EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Session 3: Post-approval pharmacogenomics: impact on Risk Management

Workshop on Pharmacogenomics: from Science to clinical care
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An agency of the European Union

Introduction

Pharmacogenomics (PGx) is defined as the study of variations of DNA and RNA characteristics as related to drug response.

- Pharmacogenomics (and pharmacogenetics*) have the potential to improve the discovery, development and use of medicines.
- Where possible, the SmPC should inform on important inter-individual variability in drug pharmacokinetics or response, and, on which extent, such variability can have a genetic basis.
- Therefore, when relevant, genetic and genomic information should be mentioned in the SmPC.

** Pharmacogenetics (PGt) is a subset of pharmacogenomics (PGx) and is defined as the study of variations in DNA sequence as related to drug response.*

Overview of Pharmacogenomics information in SmPC

4.1 Therapeutic indications	If the product's indication depends on a particular genotype or the expression of a gene or a particular phenotype, this should be stated in the indication.
4.2 Posology and method of administration	Where necessary, dosage adjustments in patients with a particular genotype should be stated (with cross-reference to other relevant sections for further detail as appropriate).
4.3 Contraindications	Linked to a particular genotype
4.4 Special warnings and precautions for use	Subjects or patients with a specific genotype or phenotype might either not respond to the treatment or be at risk of a pronounced pharmacodynamic effect or adverse reaction. These may arise because of non-functioning enzyme alleles, alternative metabolic pathways (governed by specific alleles), or transporter deficiencies. Such situations should be clearly described if known.
4.5 Interaction with other medicinal products	If interactions with other medicinal products depend on polymorphisms of metabolising enzymes or certain genotypes, this should be stated.
4.8 Undesirable effects	This section may include information on any clinically relevant differences specifically observed in patients with a specific genotype
4.9 Overdose	If applicable, counteractive measures based on genetic factors should be described.
5.1 Pharmacodynamic properties	Any relevant pharmacogenetic information from clinical studies may be mentioned here. This should include any data showing a difference in benefit or risk depending on a particular genotype or phenotype.
5.2 Pharmacokinetic properties	Variations with respect to polymorphic metabolism should be described, if clinically relevant, in quantitative terms (with cross-reference to 4.2 when applicable).

Frequently Asked Questions

1. Should the SmPC include information on pharmacogenomic testing?

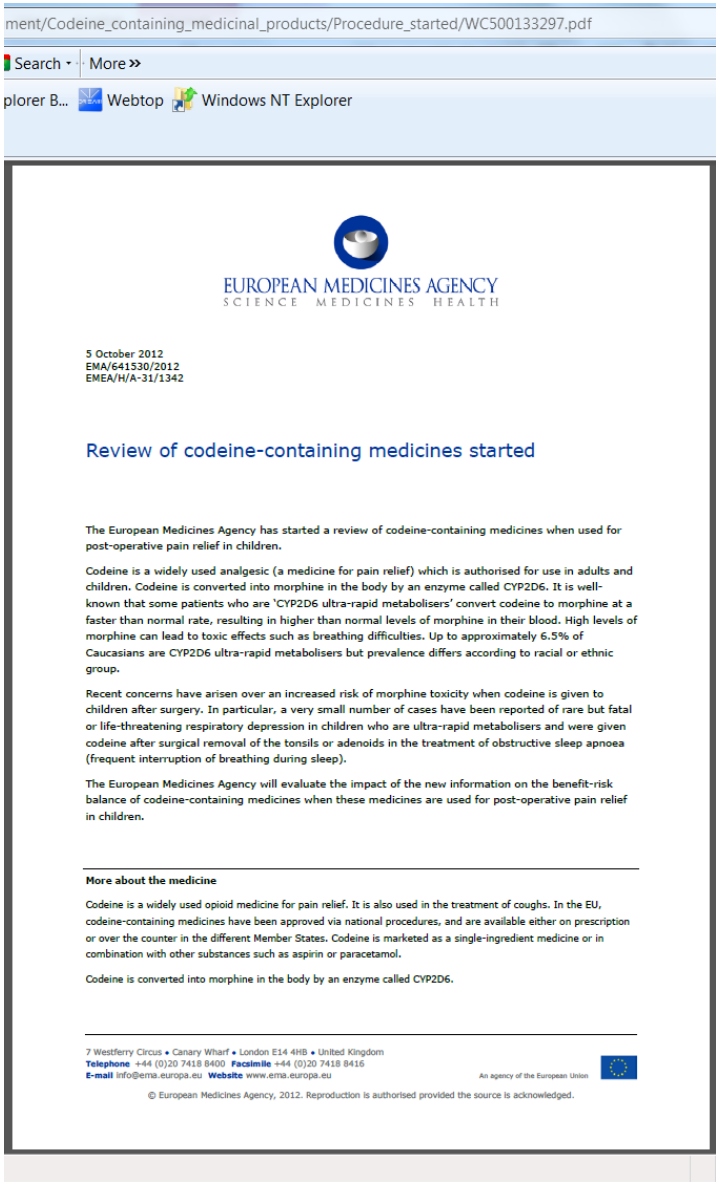
2. Should the SmPC inform on the frequency of a genotype or a phenotype?

