



Risk sharing agreements

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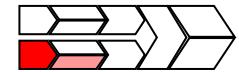
Advance-HTA Capacity building workshop



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Background

- Increasing cost of new medicines
- Presence of a significant degree of uncertainty at the time of making coverage decisions
- Need for innovative solutions to make new drugs available to patients while ensuring the long-term financial sustainability of healthcare systems



Constructing RSAs – Key sources of uncertainty

- **Uncertainty around clinical evidence**
 - More robust clinical evidence is needed about who is likely to benefit most
- **Uncertainty around cost-effectiveness**
 - Average cost-effectiveness is higher than country's WTP
- **Uncertainty around budget impact**
 - Budget impact is too high if all potentially eligible patients are treated
- **Uncertainty around price**
 - Not clear how pricing strategy results in a price that is significantly higher than BAT
- **Uncertainty around eligible patient population**
 - Not clear who is likely to benefit most
 - Not clear how many patients exist in this indication

Risk Sharing and Managed Entry Agreements

WHY?

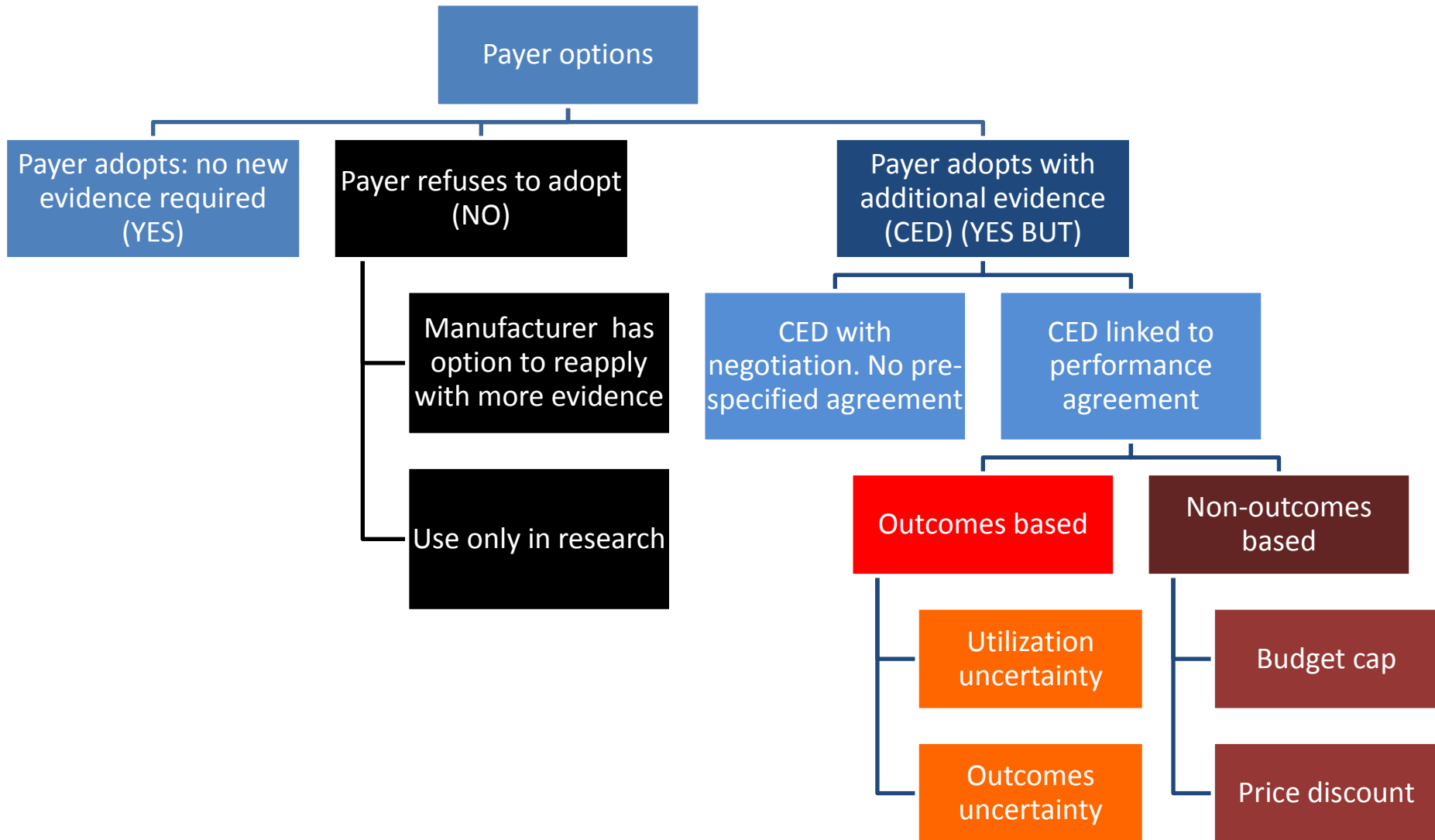
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Financial

