalence study, no further evaluation of the risk/benefit of the application was possible. This has resulted in a potential serious risk to public health.
Day 60	-
Outcome	A new bioequivalence study was initiated by the MAH in advance of the start of the CMD(h) referral procedure. This new bioequivalence study was however stopped after the first phase by the competent health authority due to severe problems in the setup of the clinical trial. As result of this failed study, the MAH withdrew the MA in the RMS and all applications for a MA in the CMS on 23 January 2008. The CMD(h) concluded, that no further action is required.

NEW APPLICATIONS**Mutual Recognition Procedure**

The CMD(h) noted that **22** Mutual Recognition Procedures were finalised during the month of January 2008. **1** Mutual Recognition Procedures was referred to CMD(h) in this period. **No** Mutual Recognition Procedure was referred to CHMP in this period.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
IS (3)	1
NL (1)	2
NL (2)	2
NL (2)	1
NL (4)	5
NL (4)	2
NL (2)	2
PT (3)	7
PT (3)	11
PT (1)	5
PT (2)	8
SE (1)	25
SE (1)	2
SE (1)	1
SE (1)	1
SE (1)	2
SE (2)	26
SE (1)	9

Decentralised Procedure

The CMD(h) noted that there were **37** Decentralised Procedures finalised during the month of January 2008 with a positive outcome. There were **no** Decentralised procedures withdrawn after Day 120. **9** Decentralised Procedures were referred to the CMD(h) in this period. **No** Decentralised Procedure was referred to the CHMP in this period.

The status as of 31st January 2008 of procedures under Decentralised Procedure is as follows:

Year	New applications finalised		New applications withdrawn ²	New applications in process	Referred to CMD(h)	Agreement reached in the CMD(h) For procedures referred in		Withdrawn during CMD(h) referral	Referred to CHMP For procedures referred to CMD(h) in	
	Positive outcome	Negative outcome				2007	2008		2007	2008
2008	37	--	--	1072	9	--	--	--	--	--

87 Decentralised Procedures (regarding **143** products) started in January 2008. The categories of these procedures are as follows:

80 abridged applications, including **32** multiple applications.

3 known active substance applications.

4 line extension applications.

The new Decentralised procedures started in January related to **68** generic, **1** informed consent, **15** hybrid and **3** full dossiers.

All of these procedures consisted of chemical substance applications.

86 of these procedures related to prescription-only medicinal products and **1** to a non-prescription medicinal product in the reference Member State³.

² After day 120.

³ 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 January 2008.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
CZ (1)	3
CZ (1)	2
CZ (1)	3
CZ (1)	2
CZ (4)	6
CZ (2)	4
CZ (2)	13
DE (1)	3
DE (2)	16
DE (4)	4
DE (4)	5
DE (1)	10
DE (1)	4
DE (1)	2
DE (1)	1
DE (1)	9
DE (1)	9
DE (1)	9
DE (5)	2
DE (2)	7
DE (2)	4
DE (2)	5
DE (1)	22
DE (2)	18
DE (3)	8
DE (1)	1
DE (1)	12
DE (1)	3
DE (1)	3
DE (2)	4
DK (1)	12
DK (2)	24
DK (3)	1
DK (3)	1
DK (3)	2
DK (3)	1
DK (3)	13
DK (3)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	3
DK (1)	3
DK (1)	3
DK (1)	2
DK (1)	2
DK (1)	3
DK (1)	1
DK (1)	1
DK (1)	1
EE (1)	17
EE (1)	7
EE (1)	3
EE (1)	2
EE (1)	8
EE (1)	1
NL (3)	5
NL (1)	19
NL (3)	20

NL (4)	10
PT (3)	19
UK (2)	1
UK (1)	6
UK (1)	6
UK (2)	13
UK (1)	6
UK (1)	8
UK (1)	5
UK (1)	8
UK (1)	9
UK (2)	1
UK (2)	4
UK (2)	6
UK (1)	1
UK (2)	6
UK (2)	6
UK (2)	3
UK (2)	3
UK (1)	1
UK (3)	23
UK (1)	1
UK (2)	15
UK (1)	10
UK (1)	1

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **494** type IA variations, **146** type IB variations and **137** type II variations were finalised during the month of January 2008. **24** renewals were finalised in this period. There was **no** procedure referred to the CHMP in this period.

The status as of 31st January 2008 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	Applications referred to CHMP
2008	494	146	137	24	--

All documents mentioned in this press release can be found at the CMD(h) website 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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Or you could visit the CMD(h) web site at:

<http://www.hma.eu/cmdh.html>