



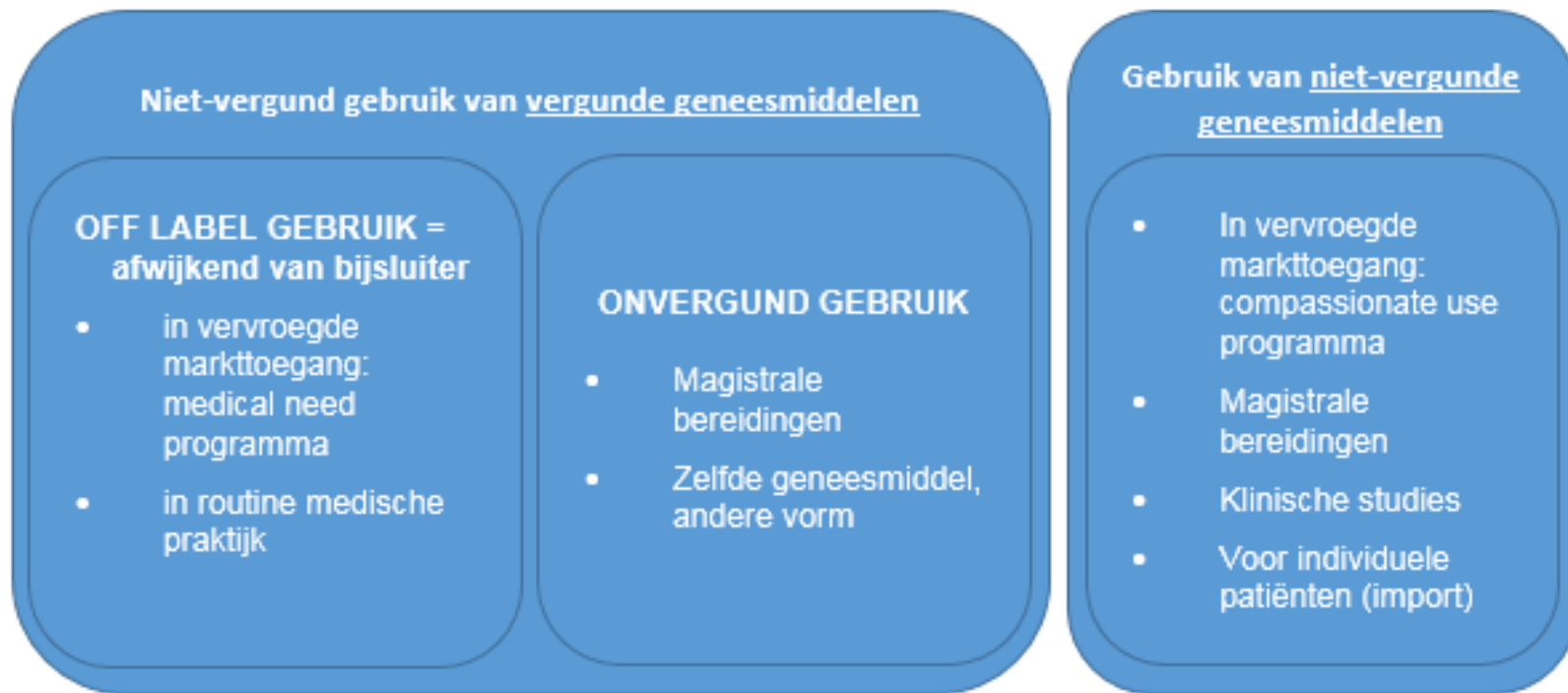
Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

TOWARDS A MANAGED OFF-LABEL USE OF DRUGS

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Unauthorised use vs use of unauthorised pharmaceuticals



Concerns parties involved

- **Authorities:** safety? efficacy?
- **Payers:** hesitate to reimburse
- **Patients:** informed?
- **Prescriber:** responsible?
- **Pharmacist:** responsible?

What did we do and how?

Research questions

- Possibilities of national authorities under EU law to manage off-label use
- Can off-label use be brought in-label through a new marketing authorisation or a variation to the existing marketing authorisation(s)?
- How can relevant evidence be gathered on off-label use of medicines?

