EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Overview of medicinal products with pharmacogenomics information in the SmPC

Multi-stakeholder workshop on Pharmacogenomics

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The contributors do not have any conflict of interests

Content

Introduction | Background

Genomic variation may be an important additional source of inter-individual variability in both the beneficial and adverse effects of medicinal products. Therefore, when relevant, genetic and genomic information should be mentioned in the Summary of Product Characteristics (SmPC).

Continuous work by EMA and European medicines regulatory network (EMRN):

- **Scientific guidelines** on pharmacogenomics to help medicine developers prepare marketing authorisation applications for human medicines
- **SmPC guideline** principles recommendations for presenting pharmacogenomics information in the **SmPC sections**

Introduction | Structure of the SmPC

1. Name of the medicinal product
2. Qualitative and quantitative composition
3. Pharmaceutical form
4. Clinical particulars
   - 4.1 Therapeutic indications
   - 4.2 Posology and method of administration
   - 4.3 Contraindications
   - 4.4 Special warnings and precautions for use
   - 4.5 Interactions with other medicinal products and other forms of interaction
   - 4.6 Pregnancy and lactation
   - 4.7 Effects on ability to drive and use machines
   - 4.8 Undesirable effects
   - 4.9 Overdose
5. Pharmacological properties
   - 5.1 Pharmacodynamic properties
   - 5.2 Pharmacokinetic properties
   - 5.3 Preclinical safety data
6. Pharmaceutical properties
   - 6.1 List of excipients
   - 6.2 Incompatibilities
   - 6.3 Shelf life
   - 6.4 Special precautions for storage
   - 6.5 Nature and contents of container
   - 6.6 Special precautions for disposal and other handling
7. Marketing authorisation holder
8. Marketing authorisation number(s)
9. Date of first authorisation/renewal of the authorisation
10. Date of revision of the text

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Introduction | Research question(s)

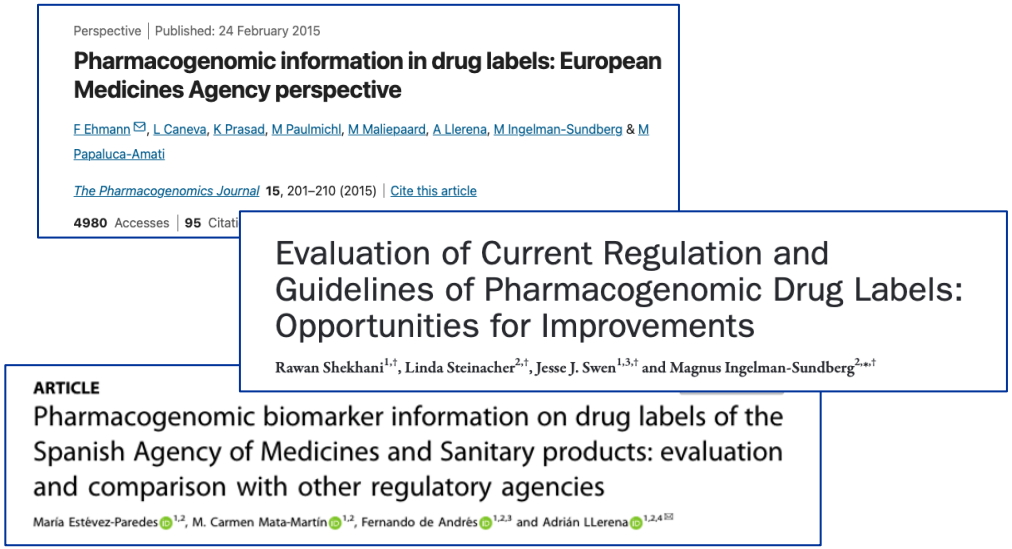
? How **many centrally authorised medicinal products** include pharmacogenomics information?

? In which **therapeutic areas** is pharmacogenomics information more prevalent?

? Which **pharmacogenes** are more often represented in the SmPC of centrally authorised medicinal products?

