



EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – authorisations, EMA

PHARM 614

PHARMACEUTICAL COMMITTEE

22 October 2012

69th meeting

SUMMARY RECORD

The Pharmaceutical Committee held its 69th meeting on 22 October 2012, in Brussels, chaired by Patricia Brunko, Head of Unit SANCO D5 - *Medicinal products – authorisations, EMA*.

1. Agenda

- **The draft agenda (PHARM 607) was adopted, with additional items under A.O.B.**

2. Legislative issues

- **1a) Hospital exemption for ATMPs (advanced therapy medicinal products) (implementation of Art 28(2) of Regulation 1394/2007): update on feedback received by the Commission**

The Commission presented the feedback received from Member States on hospital exemption for ATMP products. All Member States, with exception of Bulgaria, replied. In addition, the Commission received feedback from Croatia and Iceland. There is still a significant number of countries (13) which do not have ATMPs in the market. On average 40% of Member States have a centrally authorised ATMP on their market. This percentage is much higher than that of Member States with ATMP authorised according to national procedure with hospital exemption.

(20%). The sole centralised ATMP is Chondrocelect¹. The feedback on criteria to apply to the hospital exemption was not very detailed and, when available, there was an indication that they follow mainly the Regulation.

The next step of this exercise will be a public consultation, followed by the publication of a general report on the implementation of the legislation according to the Article 25 of the Reg.1394/2007. The summary table will be used when preparing the consultation paper. The public consultation will be launched in 2013. The consultation will also address questions to stakeholders, including industry, to gather their experience as regards the centralised procedure and the hospital exemption. Putting in place two parallel systems should be avoided.

➤ **1b) Request for information by the European Parliament on the possibility in the Member States to advertise organic origin of herbal medicinal products**

A Member of the European Parliament has asked whether it is possible to advertise the organic origin of ingredients of herbal medicinal products. To answer this question the Commission needs the feedback of the Member States. Member States were asked to provide written answer to this following question by 15/11/2012:

Is there a possibility in your Member State to advertise the organic origin of OTC medicinal products? If yes, what are the national rules for such an advertisement?

The Commission will consolidate the answers for the reply.

The Commission indicated that it is not legally possible to include in the product information (SmPC, labelling or package leaflet) the organic origin of the ingredients.

➤ **1c) Status of old marketing authorisations: oligotherapy products**

Following information received by the Commission regarding issues with mutual recognition of medicinal products of a French company in Spain, the Commission encouraged FR and ES to examine together the marketing authorisations at stake in order to solve the problem. In general, if medicinal products are legally on the market in one Member State, there should be no problem to apply for mutual recognition in other Member States.

The Commission also recalled that the MS had to carry out an evaluation programme for all medicinal products brought to the market in 1975, in order to assess whether the existing authorisations needed to be upgraded or not. All medicinal products should comply with the standards set by the Directive 2001/83.

➤ **1d) Legal and Regulatory news**

The Committee was informed about a Corrigendum to Regulation (EC) No 726/2004, some on-going public consultations and Commission implementing Acts that have been adopted since the last Pharmaceutical Committee held on 28 March 2012.

➤ **2a) Shortages of medicinal products due to quality or manufacturing issues**

The Commission provided background information on shortages of medicinal products and presented a summary of all possible best practices in case of shortages due to quality issues. HU informed that they have a national legislation to ensure the redistribution of doses between the hospitals to ensure the security of supply. UK took the view that any possible CHMP opinion on medicines subject to shortages should complement (and not be in conflict) with the national recommendation. IE pointed out that shortages can be due to other issues notably parallel trade

¹ In the meantime, a second product has been authorized by the Commission

and safety concerns. Some delegations reported difficulties to enforce the obligation of supply as laid down in Article 81 of Directive 2001/83/EC. Commission explained that the MS can put in place certain arrangements to prevent that all the supplies on their market are deviated to parallel trade (as confirmed by the Court of Justice (C-478/06, judgement 16/09/2008)). However, the measures must be proportionate with the objective of public health protection. NL pointed out that it is important to have better clarity of the roles of each actor.