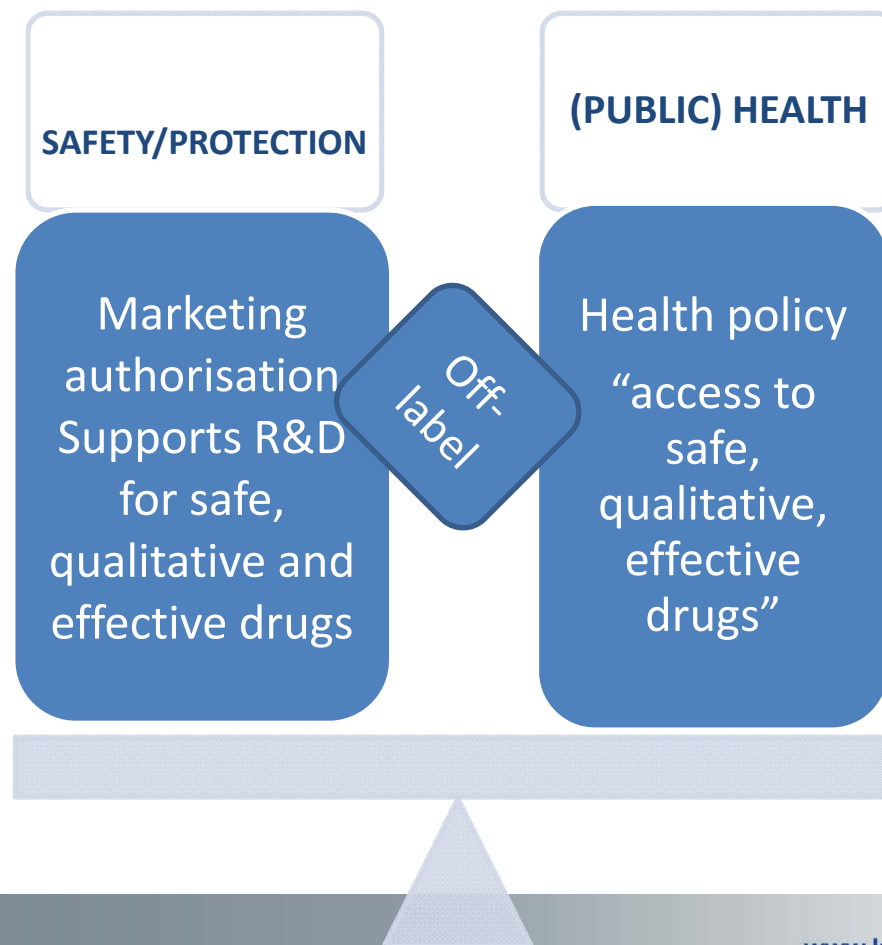
Method

- Identification of existing regulation and jurisprudence on EU level
- Identification situation in other countries
- Step-plan for Belgium

EU legal framework

- MA standard, limited exceptions
 - Medical need (CU, MN, emergency cases, special need)
 - Clinical trials
 - Magisterial formulae
- Off-label use not, as such, defined
- EU pharmaceutical law does not preclude the off-label prescription at the discretion of the doctor and at his own responsibility (therapeutic freedom)
- Increasing EU attention to off-label use, in particular in pharmacovigilance rules:
 - E.g.: Adverse reaction reporting now also includes off-label use
- Commercial promotion off-label use is prohibited for firms
- Initiatives to stimulate extensions of indications, but not always successful

SAFETY/PROTECTION



What can MS allow?

- No alternative available
 - Allowed in case of medical need, Clinical trials, Magistral formulae
 - Alternative available
 - No ECJ-judgement yet
 - Promoting solely for cost considerations not valid
 - Nevertheless:
 - Stakeholders are free to perform **research**
 - Member States are **free to provide neutral scientific information** regarding off-label used products
 - Member States can foresee **specific reimbursement schemes** enabling the public funding of off-label therapies in individual patients
 - Prescribers have **therapeutic freedom** (due diligence)
- See 8-Step plan

Liability

- **Product liability:**

- Warning of possible side effects
- Foreseeability off-label use → pharmacovigilance rules
- Unlikely for wrong decision physician

