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

Unauthorised use of authorised medicines

OFF LABEL use = deviant from leaflet/SPC

- In early market access: medical need programme
- In routine medical practice

Unauthorised use

- Magisterial formulas
- Same medicine, different pharmaceutical form

Use of unauthorised medicines

- In early market access: compassionate use programme
- Magistral formulas
- Clinical trials
- Import on prescription for individual patients

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?

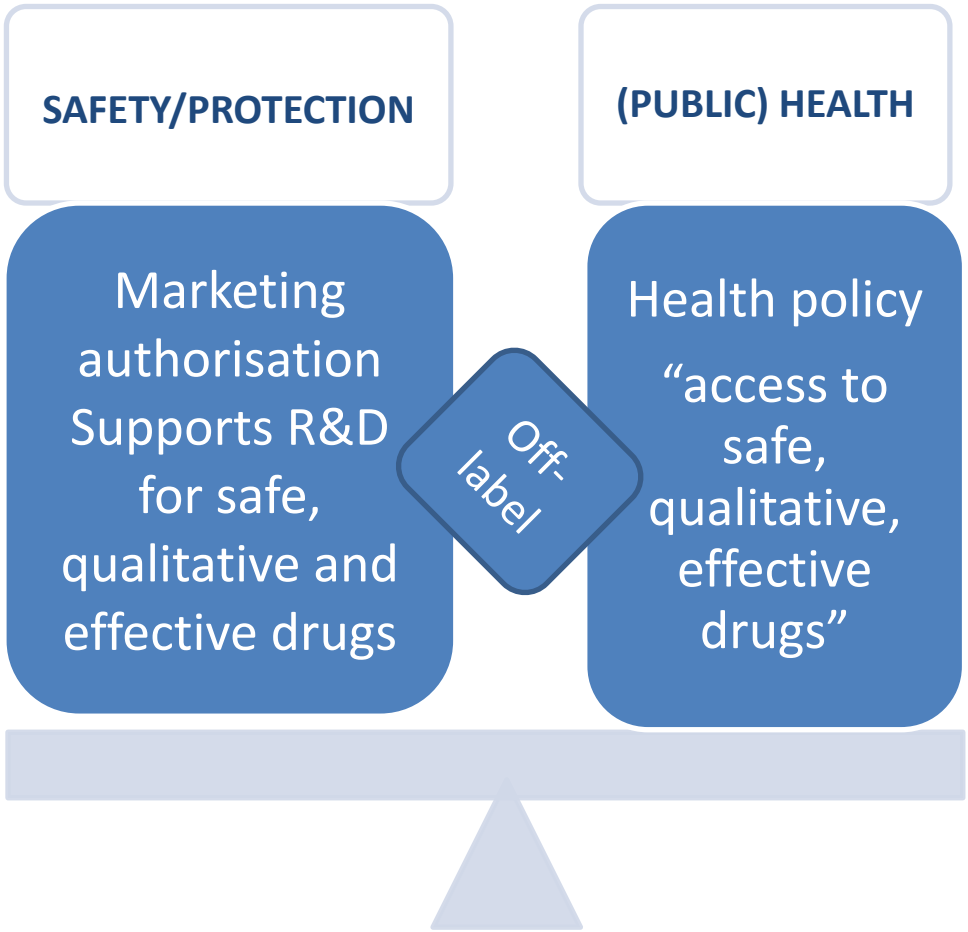
Method

- 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
  - Magistral formula
- 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



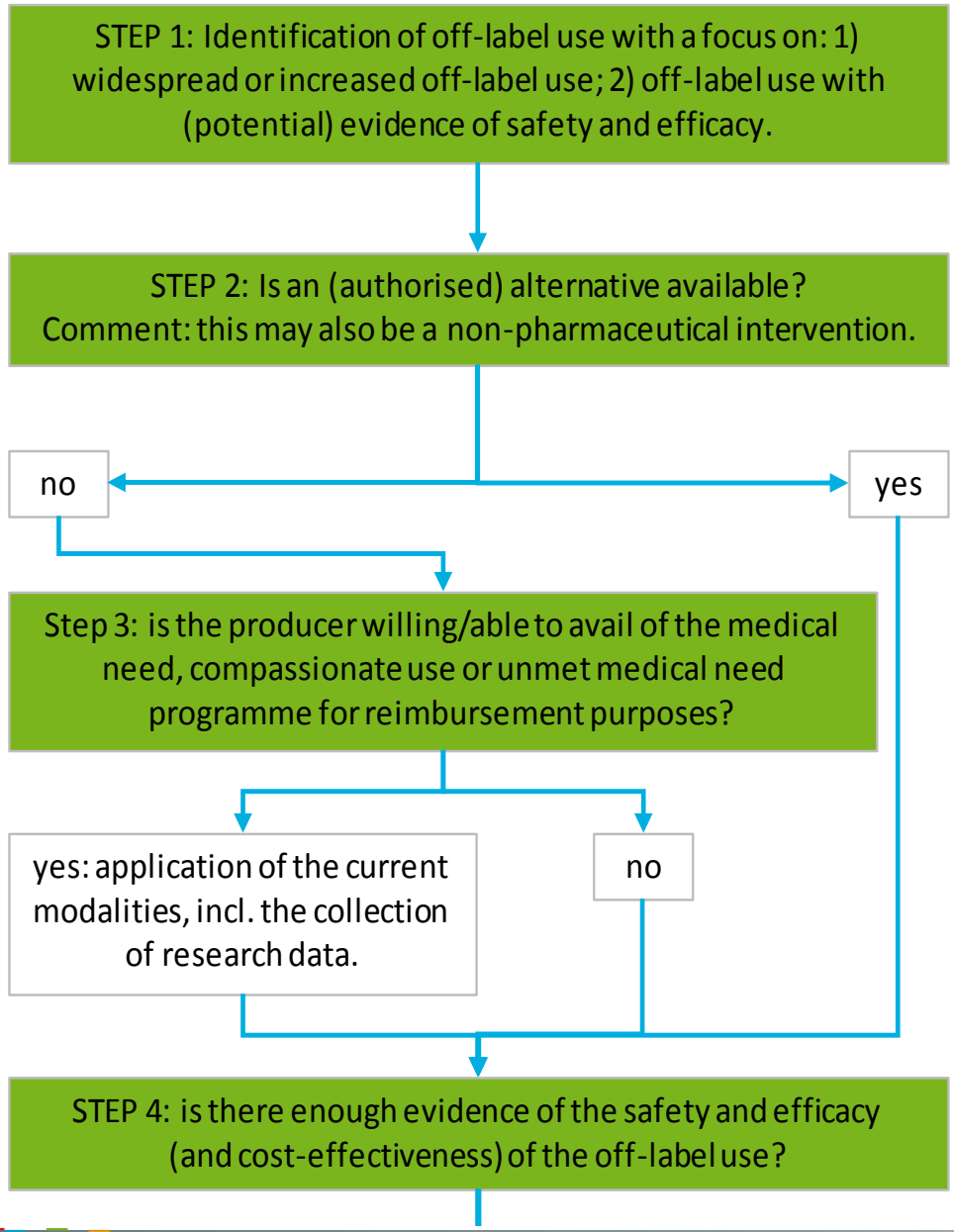
What can MS allow?