The Commission clarified that the EMA will convene a virtual working group, made up of representatives of member state authorities that will develop a decision tree to assist member states to decide whether a particular national shortage should be escalated to community level and the working group will also develop a definition or criteria of "essential medicines" which could deserve particular attention in case of shortages. The Commission proposed to convene a remote meeting of the Pharmaceutical Committee on short notice in case of serious incident of shortage as it was the case in April 2012 with cytotoxic medicines.

➤ **2b) Enforcement of pharmacovigilance obligations**

The Commission reminded the Committee that the new pharmacovigilance legislation puts a particular emphasis on the quality and reliability of the pharmacovigilance system implemented by pharmaceutical companies. For the purpose of monitoring compliance of marketing authorisation holders with pharmacovigilance obligations, competent authorities may inspect premises, records and documents. Where the outcome of the inspection is that the marketing authorisation holder does not comply, the Member States shall consider penalties. In this context the Commission asked the Committee to what extent Member States had recourse to that instrument in the past years. Following an initial discussion, the Committee was invited to provide further feedback in writing by 15/11/2012.

Additionally, the Committee was reminded of the new provisions regarding the need for periodic audits of the pharmacovigilance systems of national competent authorities.

Finally, the exchange of documents in the framework of infringement procedures initiated under Commission Regulation (EC) 658/2007 was discussed. The EMA representative explained that a press release would be published.

MS were asked to provide, by 15/11/2012, written reply to the following question:

"What is the average number of inspections in the field of pharmacovigilance per calendar year (2009-2012) in your Member State and what proportion of them was followed by an administrative infringement procedure or a penal procedure? In view of the reinforced wording of Article 111 of Directive 2001/83/EC, do you consider to make more often recourse to the instrument of administrative penalty proceedings?"

The EMA representative explained that a press release would be published, and that an advance notice had been sent to the Member States.

➤ **2c) Implementations of the new rules on importation of active substances**

The Commission provided background information on the implementation of the new rules on importation of active substances. The Commission confirmed that it is strongly committed to continue the dialogue with third countries to ensure that the new rules are fully understood and smoothly implemented. It is important to underline that the Commission is not imposing the implementation of EU rules on good manufacturing practices (GMP). The new rules, which should be seen in the context of global cooperation, aim to ensure compliance with internationally recognised GMP standards (ICH Q7, WHO) for active pharmaceutical ingredients (APIs) and equivalent regimes for all APIs on the EU market, regardless of where they are manufactured. The Commission underlined that it should be clear that third countries can base the

issuing of written confirmations on inspection results from EU or other third-country authorities applying equivalent standards for good manufacturing practices. This point is clarified in the newly introduced question 18a of the Q&A document. The Commission informed that the revised Q&A would be released on the Commission's website. UK mentioned its data collection exercise in the framework of the Heads of Medicines Agencies (HMA) task force on the implementation of the 'falsified medicines Directive'.

First figures (which will be shared with the Commission and the MS) from the UK, show that about 8,000 licenses of medicinal products, 1,000 sites and about 800-900 API manufacturers may be concerned. It is important to clarify jointly what acceptable enforcement practice is to enforce by 2 July 2013. UK and ES asked the Commission to regularly exchange information on new developments in particular as regards the listing of authorities.

➤ **2d) Joint action 'Facilitating collaboration among the Member States for the effective operation of the pharmacovigilance system in the EU' : state of play and next steps**

The Commission informed MS that the joint action on pharmacovigilance had been agreed as part of the 2013 Health Programme. The call for proposals would be formally launched towards the end of 2012. Workshops will be organised by the Executive Agency for Health and Consumers to present the administrative activities. The Committee members were encouraged to contact their coordinators for the health programme to confirm registration of their interest to participate in the joint action.