Kalydeco Risk Management Plan (extract from EPAR)

Kalydeco is indicated for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have a G551D mutation in the CFTR gene

Safety issue	Agreed pharmacovigilance activities
Off label use in children less than 6 years old of age and in patients with other mutations (non-G551D CFTR gating mutations and non-class III mutations)	Ongoing surveillance through routine pharmacovigilance practices Long-term safety study: An Observational Study to Evaluate the Long-Term Safety of Ivacaftor in Patients With Cystic Fibrosis Study 110 Study 111

Study VX11-770-110: Phase 3 Study in subjects with cystic fibrosis who have the R117H-CFTR mutation
Study 111: Phase 3 Study In subjects with cystic fibrosis who have a non-g551d CFTR gating mutation



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5 October 2012
EMA/641530/2012
EMEA/H/A-31/1342

Review of codeine-containing medicines started

The European Medicines Agency has started a review of codeine-containing medicines when used for post-operative pain relief in children.

Codeine is a widely used analgesic (a medicine for pain relief) which is authorised for use in adults and children. Codeine is converted into morphine in the body by an enzyme called CYP2D6. It is well-known that some patients who are 'CYP2D6 ultra-rapid metabolisers' convert codeine to morphine at a faster than normal rate, resulting in higher than normal levels of morphine in their blood. High levels of morphine can lead to toxic effects such as breathing difficulties. Up to approximately 6.5% of Caucasians are CYP2D6 ultra-rapid metabolisers but prevalence differs according to racial or ethnic group.

Recent concerns have arisen over an increased risk of morphine toxicity when codeine is given to children after surgery. In particular, a very small number of cases have been reported of rare but fatal or life-threatening respiratory depression in children who are ultra-rapid metabolisers and were given codeine after surgical removal of the tonsils or adenoids in the treatment of obstructive sleep apnoea (frequent interruption of breathing during sleep).

The European Medicines Agency will evaluate the impact of the new information on the benefit-risk balance of codeine-containing medicines when these medicines are used for post-operative pain relief in children.

More about the medicine

Codeine is a widely used opioid medicine for pain relief. It is also used in the treatment of coughs. In the EU, codeine-containing medicines have been approved via national procedures, and are available either on prescription or over the counter in the different Member States. Codeine is marketed as a single-ingredient medicine or in combination with other substances such as aspirin or paracetamol.

Codeine is converted into morphine in the body by an enzyme called CYP2D6.

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EMA SmPC webpages

- To promote compliance with SmPC guideline
- EudraSmPC webpage
  - Training presentations
    - Introduction to SmPC, guideline principles/section
    - Paediatrics, Older people, Pharmacogenomics
  - Useful links (*e.g.* guidelines)
  - System of Query and Answer (regulatory network)
- Public interface of the SmPC webpage on Agency's website by the end of 2012.

index - Windows Internet Explorer

http://eudrasmpc.eudra.org/

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index

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Welcome to EudraSmPC

This website helps you review SmPCs (Summary of Product Characteristics) – in line with the SmPC Guideline. You can get advice from the SmPC Advisory Group by submitting a query form or by searching the database. And you can access training presentations and useful links.

Key Documents

- SmPC Guideline
- Guideline on excipients
- Annex II advanced therapy regulation

Scientific guidelines with SmPC recommendations:

- - Quality and Biologicals
- - Non-clinical
- - Clinical efficacy and safety

Links

- EudraLex
- QRD
- Herbal Medicinal Products
- Centrally authorised products
- European Medicines Agency
- HMA

SmPC Advisory Group

- Mandate and Rules of Procedure
- List of Members
- CHMP SmPC Implementation Plan

Training Presentations

Introduction to SmPC Guideline			
Presentation User Guide	1. Name of medicinal product	2. Qualitative and quantitative composition	3. Pharmaceutical form
4.1 Therapeutic indications	4.2 Posology & method of administration	4.3 Contraindications	4.4 Special warnings & precautions for use
4.5 Interactions	4.6 Fertility, Pregnancy and Lactation	4.7 Effects on ability to drive and use machines	4.8 Undesirable effects
4.9 Overdose	5.1 Pharmacodynamic Properties	5.2 Pharmacokinetic Properties	5.3 Preclinical safety data
6. Pharmaceutical particulars	Section 7-12	Paediatrics	Pharmacogenomics

SmPC Advisory Group Query and Search

Do you have a specific SmPC related query?

We will be pleased to advise you, within a short timeframe, on all matters relating to the SmPC Guideline (e.g. on the application of the guideline for a specific SmPC)

click here

Search database of previous advice

click here

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