EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – authorisations, EMA

PHARM 600

PHARMACEUTICAL COMMITTEE
28 March 2012

Subject: **Hospital exemption for ATMPs (implementation of Art 28(2) of the ATMP regulation): update on feedback received by the Commission**

Agenda item 1a)

Member States were requested to provide information on the following points regarding Advanced Therapy Medicinal Products:

- How many products are legally on the market of each Member State?
- Which of the products legally on the market are prepared on a routine basis?
- Which of the products legally on the market fall under the hospital exemption?
- Criteria applied for products under the hospital exemption.

Annex 1: Responses from Member States on the Status of ATMPs in their territory (December 2011)

Country	How many products legally on the market	Prepared on a routine basis	Which fall under the hospital exemption	Criteria applied for HE
Belgium	In Belgium there are no ATMP's legally on the market at the moment. .		As for the products falling under the hospital exemption, 16 cell and tissue banks have been authorized to continue their activities for the products they are allowed to process at this moment. This authorization is temporary until further examination of the exact nature of their activities has been carried out (on the basis of a dossier introduced). The purpose of this examination is to identify products that clearly fall under the exemption and others which would not meet the requirements of the exemption.	Furthermore, the purpose of this examination is to define more specific requirements for the 'hospital exemption'
Croatia	There are no ATMP in the Croatian Medicinal Products Database for 2011, nor in pharmacotherapy manuals nor Croatian pharmacovigilance database. Currently, our Agency is performing PALC (Pre-accession linguistic checking of centrally authorised medicinal products) and we have received an application for the medicinal product ChondroCelect®, so with the EU accession we will definitely have an ATMP approved by EMA.			

Country	How many products legally on the market	Prepared on a routine basis	Which fall under the hospital exemption	Criteria applied for HE
Czech Republic	1) Gene Therapy Medicinal Products – none 2) Cell Therapy Medicinal Products: a) Clinical Trials - 3 medicinal products of anticancer immunotherapy (2 dendritic cells therapy, 1 tumor infiltrating lymphocytes) – will fall under centrally authorized products b) hospital use – 1 medicinal product – extracorporeal phototherapy in indication of graft versus host disease (GVHD), comment – this medicinal product should be re-evaluated, whether it falls under ATMPs (some EU states does not have it as ATMP, re-evaluation should occur in February CAT Meeting) – if considered as ATMP, will fall under scope of hospital exemption, prepared on non-routine basis 3) Tissue Engineered Medicinal Products: 2 medicinal products – autologous cultivated chondrocytes for treatment of chondral defects, these will fall under centrally authorized products and can be present on the market only to 30 December 2012 (for this transitional period under scope of article 49 Pharmaceutical Act 378/2007 Coll.)			- patient specific (tailored for concrete patient) - the overall numbers of the particular product prepared, the regularity/frequency of production, and the time period over which the preparation of that product has become established - progression of the rate of manufacturing
Denmark	In Denmark we have one product on the market under the hospital exemption: Genzymes MACI. They have informed us that they will apply for MA authorisation with EMA before the end of 2011.			
Estonia	There are no ATMP-s legally in the market in Estonia			

Country	How many products legally on the market	Prepared on a routine basis	Which fall under the hospital exemption	Criteria applied for HE
Finland	There are no ATM products legally on national markets in Finland. Marketing of the first centrally authorised product, ChondroCelect, is going to start soon in Finland. Still, it is known that Finnish university hospitals, orthopaedic clinics are using autologous chondrocyte preparations, for which patient biopsies are collected in Finland, exported for processing to a Swedish cell laboratory in Gothenburg and imported back to Finland for the clinical use. A license for tissue establishment is required for the procurement and exportation of the chondrocytes. The number of patients treated by using this optional method is approximately 10to20/year.	Production of the chondrocyte preparations in Sweden are prepared using a routine process, but the cells and serum in each case are from different donors.	None of the above-mentioned preparations are approved under the hospital exemption. Fimea has given a license for ATMP manufacturing under hospital exemption currently to one applicant producing an oncolytic virus product for cancer therapy and to one applicant producing six different tissue engineering products mainly for bone regeneration. Our interpretation is that the collaboration between the Finnish hospitals and the Swedish production site can continue until the end of the transitional period for TEPs (end of 2012) or until similar, centrally authorised product enters our markets.	The main criterion is an initial phase of drug development before entering into a clinical trial. The oncolytic viruses are used for single patients having different diagnosis of cancer and no option for conventional therapies. The treatment is offered individually in a private hospital under the responsibility of a treating physician. The tissue engineering products are prepared for individual patients in a non-routine basis for experimental treatment of facial defects. The aim of this experimental treatment is to find the most suitable combination of stem cells and biomaterial to be taken into the future clinical trial.