The Commission underlined that the information workshop to be organised in Luxembourg is extremely important and useful and suggested to Member States to monitor the website of the EAHC, <http://ec.europa.eu/eahc/index.html>. The joint action falls under the group 'call for proposals'.

➤ **2e) Presentation from France: new framework in France for regulating off-label use**

France informed the Committee that a law was voted in in 2011 to reinforce safety in the use of medicinal products. One of the axis covered concerned off-label use. A framework for off-label use is now possible (when there is no appropriate alternative), whereby the French national agency produces a recommendation for temporary use.

The health professional has the obligation to inform the patient of the off-label use, on the risks-benefits and that there is not an appropriate alternative medicine.

The French agency sets a temporary recommendation for use when deemed necessary. The temporary recommendation cannot be valid for more than 3 years. Industry is requested to provide all information on safety and efficacy data available before a temporary recommendation is issued. The MAH may make a binding agreement to submit a request for an extension of the indication within by a specified period of time. The recommendation is published on the website of the agency. By means of a contract between the company and the *Comité économique des produits de santé (Health products economic committee)*, the company may undertake to implement ways in order to limit off label use; financial penalties may be imposed by the *economic committee* if the company fails to meet its commitments.

The Commission asked FR to verify whether this new legislation had been formally notified to the Commission under 98/34 notification procedure.

Hungary informed of a similar system, put in place three years ago.

The Commission asked all MS to provide feedback on the following question:

"In your Member State, what is the approach to off-label use and what are its main characteristics? Please also specify if there is none."

Written replies should be sent to SANCO-Pharmaceuticals-D5@ec.europa.eu by 15/11/2012.

3. Interpretation of pharmaceutical legislation

➤ 3a) Recent judgements of the European Court of Justice

The Commission called the Committee's attention to some recent rulings of the European Court of Justice and the EFTA Court, especially:

- Case C-221/10P, judgment of 19 April 2012
- Case C-145/11, judgment of 19 July 2012
- Case C-308/11, judgment of 6 September 2012
- Case E-7/11, Efta Court ruling of 29 March 2012

4. A.O.B.

➤ AOB 1 – Health claims on botanicals: feedback from the expert group meeting on the discussion paper of the legal framework for botanicals with health claims

The Commission provided clarification to Member States' experts on the on-going reflection on health claims made on plant preparations, or plant extracts (so-called 'botanicals') in foods.

The Commission described the legal framework applicable to health claims made on foods pursuant to Regulation (EC) No 1924/2006 on nutrition and health claims and the process under Article 13 for establishing the list of permitted health claims. In this context, it recalled the decision of September 2010 to put Art. 13 health claims made on botanicals 'on hold' while it continued with the process that led to the adoption of Commission Regulation (EU) No 432/2012 establishing the above-mentioned list of permitted claims. It explained that claims on botanicals 'on hold' are listed on the website of the Commission and may continue to be used in accordance with the transition periods foreseen in Regulation (EC) No 1924/2006 and subject to the responsibility of operators until a decision on them is taken.

The Commission explained that it decided to begin a reflection on health claims on botanicals after many concerns were raised by a number of Member States and stakeholders. These related to a difference in the consideration given to evidence based on 'traditional use' for botanicals under the legislation on health claims and that on Traditional Herbal Medicinal Products (THMPs). In the context of its reflection, the Commission considered it appropriate to seek Member States' views on the subject and, to this purpose, it submitted a discussion paper to Member States in which the issue was described and two possible scenarios to proceed were identified. While the first scenario described a situation in which no change to the approach would be made, the second scenario described a situation in which the issue would be addressed in a comprehensive manner through a legislative action.

The discussion paper was also the subject of a meeting with Member States' experts on 17 September in which questions were asked and views were exchanged. The Commission asked Member States to provide comments in writing to the discussion paper and such comments are currently being collected and scrutinised.

Questions for clarification on the procedure followed were raised by the Committee but no comments on the substance of the on-going reflection were made.