**Outcomes-
related**

**Combination
of both**

Payer option flow diagram



Coverage with Evidence Development

- Product is covered or reimbursed when used under controlled circumstances:
 - RCTs
 - Utilisation Management Schemes (UMS)
 - Evidence-providing Registries
- Examples
 - Coverage of CRC agent by Medicare via RCT and UMS
 - Coverage of prostate cancer “vaccine” by Medicare via building evidence-providing registry

Conditional Coverage

- Price and reimbursement are (temporary) granted but failure to achieve set targets can result in price and reimbursement changes and/or rebates
- Examples
 - Pfizer on statins in the UK
 - UK NICE MS scheme
 - France: Acomplia

Outcome Guarantee

- Rebates or free product are given by the manufacturer when outcomes are not achieved for individual patients
- Presupposes ability to monitor eligible patients well
- Example: Bortezomib case in UK through NICE guidance (case study separately)

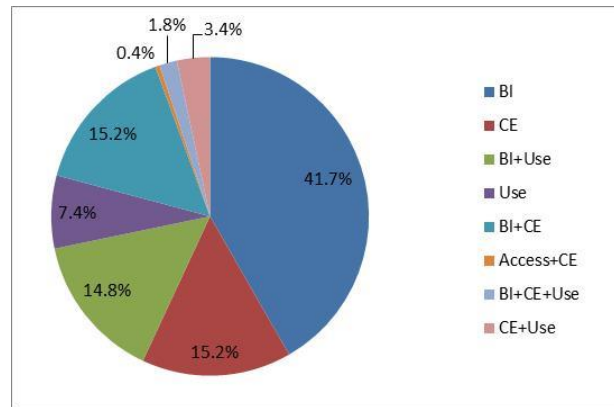
Price and Volume (Budget) Agreements

- A penalty is foreseen when a new drug is overshooting a pre-set budget (PxQ)
- Penalty can take the form of
 - Rebate or payback
 - Lower price for volume above agreed limit
 - Lower future price
- Variety of payback clauses
 - Supplier is fully accountable
 - Prescriber and supplier are jointly accountable
 - Rebate/Payback to be shared among suppliers
- Examples: Australia, France, Italy, Austria, Portugal

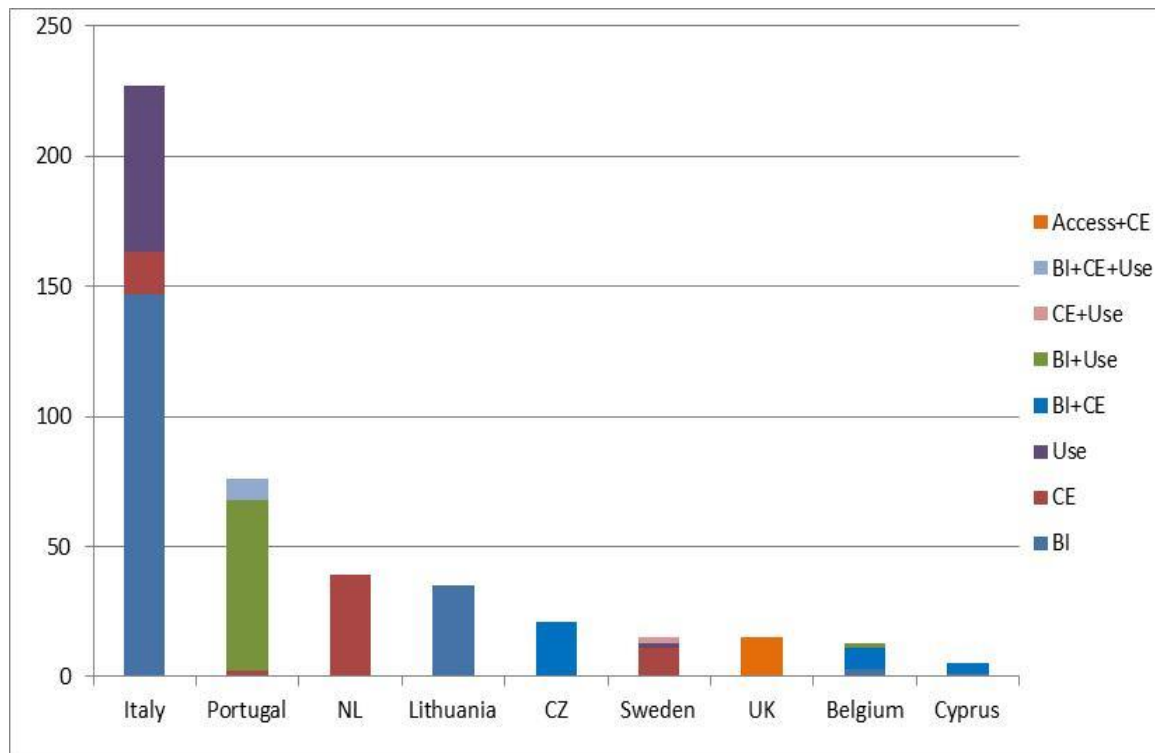
Risks addressed by individual scheme types

