Wyss Zürich Regulatory Affairs Seminar

Hospital Exemption & Compassionate Use

EU Framework

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Introduction

- What are ATMPs?
  - Regulation (EC) No. 1394/2007 of 13 November 2007 on **a**dvanced **t**herapy **m**edicinal **p**roducts and amending Directive 2001/83/EC and Regulation (EC) No. 726/2004 (the "ATMP Regulation")
  - ATMPs: gene therapy medicinal products, tissue engineered products and somatic cell therapy medicinal products
- Central marketing authorisation (MA) mandatory for all ATMPs
- Exception to MA: hospital exemption ("HE")

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Hospital Exemption - Definition & Conditions

- Article 3(7) of Directive 2001/83/EC of 6 November 2001 on the Community Code relating to medicinal products for human use

  "Any advanced therapy medicinal product, as defined in Regulation (EC) No 1394/2007, which is prepared on a non-routine basis according to specific quality standards, and used within the same Member State in a hospital under the exclusive professional responsibility of a medical practitioner, in order to comply with an individual medical prescription for a custom-made product for an individual patient.

  Manufacturing of these products shall be authorised by the competent authority of the Member State. Member States shall ensure that national traceability and pharmacovigilance requirements as well as the specific quality standards referred to in this paragraph are equivalent to those provided for at Community level in respect of advanced therapy medicinal products for which authorisation is required pursuant to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency."

- Introduced by Article 28(2) of ATMP Regulation

Hospital Exemption - Definition & Conditions

- Conditions
  - an **advanced therapy medicinal product**, as defined in the ATMP Regulation
  - prepared on a **non-routine basis**
  - according to **specific quality standards**
  - used **within the same MS**
  - **in a hospital**
  - **under the exclusive professional responsibility** of a medical practitioner
  - which complies with an **individual medical prescription** for a custom-made product for an individual patient
- If satisfied, no MA required

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Hospital Exemption – Implementation by MS

- Manufacture of ATMPs under HE **must be authorised by competent authority of MS** concerned

- MS should ensure that **national traceability and pharmacovigilance requirements** as well as **specific quality standards** are **equivalent** to those provided for at EU level in respect of ATMPs for which authorisation is required pursuant to Regulation (EC) No. 726/2004

- Implementation by MS

- Example : Belgium

  → Article *6quater*, §3, indent 1, 6/1 of Law on Medicinal Products of 25 March 1964 and Royal Decree of 8 January 2017 on the HE for ATMPs (entry into force: 1 September 2017)

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Hospital Exemption – Discussion

- MS apply HE in different manners
- Similarities ✓ vs. discrepancies ✗
  - an **advanced therapy medicinal product**, as defined in the ATMP Regulation ✓
  - prepared on a **non-routine basis** ✗
  - according to **specific quality standards** ✗
  - used **within the same MS** ✓
  - **in a hospital** ✗
  - **under the exclusive professional responsibility** of a medical practitioner ✗
  - which complies with an **individual medical prescription** for a custom-made product for an individual patient ✗

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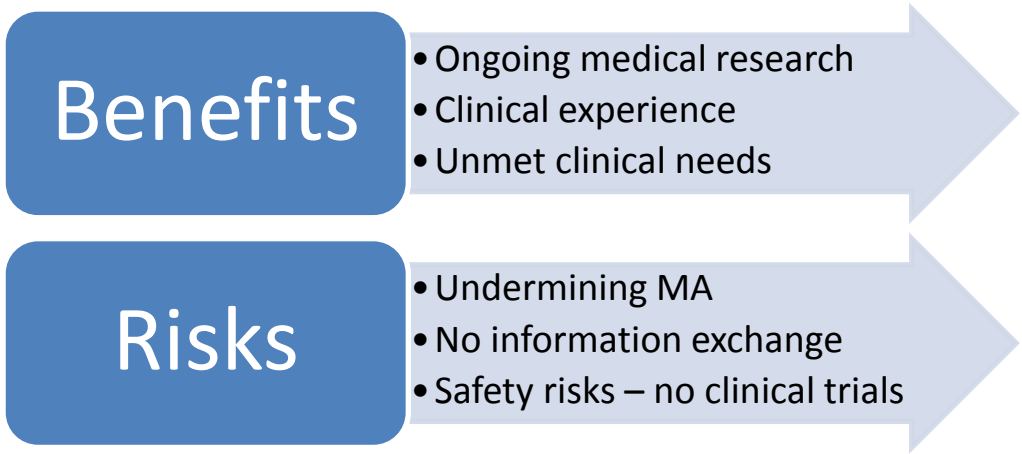
Hospital Exemption – Discussion