➤ AOB 2 – E-health network and interoperability

The Commission provided a presentation on the eHealth Network set up by Article 14 of the Directive on patients' rights in cross-border healthcare 2011/24/EU. All 27 Member States'

national authorities responsible for eHealth joined the Network (represented at higher level of Secretaries of State and Director General). The Network aimed to achieve health, social and economic benefits of eHealth systems and interoperable applications. The Directive specifies some specific priorities for the Network, such as to work towards common measures for eIdentification for eHealth, interoperable ePrescriptions and access to patient summary data, methodologies for reuse of data for research. The Network members can however agree on further priorities.

The Commission highlighted that the Network decided to work towards interoperability between the European and national databases for medicinal products. It was pointed out that:

1. Interoperability and connectivity between the European and the national databases for medicinal products will bring quality and efficiency gains, strengthen the protection of public health and foster EU research.
2. ISO/CEN IDMP standards will provide an integrated and distributed data model for medicinal products and facilitate the development of well defined, harmonised EU reference terminologies
3. The use of the new ISO/CEN IDMP standards (Commission implementing Regulation 520/2012 on the performance of pharmacovigilance activities) could provide an important tool to enhance interoperability, data exchange and retrieval across EU and national databases
4. Open access to interoperable medicinal products databases for doctors and pharmacists could enhance unambiguous identification (and safe substitution) of medicinal products in the frame of ePrescriptions in cross-border setting

Interoperability of databases will be discussed in the 2nd eHealth network meeting which will take place on 7 November 2012 in Brussels, with the participation of EMA to present current streamlining work on IT systems under the pharmacovigilance legislation and a vision on how to contribute to the Network's objective on interoperability of databases. Vanessa Biname, Belgian Director General for post authorisation of medicines will present the views of the Member States on the issue.

The EC encouraged National Medicines Agencies to establish contact with their MS representatives in the eHealth Network and possibly discuss the approach prior to the eHealth Network meeting on 7 November.

➤ **AOB 3 – Medicinal products for human use which contain the active substance "methylphenidate"**

In the last three years the Commission has received several letters from a Swedish journalist regarding methylphenidate containing medicinal products.

Medicinal products containing methylphenidate are used as part of a comprehensive treatment programme for attention-deficit / hyperactivity disorder (ADHD) in children aged 6 and above. These products have only national marketing authorisations.

The Commission Decision C(2009)4242 of 27/05/2009 in the framework of Art 31 of Directive 2001/83/EC included binding amendments of the summary of the product characteristics and the package leaflet and the conditions of the marketing authorisations.

Member States have been informed by the Commission about issues raised in the above-mentioned correspondence, which included:

- Compliance of the Member States with the Commission Decision, particularly regarding long-term safety study in children,
- Off-label use, prescription of methylphenidate to adults in Sweden,
- Increasing prescription and sales figures in Sweden and related marketing strategies of the marketing authorisation holder.

In the Standing Committee on medicinal products for human use of 13 September 2011, Member States have been asked to check how the Commission decision has been implemented and provide that information on the occasion of the following Standing Committee meeting. At the date of this meeting of the Pharmaceutical Committee, the Commission had received responses from 8 Member States (AT, DK, DE, FR, IT, LV, SI, UK).

As the most recent letter of July 2012 received by the Commission relates to issues to be addressed at the Member State level, the Commission has forwarded it to the Member States authorities.

➤ **AOB 4 – Fees for Pharmacovigilance**

The Commission recalled that the Parliament amendment to enable the Commission to adopt fees for pharmacovigilance activities of EMA through a delegated act has been rejected by the Council. Consequently the Commission needs to prepare a proposal to Parliament and the Council based on a full impact assessment. Currently the Commission is working at the impact assessment in close collaboration with EMA. After the publication of a roadmap mid-2011, the Commission developed in collaboration with the EMA a concept paper for public consultation. The concept paper indicated a number of pharmacovigilance tasks for which the legislation allows EMA to collect fees from industry. The concept paper was issued for public consultation in June 2012 and the deadline for comments was mid-September. The Commission is now analysing responses which will be published on the Commission website. Work with EMA is in progress to refine the figures in order to be able to proceed with the Impact assessment, which will be followed by a formal proposal in 2013.