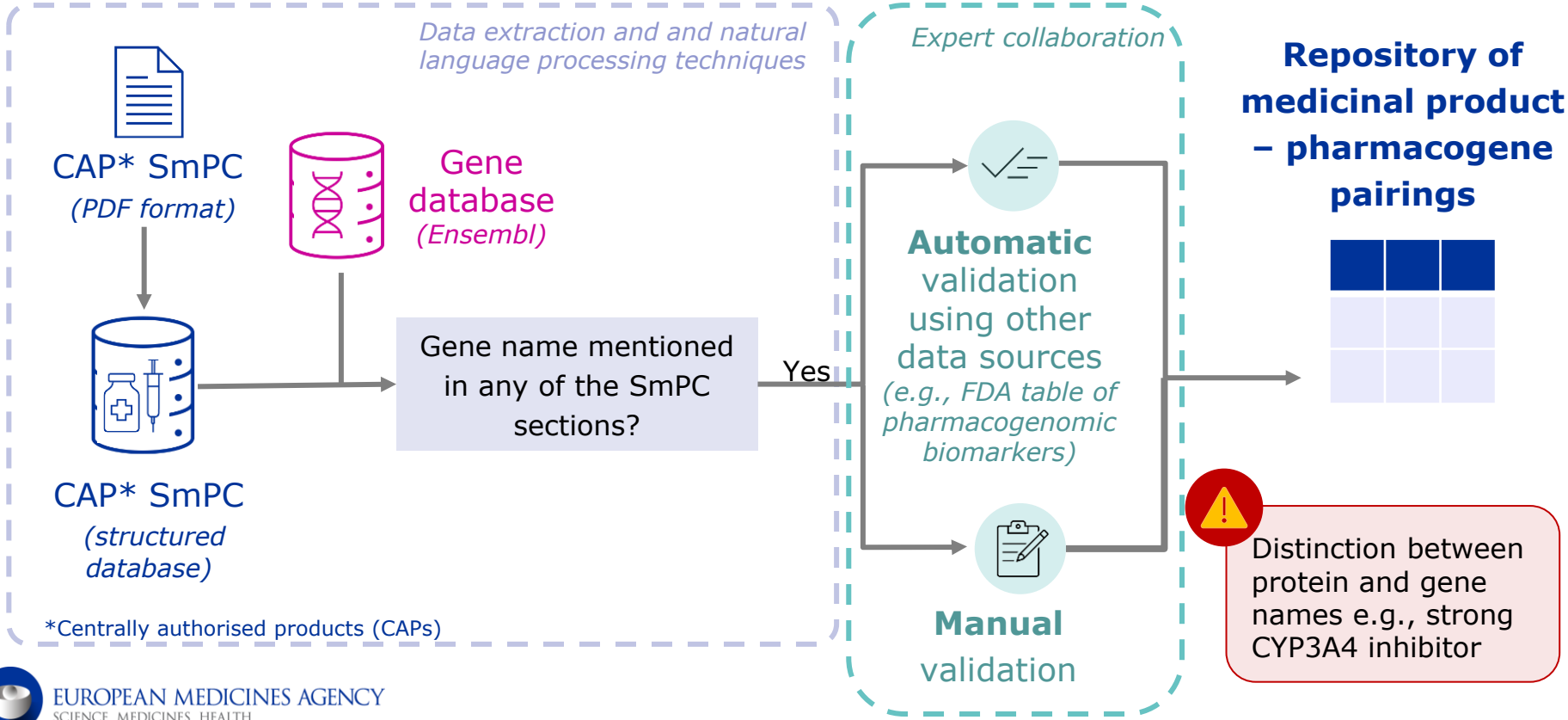
Aim | To create a repository of centrally authorised medicinal products with pharmacogenomics information in the SmPC

Previous work…



An **up-to-date review** of the pharmacogenomics (PGx) information in the SmPC of centrally authorised medicinal products has been requested in different occasions by **PGx experts of the Methodology European Specialised Expert Community (ESEC), assessors and academia**