Countries	Non-routine preparation	Scope and purpose
BELGIUM	No definition; case-by-case assessment Depends on: number of patients treated, number of batches released & frequency of manufacturing	Exceptional regime HE will be refused if : - patient can participate in ongoing trial; - compassionate use program or medical need program exists; - MA or HE already granted; - ATMP has not been used in humans before (no first-in-men trials)
THE NETHERLANDS	Definition Maximum 10 treatments during maximum 1 year 5 patients per order	Small scale clinical use as experimental treatment Only for patients not eligible for clinical trials
THE UNITED KINGDOM	No definition; case-by-case assessment Depends on: scale and frequency of the preparation of the specific ATMP	Supply of unlicensed ATMPs at small scale and with developmental nature of activity

Hospital Exemption - Discussion

- Commission public consultation in 2012 & EMA workshop in 2016
- Need for harmonisation, transparency and better clinical data collection



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Compassionate Use (CU) – Definition & Conditions

- Article 83 of Regulation No. 726/2004 of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

  "1. By way of exemption from Article 6 of Directive 2001/83/EC Member States may make a medicinal product for human use belonging to the categories referred to in Article 3(1) and (2) of this Regulation available for compassionate use.

  2. For the purposes of this Article, 'compassionate use' shall mean making a medicinal product belonging to the categories referred to in Article 3(1) and (2) available for compassionate reasons to a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who can not be treated satisfactorily by an authorised medicinal product. The medicinal product concerned must either be the subject of an application for a marketing authorisation in accordance with Article 6 of this Regulation or must be undergoing clinical trials.

  […]."

Compassionate Use – Definition & Conditions

- making a **medicinal product that can qualify for a central MA available for compassionate reasons**
- to a **group of patients**
- with **a chronically or seriously debilitating disease** or **whose disease is considered to be life-threatening**
- and who **cannot be treated satisfactorily by an authorised medicinal product**

Compassionate Use – Definition & Conditions

- Medicinal product must be subject of application for central MA

OR

- Medicinal product must be undergoing clinical trials

+

- Patients taking part in CUP should have access to new medicinal product during period between authorisation and placing on market

Compassionate Use - Definition & Conditions

- **Facultative opinion** of Committee for Medicinal Products for Human Use (CHMP)
  - The CHMP, after consulting the manufacturer or the applicant, may adopt opinions on the conditions for use, the conditions for distribution and the patients targeted. The opinions shall be updated on a regular basis.
- CHMP Guideline on compassionate use of medicinal products pursuant to Article 83 of Regulation No. 726/2004

Compassionate Use - Definition & Conditions

- Comparison between early access tools

	CUP	HE	Named Patient Use
MA?	Not yet (<-> MNP)	No	No
Patients	Group	Individual	Individual
Medicinal products	Any under Regulation (EC) No. 726/2004	ATMPs	Any
Disease	Chronically or seriously debilitating or life threatening disease	Any	Special needs

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Compassionate Use – Discussion

- **Positive aspects:**
  - Facilitate access to new medicines for patients suffering from life threatening disorders or diseases
  - Clinical experience

- **Negative aspects:**
  - Diverging and complex national legislations

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Conclusion

- HE and CU are two different mechanisms with different objectives
- They are both useful and could be beneficial to both patients and pharmaceutical companies
- Especially for HE, more uniformity needed across EU to tackle fragmentation

ANY QUESTIONS?