➤ **AOB 5 – Implementing directive on recognition of prescriptions**

On 22 October 2012 a proposed implementing Directive on the recognition of medical prescriptions issued in another Member States (“cross-border prescriptions”) was discussed in the cross-border Healthcare Committee with Member State delegates.

The proposal aims to improve the recognition of cross-border prescriptions by means of a non-exhaustive list of elements that cross-border prescriptions must contain. The scope of application for this list is limited to those prescriptions where a patient indicates the intended cross-border use at time of prescribing. The list covers items related to patient identification, prescription authentication, prescriber identification and prescribed product identification.

Of relevance to the Pharmaceutical Committee are provisions related to the identification of medicinal products. In particular the following wording is of interest, implying the mandatory inclusion of the INN, possibly complemented by brand name for specific cases:

“Non-exhaustive list of elements to be included in medical prescriptions [...]

Common name" as defined by Article 1 of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2011 on the Community code relating to medicinal products for human use.

The brand name if:

(a) the prescribed product is a biological medicinal product, as defined in point 3.2.1.1.(b) of Annex I (Part I) to Directive 2001/83; or

(b) the prescribing health professional deems it medically necessary; in that case the prescription shall shortly state the reasons justifying the use of the brand name”

Overall, Member State delegates expressed a favourable opinion on the proposed text. The Commission is planning present the text for the opinion of the Standing Committee on 28 November 2012. Member States would have to comply with the proposed implementing

Directive by 25 October 2013, which coincides with the overall transposition date of Directive 2011/24/EU.

➤ **AOB 6 – Exchange of correspondence with a MAH on medicinal product for leukemia**

The Commission informed the Committee about the request of withdrawal of the marketing authorisation of the product 'Mabcampath' by the MAH. This product is authorised for a certain type of leukaemia (B-cell chronic lymphocytic leukaemia). The company argued in a letter sent to the Commission in June 2012 that the withdrawal was necessary in view of the company's new application for a marketing authorisation for the same molecule with the indication for multiple sclerosis. The company stated that it does not want to keep double indications, to avoid confusion in the market. The Commission expressed its concern on the matter, especially in the interest of patients, and asked the CHMP to assess the consequences of the withdrawal of the marketing authorisation for the patients being treated with this medicinal product. The CHMP highlighted that the withdrawal of the product is considered not to be in the patients' interest. In September 2012 the Commission wrote to the company communicating that it is possible to have two separate MAs for the two indications and asked to reconsider the withdrawal of the MA, in the interest of the patients. A reply from the company has not been yet received. The Committee will be informed on the follow-up.

Some Member States congratulated the Commission on its intervention on this matter. Others reported that the withdrawal of product for economic reasons is more and more frequent and that they regularly endeavour to persuade companies not to withdraw products of vital importance for the patients.

➤ **AOB 7 – Audit from Canada and Japan in Bulgaria**

The Commission recalled that there is a mutual recognition on GMP between the EU, Canada and Japan. This has considerable advantages because the inspection reports are mutually accepted by the parties. The EU authorities do not have to go in these third countries for on-site inspections. In addition, the manufacturers do not have to test each batch coming from Canada and Japan. Not all MS are recognised at the moment. Canada will carry out audits of Romania and Bulgaria and Japan has decided to audit Bulgaria only. The Commission asked BU and RO to give their agreement to launch this audit as soon as possible, beginning of 2013, in order to allow this important agreement to be operational for the whole EU.

➤ **AOB 8 – High-level contact points on pharmaceutical policy in MS**

The Commission asked MS to provide feedback of relevant contact points on pharmaceutical dossiers and policy at Director-General level by 15 November 2012.

Next meeting of the Pharmaceutical Committee (human) is **tentatively** planned for **27 March 2013 (no travel arrangements should be made until final date is confirmed by the Commission in February 2013)**.