Introduction to the European Medicines Agency

EFA training for patient experts on allergy, asthma and COPD on getting involved with the EMA, 18 February 2014

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Head of patients and healthcare professionals department
Key Principles

• The EU is a Single Market for pharmaceuticals
  ~ 0.5 billion people

• In order to market a medicinal product in the EU, a company
  needs a Marketing Authorisation

• There are different ways (‘Procedures’) for a company to
  obtain a Marketing Authorisation

• The main scientific principle used in the evaluation of
  medicines is the benefit/risk balance, based on quality,
  efficacy and safety aspects

• Economic considerations are excluded from the assessment
A European agency and medicines system: Why?

- Protect and promote public and animal health
- Pooling of best scientific expertise from across Europe for evaluation of medicines
- Facilitate availability of new medicines to patients
- Same product information to patients and healthcare professionals
- Single market for pharmaceuticals
- Benefits R&D industry
- Platform for discussion of public health issues
A European agency and medicines system: How?

‘One system, two routes for approval’

- **Centralised European route** - attracts nearly all innovative medicines

- **Mutual recognition + decentralised national routes** - mostly generics and some new indications for existing products
European Medicines Agency: focal point of the centralised procedure

- 1 application
- 1 evaluation
- 1 authorisation for all EU
- 1 invented name
- 1 product information (SPC, Labelling, PL)
- All EU languages

The EMA is not responsible for pricing or reimbursement

Marketing Authorisation is granted by the European Commission
The Agency is responsible for:

- The **evaluation of marketing authorisation** for **human and veterinary** applications submitted by pharmaceutical companies
- The coordination of European **pharmacovigilance** (supervision of the medicines on the market)
- The provision of **scientific advice** on the development of medicines
- The evaluation of applications for **orphan** designation in EU
- The evaluation of **paediatric investigation** plans (or waivers)
- The evaluation of **arbitration** and **referral** procedures
- The provision of good quality and independent **information** on the medicines it evaluates to patients and health
- The coordination of Member States’ **inspections** (**GMP, GCP, GLP**)
Eligibility: “Mandatory Scope”

<table>
<thead>
<tr>
<th>ADVANCED THERAPY MEDICINAL PRODUCTS:</th>
<th>Gene therapy products</th>
<th>Somatic Cell therapy products</th>
<th>Tissue engineered products</th>
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<tbody>
<tr>
<td>Auto-immune diseases and</td>
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<td>Other immune dysfunctions</td>
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<td>AIDS</td>
<td>Recombinant DNA technology</td>
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<td>Cancer</td>
<td>Controlled gene expression</td>
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<td>Neurodegenerative disorders</td>
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<td>Viral diseases</td>
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<td>Orphan medicines</td>
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Since Jan 95

Since May 08

Since Dec 08
Eligibility “Optional Scope”

- New Active Substances
- Significant Innovation (Therapeutic, &/or Scientific, &/or Technical)
- Interest of Patients at Community Level

Art 3(3) Generic of a product authorised via EMA

The centralised procedure attracts most innovative medicines. Decentralised and MRP mainly do generics and new indications for existing products
A networking Agency

Member States have pooled their sovereignty for authorisation of medicines

• The Agency is designed to coordinate the existing scientific resources of Member States

• It is not intended to replace national authorities, but to be a partner in the system

• It is a networking agency, providing an interface between all partners

• All parties linked by an IT network (EudraNet)
Our partners in Europe

- More than 45 national competent authorities dealing with human and veterinary medicines and access to a network of more than 2,500 European experts
- EU institutions: European Commission, European Parliament, other EU agencies (EMCDDA, EFSA, ECDC, Translations Centre)
- European Pharmacopoeia (Council of Europe)
- Medicines Control Laboratories Network
A dynamic and constantly changing Agency

Taking on new tasks and responsibilities

- 2001: Orphan medicines (+ new committee)
- 2005 & 2008: Extended mandatory scope
- 2005: ‘Biosimilar’ and generic medicines
- 2005: Herbal medicines (+ new committee)
- 2007: Paediatric medicines (+ new committee)
- 2008/2009: Advanced therapies (+ new committee)
- 2012: Pharmacovigilance (+ new committee)
- 2013: Falsified medicines legislation
Development of Medicines
Drug Development Overview