Country	How many products legally on the market	Prepared on a routine basis	Which fall under the hospital exemption	Criteria applied for HE
Germany	Presently, 17 products are legally on the market in Germany. They fall in the scope of the German transitional provisions, i.e. these products were legally on the market when the hospital exemption came into force in Germany (July 23, 2009). For these products an application for authorisation was made either until August 1, 2010 (gene therapy medicinal products and somatic cell therapy medicinal products) or until January 1, 2011 (tissue engineered products).	None. German authorities do not have any data how many ATMP prepared on a routine basis are legally on the market in Germany.		In addition to the criteria laid down in Article 3 Nr. 7 of Directive 2001/83/EC (Article 28 of Regulation (EC) Nr. 1394/2007), in Germany for hospital exemptions an authorisation of the product by the higher federal authority is necessary.
Greece	No Advanced Therapy Medicinal Product has been approved in Greece. Concerning new ATMPs, there is one clinical study in process (genetically modified somatic cells).			The implementation of the hospital exemption status is still ongoing. Consequently, at this time point, we cannot specify the products that will fall under this category.

Country	How many products legally on the market	Prepared on a routine basis	Which fall under the hospital exemption	Criteria applied for HE
Hungary	There are no ATMPs marketed in Hungary		No "hospital exemption" request have been received until now.	Their hospital exemption is defined at the level of an Act saying that the human medicines competent national authority has to licence the "manufacturing site" of such products in the in-patient institutions. This is valid since 1 January of 2011. There is an agreement on that some Good Manufacturing Practice rules, specially adjusted to this purpose (not the GMP 'per se'!) will apply, but no details have been issued yet.
Ireland	There is only one product under supplied hospital exemption (article 28) the MACI product which is currently going through the centralized procedure			

Country	How many products legally on the market	Prepared on a routine basis	Which fall under the hospital exemption	Criteria applied for HE
Italy	Three advanced therapy products have been granted the status of "legally on the market by the Italian Medicines Agency on November 25th, 2008. The three products are Hyalograft C autograft (cartilage), Hyalograft 3D autograft e Laserskin autograft (skin). The Applicant, Anika Therapeutics (former Fidia Advanced Biopolymers (FAB)) is planning to submit a file for authorization only for Hyalograft C auto graft in March 2012, hence before December 2012 that is the deadline for tissue engineering products.			Concerning the national legislation for "hospital exemption" a draft technical text is available; the verification of legal aspects is currently in progress.
Latvia	In Latvia till this day there were no such products on the market therefore no use in hospitals products are prepared on a routine basis or which fall under the hospital exemption.			

Country	How many products legally on the market	Prepared on a routine basis	Which fall under the hospital exemption	Criteria applied for HE
Lithuania	According to the statistic data of the State Medicine Control Agency ATMPs registered centrally have not been supplied to the Lithuanian market.		The Agency has not received any applications to get a permit for manufacture of ATMPs for individual patients yet.	The rules on manufacture of advanced therapy medicinal products for individual patients were approved by the Minister of Health of Lithuania in 2010. An entity is allowed to manufacture ATMPs on non-routine bases for individual patients if it possesses a permit issued by the State Medicine Control Agency at the Ministry of Health of the Republic of Lithuania. ATMPs must be prepared on non-routine bases, when different (modified) manufacturing processes are applied for every MP or when the same ATMP is manufactured with the frequency that may not be attributed to the routine manufacture. An entity is eligible to get a permit if it possesses a health care licence and meets manufacturing and control requirements approved by the Minister of Health.

Country	How many products legally on the market	Prepared on a routine basis	Which fall under the hospital exemption	Criteria applied for HE
Netherlands	The Inspectorate approved approximately 5 hospital exemptions.			In the Netherlands a request for a hospital exemption has to be submitted at the Health Care Inspectorate.
Portugal	At present Portugal has no ATMP products legally on the market			
Romania	in Romania there are no ATMP products legally on the market.			
Spain	We only have ChondroCelect, as it has been centrally authorised. We also have other products in hospital use, belonging to one of the following three categories: corneal limbai stein cells, chondrocytes and skin keratinocytes. These products are manufactured by a non-industrial process and have a "historical", consolidated use previous to the ATMP Regulation 1394/2007, and will be regulated under the hospital exemption clause by a project currently under development in Spain.	Only ChondroCelet	For the moment, we only envision to regulate under the hospital exemption the non-industrially produced ATMPs that have been "historically" used in Spain, as described above.	In the future, once that the project of regulation in Spain is approved, we expect other products could apply for authorisation under the HE.

Country	How many products legally on the market	Prepared on a routine basis	Which fall under the hospital exemption	Criteria applied for HE
Sweden	In Sweden one can identify two types of products that can be considered legally on the market although no formal decision has been made: These products are: Mesenchymal stem cells for Graft versus Host disease and a Chondrocyte implantation product.	The Chondrocyte implantation product can be considered to be produced on a routine basis.		From May 1st the manufacturers need to apply for a manufacturing licence for "hospital exemption products". Provisions from the Medical Products Agency sets up the specific requirements for the "hospital exemption products". So far (Dec. 2011) only one manufacturer has applied for a manufacturing licence for a tissue engineered product.
United Kingdom	18 authorisations to manufacture and supply unlicensed ATMPs under the terms of the exemption provided by Article 5(1) of Directive 2001/83/EC (the UK's Specials scheme) have been granted.		To date, the UK has not issued any authorisations for ATMPs to be made under the hospital exemption.	The UK has developed guidance for arrangements under the hospital exemption scheme which we notified to the Commission.

Countries which have not sent any information on the status of ATMPs on their territory:
Austria, Bulgaria, Cyprus, France, Luxembourg, Malta, Poland, Slovakia, Slovenia