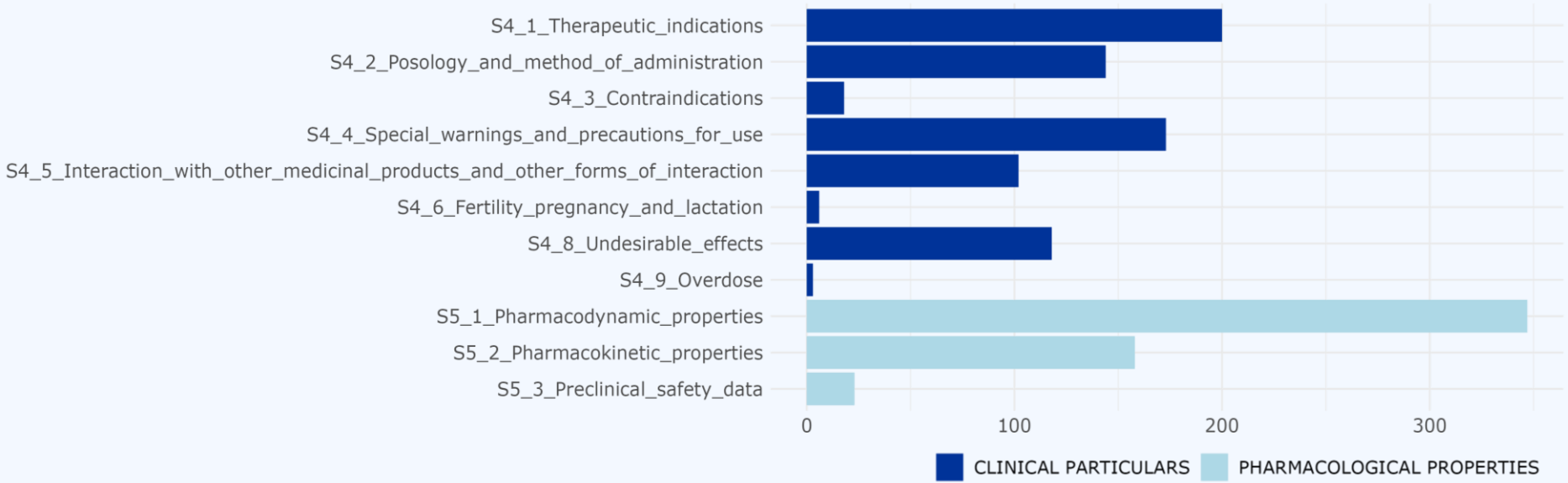
Methodology and data sources | An overview



Results | Overall findings

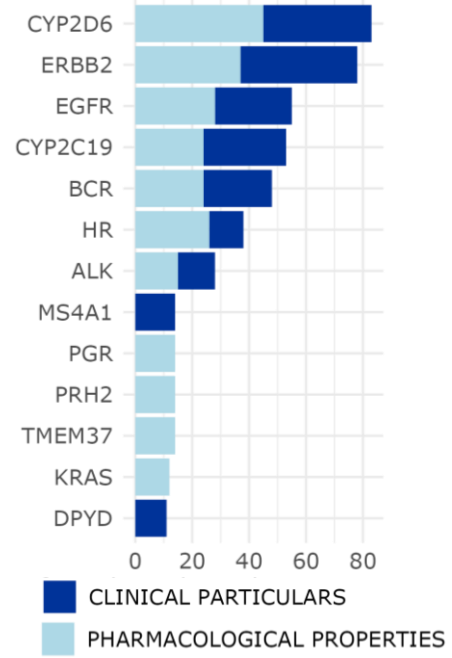
→ As of December 2023, approx. 24% medicinal products mention pharmacogenomics information in their SmPC