Discovery/Manufacture

Non-clinical

Clinical

Human Pharmacology

Therapeutic Exploratory

Therapeutic Confirmatory

Therapeutic Use

(“Phase I”) (”Phase II”) (”Phase III”) (”Phase IV”)

Scientific Advice

Paediatric Investigation Plan

Orphan Drug Designation

Pharmacovigilance Risk Management

Marketing Authorisation Application

Maintenance Procedures

Extension Application
EMA Scientific Committees and working parties
**CHMP**
(Committee for Human Medicinal Products)
Members: 1 per Member State + 1 alternate + 5 co-opted Members
Non-voting members: ICE/NO; Chair: T. Salmonson – Vice Chair: P. Demolis

**PRAC**
(Pharmacovigilance Risk Assessment Committee)
Members: 1 per Member State + 3 additional Members + 1 Patient Organisation + 1 Healthcare Professionals Organisation
Non-voting Members: ICE/NO; Chair: J. Munro Raine – Vice Chair: Almath Spooner

**COMP**
(Committee for Orphan Medicinal Products)
Members: 1 per Member State + 3 additional Members + 3 Patient Organisations
Non-voting Members: ICE/NO; Chair: B. Sepodes – Vice Chair: L. Greene

**HMPC**
(Committee for Herbal Medicinal Products)
Members: 1 per Member State + 1 alternate + max. 5 Co-Opted Members
Non-voting members: ICE/NO/possible intl. org.; Chair: W. Knöss - Vice-Chair: M. Delbò

**PDCO**
(Paediatric Committee)
Members: 5 CHMP, 1 per other Member States
2 HCP, 3 Patient Organisations + 1 Alternate per member
Non-voting members: ICE/NO; Chair: D. Mentzer - Vice-Chair: K. Norga

**CAT**
(Committee for Advanced Therapies)
Members: 5 CHMP, 1 per other Member States
2 clinicians appointed by EC + 2 alternates, 2 Patient Organisations appointed by EC
Non-voting members: ICE/NO; Chair: C. Schneider - Vice-Chair: P. Salmikangas
EMA-EU Network

28 EEA Member States + 4,500 European experts

EU institutions: Commission - Parliament

Committee for Human Medicinal Products (CHMP)

Paediatric Committee (PDCO)

Committee for Herbal Medicinal Products (HMPC)

Management Board

EMA Secretariat

Pharmacovigilance Risk Assessment Committee (PRAC)

Committee for Veterinary Medicinal Products (CVMP)

Committee for Orphan Medicinal Products (COMP)

Committee for Advanced Therapies (CAT)
Scientific Committee CHMP

- Formulate scientific opinions to the EC
  . on medicinal products for human use (CAP)
  . on arbitration/referral procedures

- Scientific Advice

- EU scientific and regulatory guidelines

- Chair (Dr. Tomas Salmonson)
- 1 member (+ 1 alternate) per MS
- 1 member (+ 1 alternate) NO - IS
- 5 co-opted members
Committee Plenary Meeting
Scientific Advice
Scientific Advice

- Advice to development
- Agreement on future strategy (when no guideline)
- Not a pre-evaluation
- Fee-related activity (fee reduction for orphan products)
- Working Party of the CHMP

[Diagram showing CHMP, COMP, SAWP, CAT, PDCO, PRAC, WPs, Experts, SAGs]
Paediatric Development
Paediatric Initiative - Objectives

**Improve the health of children**

- Increase high quality, ethical research into medicines for children
- Increase availability of authorised medicines for children
- Increase information on medicines

**Achieve the above**

- Without unnecessary studies in children
- Without delaying authorisation for adults
Paediatric Initiative

- Obligation to study products in children
- Paediatric Investigation Plan (PIP) or Waivers for products for new marketing authorisation, extension of indications, new pharmaceutical forms
- Rewards in the form of extension of supplementary patent certificate
- PIP/Waivers requests to be submitted by end of human PK studies
- Incentives for old products of paediatric interest
- Coordination of a Network of EU paediatric networks
- Paediatric Committee (PDCO)
Integration into Development Plan

Phase 1

Phase 2

Phase 3

Post approval

MAA

PIP Amendments

PIP Agreement

Compliance/Deferral/Waiver
Orphan Drugs
Orphan Medicinal Products

Criteria:

– Life threatening or debilitating condition
– Epidemiological – Prevalence <5/10,000
– No satisfactory methods exist or significant benefit over authorised products/methods

Or
– Economical: unlikely to generate sufficient return on investment

• Committee for Orphan Medicinal Products (COMP) 2000

IMPORTANT:

• Designation for Orphan status (not Marketing Authorisation)
• Confirmation of Orphan status before Marketing Authorisation
Advanced Medicines
Advanced Therapies Medicinal Products (ATMPs)

- Gene therapy products
- Somatic Cell therapy products
- Tissue engineered products
Scientific Committee CAT

- Formulate draft opinion on Advanced Therapy
- Medicinal Products for final approval by CHMP
- ATMP classification (gene, cell, tissue)
- ATMP quality and clinical data certification

- Chair (Dr. C. Schneider)
- 5 CHMP members (with alternates)
- 1 member (+ 1 alternate) per MS (not represented by CHMP member)
- 1 member (+ 1 alternate) NO - IS
- 2 members (+ 2 alternates) patients organisations
- 2 members (+ 2 alternates) healthcare professionals
Monitoring and supervision of medicines
Pharmacovigilance and Risk Management

Pharmacovigilance

⇒ the science and activities relating to the detection, understanding and prevention of adverse drug reactions or any other drug-related problems

Risk Management System

⇒ a set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicinal products, including the assessment of the effectiveness of those interventions
Pharmacovigilance and Risk Management

What we know at the end of the clinical trial programme...

What we don’t know!
- What happens when the medicinal product is used in normal practice?
- What is its adverse event profile?
Pharmacovigilance and Risk Management
Data Collection and Management

Patient with ADR

Reporting physician

Original Report

MAH OR

NCA

Patient Safety Monitoring Schemes?

EudraVigilance Human

ICSR
Pharmacovigilance and Risk Management; Signal Detection and Data Analysis

Signal detection → EU Assessors → MAH

Assessment of the signal

Other MS

PRAC

CHMP

Propose appropriate regulatory action
Scientific Committee
PRAC

- Assess aspects of risk management (detection, assessment, minimisation and communication of risk of adverse reactions)
- PASS and pharmacovigilance audit
- Recommendations on questions on PhV activities

- Chair (Dr. June Raine)
- 1 member (+ 1 alternate) per MS
- 1 member (+ 1 alternate) NO - IS
- 6 experts nominated by EC
- 1 member (+ 1 alternate) healthcare professionals
- 1 member (+ 1 alternate) patients organisations
How does the PRAC Work?

CMDh -> PRAC

PRAC -> CHMP

Recommendations

EU Member States

European Commission
Transparency and communication
What information does EMA provide?

- EMA website – main channel of communication
- Different information at different stages of life-cycle of medicines
- Information on medicines authorised via EMA
- Safety communication for all medicines authorised in the EU
- Agendas and minutes of all scientific committees
EMA website: www.ema.europa.eu
Pre-authorisation (1): orphans and paediatrics

• Information on orphan designation
• Information on review of orphan designation at the time of marketing authorisation.
• Opinions and decisions on paediatric investigation plans.
• Information available in English.
Public summary of opinion on orphan designation on EMA website

EU/3/12/1055

Orphan designation

On 10 October 2012, orphan designation (EU/3/12/1055) was granted by the European Commission to Topotarget A/S, Denmark, for belinostat for the treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic / disseminated).

What is peripheral T-cell lymphoma?

Peripheral T-cell lymphoma is a cancer of the lymphatic system, a network of vessels that transport fluid from tissues through the lymph nodes and into the bloodstream. In peripheral T-cell lymphoma there is uncontrolled growth of T lymphocytes (T cells), a type of white blood cell found in the lymphatic system. Different types of peripheral T-cell lymphoma have been identified and categorised as nodal, other extranodal and leukaemic / disseminated.

The symptoms of the disease vary according to the type of lymphoma, but the first sign is usually a lump in the neck, under the arm or in the groin area, which is caused by an enlarged lymph node. The lymphoma may also affect other organs in the body such as the bone marrow, liver and the skin.

Peripheral T-cell lymphoma is a long-term debilitating and life-threatening condition because in most cases the disease does not respond well to therapy and comes back within one year after initial treatment and is associated with poor overall survival.

What is the estimated number of patients affected by the condition?