- **Practitioner's liability:**

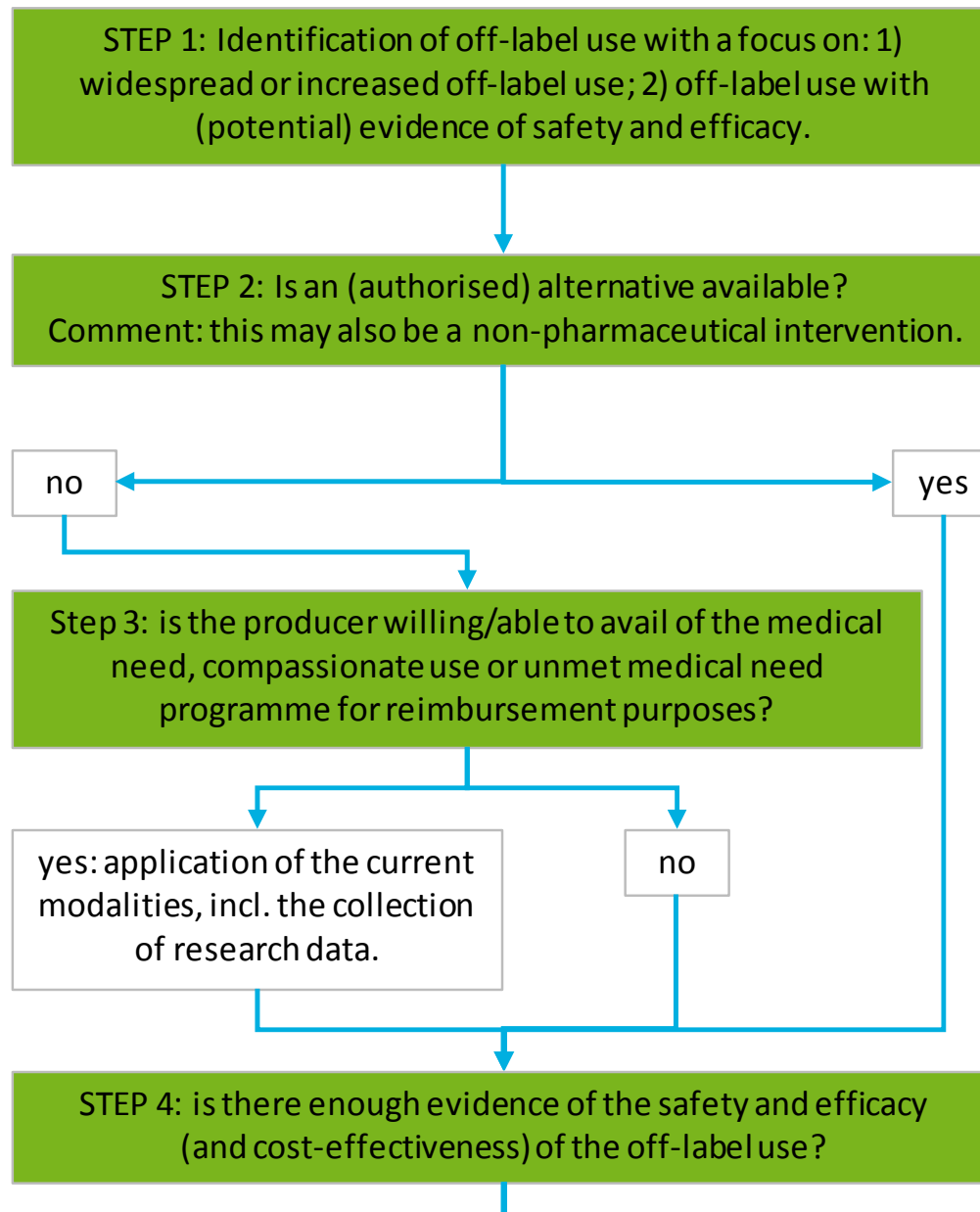
- No prohibition of off-label prescription, sometimes sole option
- Solid scientific basis
- Informed consent