Number of medicinal product-gene pairs by SmPC section

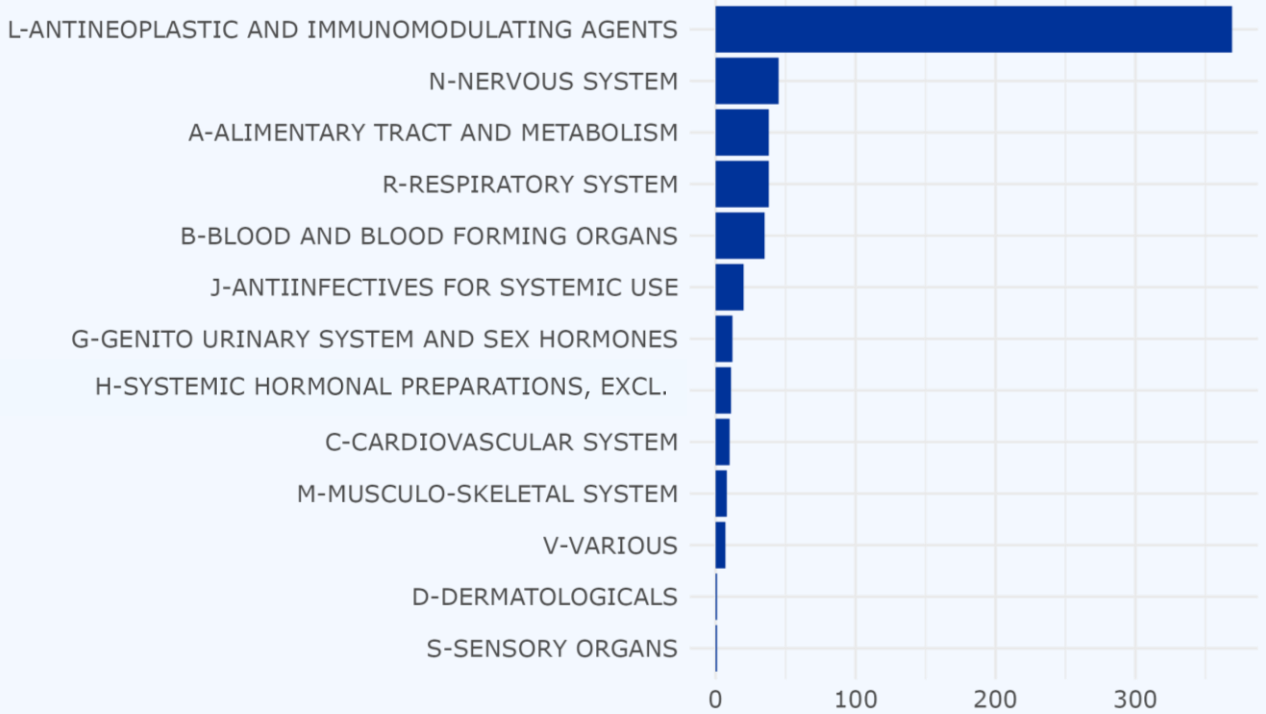


Results | Overall findings

Most recurrent pharmacogenes in SmPC



Number of medicinal product-gene pairs by ATC index



Results | Examples

Zokinvy

lonafarnib

Authorised

This medicine is authorised for use in the European Union

4.1. Therapeutic indications 	Zokinvy is indicated for the treatment of patients 12 months of age and older with a genetically confirmed diagnosis of Hutchinson-Gilford progeria syndrome or a processing-deficient progeroid laminopathy associated with either a **heterozygous *LMNA* mutation** with progerin-like protein accumulation or a **homozygous or compound heterozygous *ZMPSTE24* mutation**.
4.2. Posology and method of administration 	Dose adjustment for patients with known **dysfunctional polymorphisms in *CYP3A4*.** The patient's daily dose of lonafarnib should be reduced by 50%, and the reduced daily dose should be divided into two equal doses.

Results | Examples

Zebinix

eslicarbazepine acetate

Authorised

This medicine is authorised for use in the European Union

4.4. Special warnings and precautions for use

HLA-B*1502 allele in individuals of Han Chinese and Thai origin has been shown to be strongly associated with the risk of developing the severe cutaneous reactions known as Stevens Johnson syndrome (SJS) when treated with carbamazepine. The chemical structure of eslicarbazepine acetate is similar to that of carbamazepine, and it is possible that patients who are positive for HLA-B*1502 may also be at risk for SJS after treatment with eslicarbazepine acetate. If patients of these ethnic origins are tested positive for HLA- B*1502 allele, the use of eslicarbazepine acetate may be considered if the benefits are thought to exceed risks.

Results | Examples

Neofordex

dexamethasone

Authorised

This medicine is authorised for use in the European Union

4.5 Interaction with other medicinal products and other forms of interaction

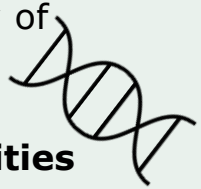
Effects of dexamethasone on other medicinal products:

Dexamethasone is a moderate inducer of CYP3A4 and of P-gp. Concomitant administration of dexamethasone with substances that are metabolised via CYP3A4 or transported by P-gp could lead to increased clearance and decreased plasma concentrations of these substances:

Erythromycin, due to increased metabolism of erythromycin in **non-carriers of the CYP3A5*1 allele** after dexamethasone treatment.

Benefits and challenges

- Standardised **repository** of PGx biomarkers
- Better **understanding** of the frequency of PGx information
- Inform future pharmacogenomics **activities** at EMA/EMRN



- Lack of **standardisation** → Gene names and genetic variation nomenclature
- Coverage → only centrally authorised products were reviewed

- A state-of-the-art **methodology** to analyse and harmonise unstructured data
- Open access publication and code repository → Advocate for **reproducibility** and transparency in the activities performed by EMA and collaborators

Key messages

1. 24% of the centrally authorised medicines include pharmacogenomics information

2. Pharmacogenomics information in the SmPC is guiding patients' treatment and contributes to the safety of medicines

3. Publicly available repository of pharmacogenomics information

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Thank you for your attention

Further information

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