Sponsor’s contact details:
Topotarget A/S
Friebjergvej 3
DK-2100 Copenhagen
Denmark
Telephone: +45 39 17 6392
Telefax: +45 39 17 94 92
E-mail: enquiries@topotarget.com

Patients’ organisations
For contact details of patients’ organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases which includes a directory of patients’ organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.
Pre-authorisation (2): clinical trials (CT)

- Information on CT – the EU Clinical Trials Register website: [https://www.clinicaltrialsregister.eu/](https://www.clinicaltrialsregister.eu/)
- The Register allows to search for information on CT in the EU Member States.
- Information on:
  - trial design;
  - sponsor;
  - investigated product and therapeutic area;
  - the status of the trial.
EU Clinical Trials Register:
https://www.clinicaltrialsregister.eu/
Authorisation/ Licensing

- EPAR summary – in all EU languages
- Assessment report (scientific discussion)
- Product Information – in all EU languages:
  - Summary of Product Characteristics;
  - Package leaflet;
  - Labelling.

- Risk Management Plan (soon!)
EPAR summary on the EMA website

This is a summary of the European public assessment report (EPAR) for Betaferon. It explains how the Committee for Medicinal Products for Human Use (CHIMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Betaferon.

What is Betaferon?
Betaferon is a powder and solvent that are made into a solution for injection. It contains 250 micrograms (8 million international units - MIU) per millilitre of the active substance interferon beta-1b.

What is Betaferon used for?
How is Betaferon used?
How does Betaferon work?
How has Betaferon been studied?
What benefit has Betaferon shown during the studies?
Post-authorisation

- New therapeutic indications;
- New contraindications;
- Other variations.

- Update of the EPAR summary;
- Update of Product information;
- Publication of relevant assessment report.
Communication about safety referrals

Procedure

Start of safety referral by PRAC

PRAC recommendation

CHMP/CMD(h)
Communication about safety referrals

- 'EMA public health communication'
- Single piece of information (integrates PR+Q&A into one document), composed of three sections:
  - Summary of the issue (for press and general public)
  - Information to patients
  - Information to healthcare professionals
- Explain any divergence with PRAC recommendation if applicable
- Syndicated to press, patients and healthcare professionals contacts

Example: Tredaptive
Information on adverse drug reactions: http://www.adrreports.eu/

- This EU database displays information on ‘suspected adverse drug reactions’ for medicines authorised in the EU.
- A phased development: so far, only for medicines approved via centralised procedure.
- The reports are constantly updated.
European database of suspected adverse drug reaction reports: [http://www.adrreports.eu/](http://www.adrreports.eu/)
This newsletter is addressed primarily to organisations representing patients, consumers and healthcare professionals. It provides a summary of key information relating to medicines for human use published during the previous month by the European Medicines Agency. Information is selected based on recommendations from consulted patients, consumers and healthcare professionals, and does not necessarily cover all relevant information published by the Agency.

To receive an e-mail alert when each new issue of the newsletter is published, send a request to: HMDNewsletter@ema.europa.eu

Information on medicines

Antivirals/anti-infectives

Negative CHMP opinions on new medicines
- Delamanid (delamanid)
   Intended for the treatment of multidrug-resistant tuberculosis
Conclusions

Information on medicines is a key factor of the safe and rational use of medicines. EMA provides understandable, up-to-date, evidence-based information on medicines.

Patients play a key role in the evaluation of medicines and the provision of information by the EMA.
**Acronyms**

- **ADR** = Adverse Reaction
- **AR** = Assessment Report
- **CHMP** = Committee for Medicinal Products for Human Use
- **CD** = Commission Decision
- **D1, etc** = Day 1 (procedural timeline)
- **GCP** = Good Clinical Practice
- **GLP** = Good Laboratory Practice
- **GMP** = Good Manufacturing Practice
- **LoQ** = List of Questions
- **LoOIs** = List of Outstanding Issues
- **MAH** = Marketing Authorisation Holder
- **MS** = Member State
- **OE** = Oral explanation
- **PASS** = Post Authorisation Safety Study
- **PI** = product information
- **PRAC** = Pharmacovigilance Risk Assessment Committee
- **PSUR** = Periodic Safety Update Report
- **RMP** = Risk Management Plan
- **SmPC** = Summary of Product Characteristics
Any Questions?

Thank you for your attention