- **Pharmacist + Medical Pharmaceutical Committee:**

- Advising patient => able to be aware of off-label?
- Carefull preparation

- **Public health authorities' liability:**

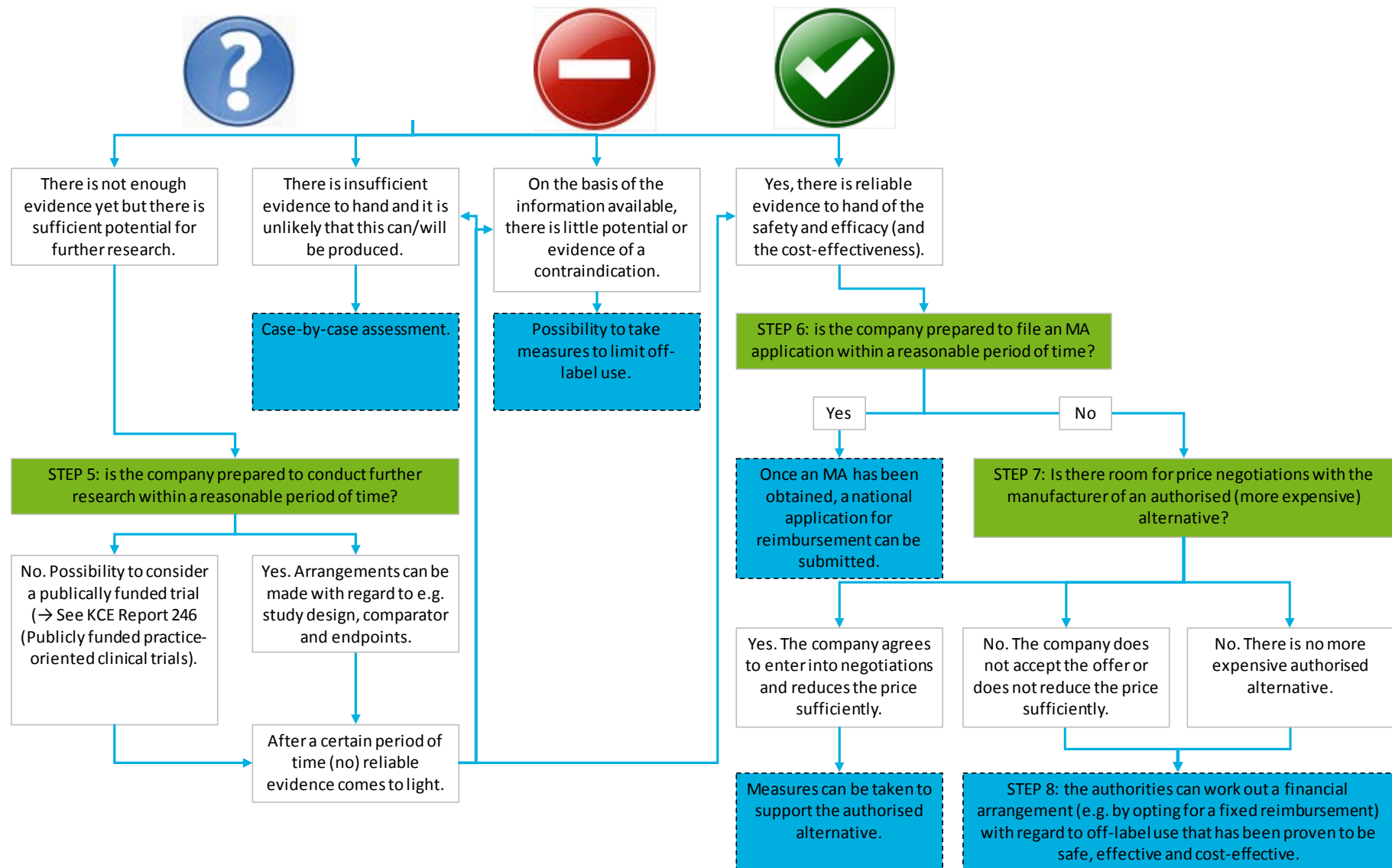
- Unlawful or careless policy: Promoting off-label use for budgetary reasons



- Start: use of off-label

➔ **Priority is public health**

- Evaluation of (quality), safety, efficacy (and cost-effectiveness)



- Discussion with MAHs
- Financing

Recommendations

- Inform prescriber that off-label prescribing is possible
 - Informed consent + diligence + note in patient file
- The roadmap should help to manage the off-label use of drugs
 - FAMHP/EMA to evaluate quality, safety and efficacy (to be discussed at STAMP)

Recommendations

- Reevaluate policy for price reduction in case of extension of indication
- Manufacturers to include all information about off-label use in the application file for an MA.
- Research agenda: how to make relevant non-clinical data available for non-commercial trials



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Bedankt, Merci, Thank you!



Colophon

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- **Publication date:** 8 October 2015
- **Domain:** Health Services Research (HSR)
- **MeSH:** Off-label use; Drug approval ; Jurisprudence ; Liability, legal
- **NLM Classification:** QV 771
- **Language:** English
- **Format:** Adobe® PDF™ (A4)
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