- No alternative available
  - Allowed in case of medical need, Clinical trials, Magistral formula
- 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

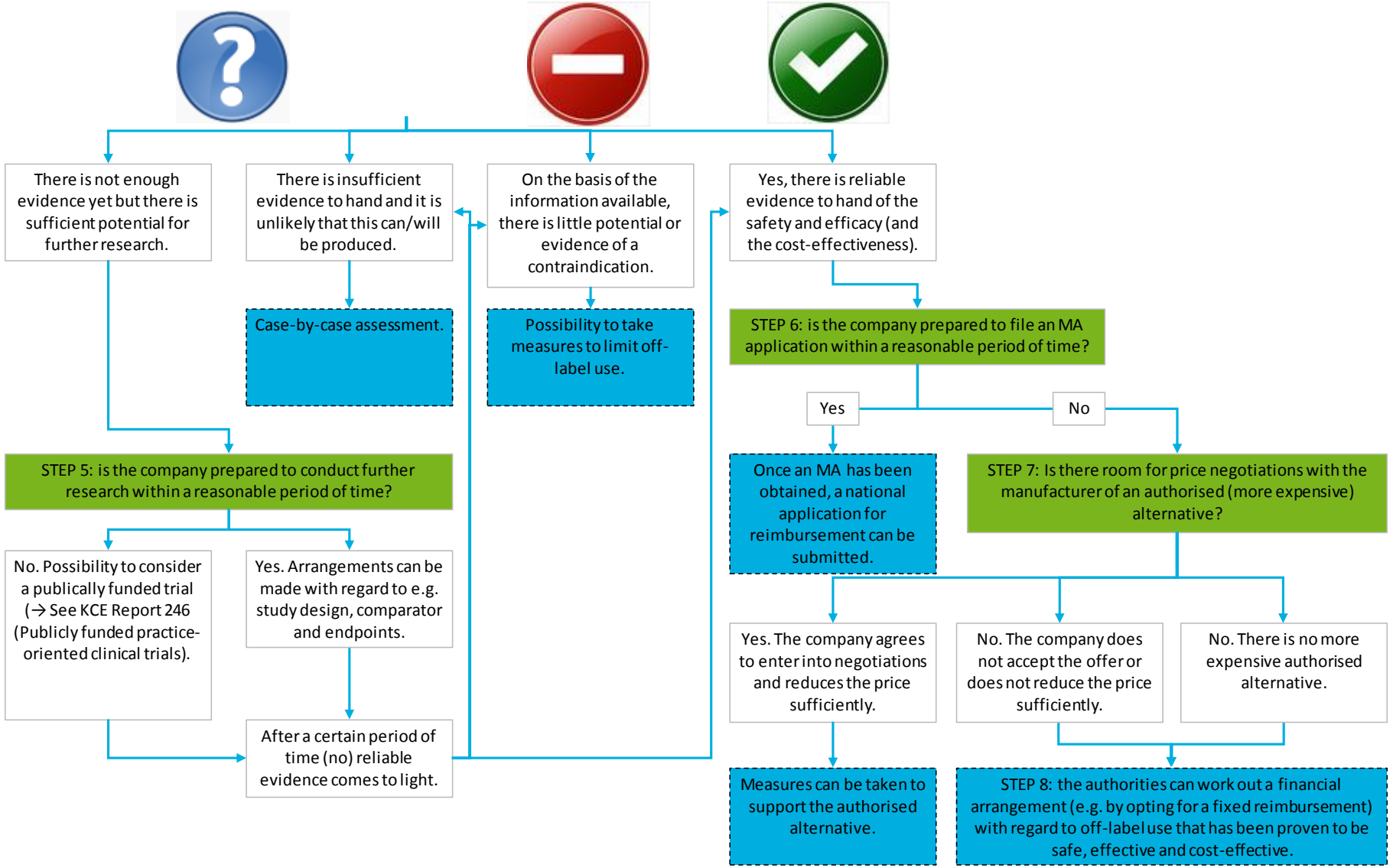
Liability

- **Product liability**:
  - Warning of possible side effects
  - Foresee ability 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
  - Competent authorities 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!

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Colophon

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