	Right patients	Uncertain clinical value	Low cost effectiveness	Budget overspend
Coverage with ED	Yes	Yes	Yes	x
Conditional coverage	Yes	Yes	Yes	Yes
Outcome guarantee	Yes	Yes	Yes	x
Price-volume deal	x	x	X	Yes

Main objectives of MEAs

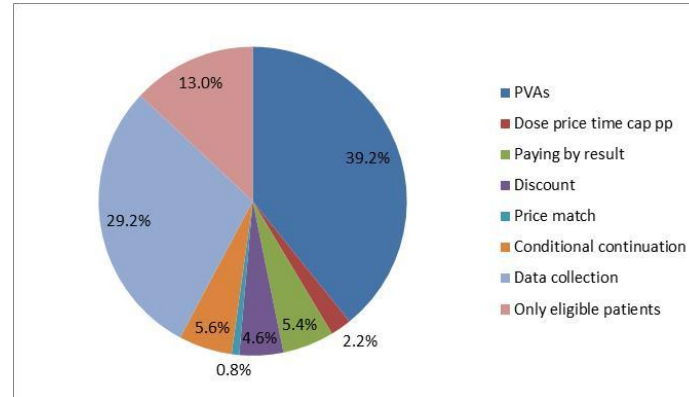


BI: Budget impact
CE: Cost-effectiveness

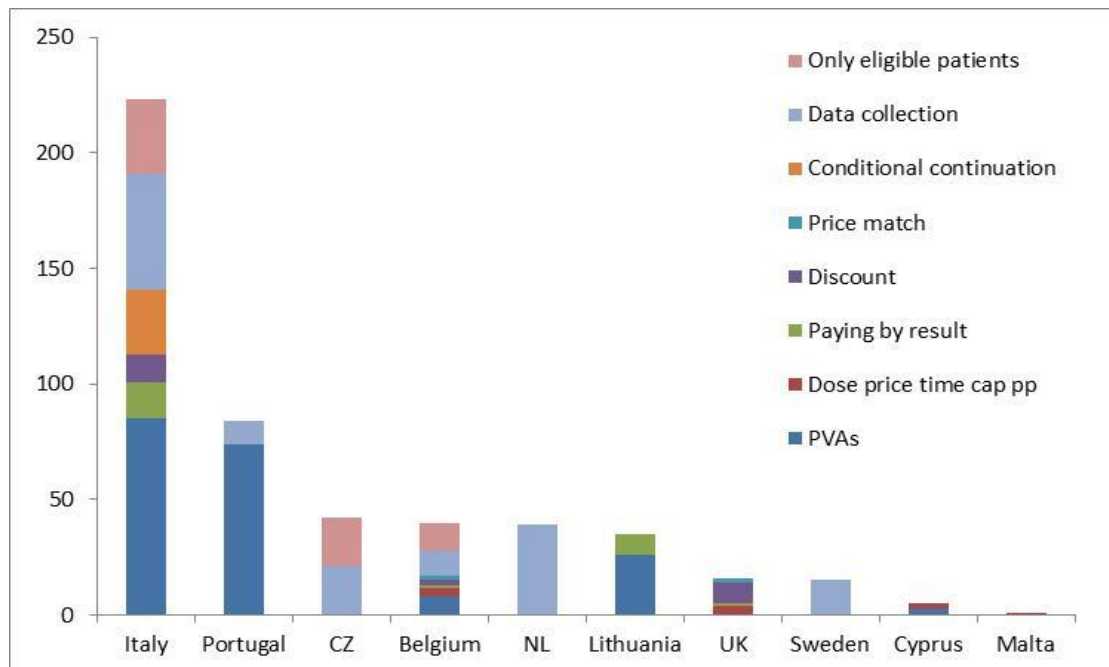


Source: Ferrario
& Kanavos, 2013

Common elements of MEAs

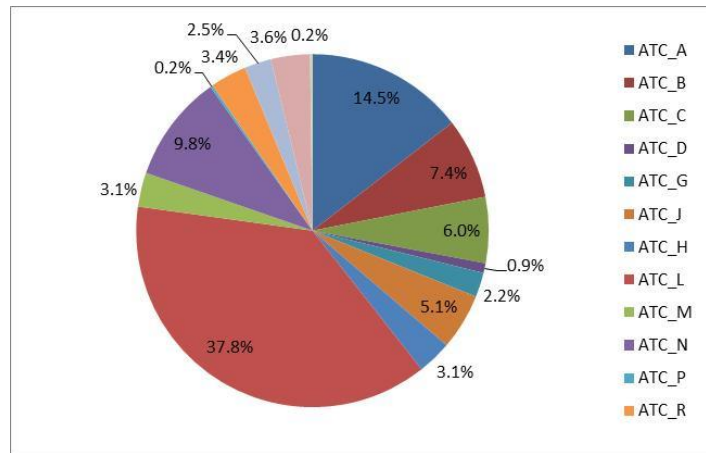


PVAs: Price-volume agreements
pp: per person



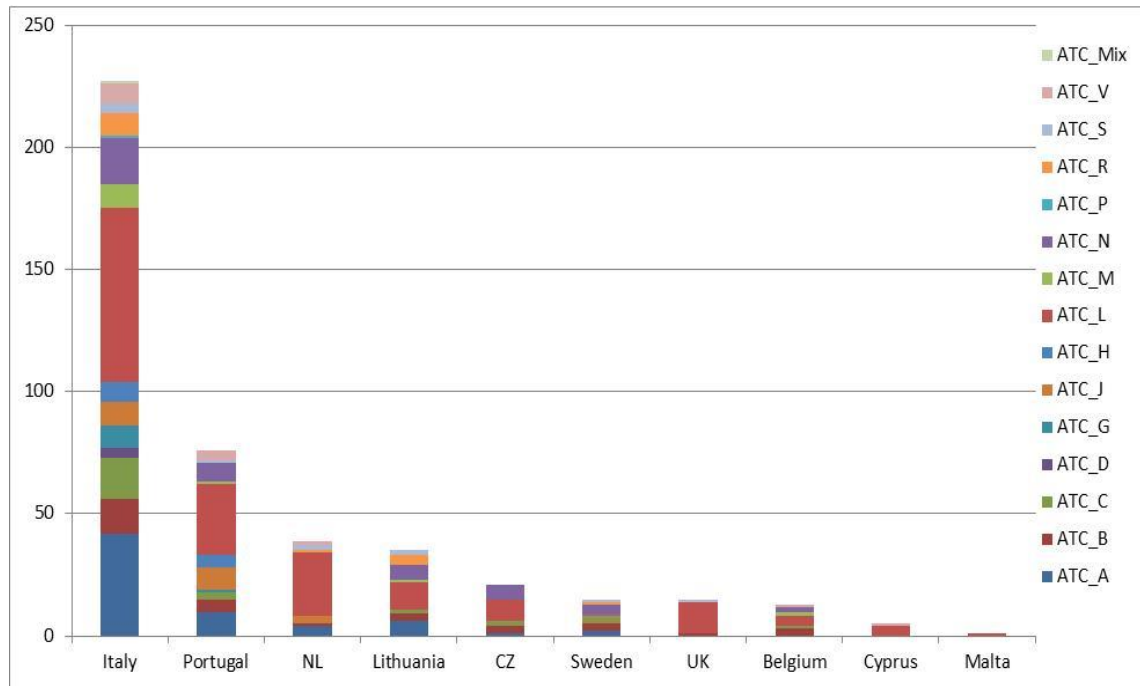
Source: Ferrario & Kanavos, 2013

Therapeutic classes



ATC groups (according to ATC-index 2011)

- A: Alimentary tract and metabolism
 - B: Blood and blood forming organs
 - C: Cardiovascular system
 - D: Dermatologicals
 - G: Genito urinary system and sex hormones
 - H: Systemic hormonal preparations, excl. sex hormones and insulins
 - J: Anti-infectives for systemic use
 - L: Antineoplastic and immuno-modulating agents
 - M: Musculo-skeletal system
 - N: Nervous system
 - R: Respiratory system
 - S: Sensory organs;
 - V: Various
- ATC_Mix: There was one case in Italy where a particular AIFA-note contained medicines from different ATC-groups.



Source: Ferrario & Kanavos, 2013

Duration

- The average duration of MEAs varies between Member States, ranging from one year in Belgium (renewable) to up to four years in the Netherlands or for an indefinite period of time subject to review (France, Malta, UK).

Main instruments linked to MEAs

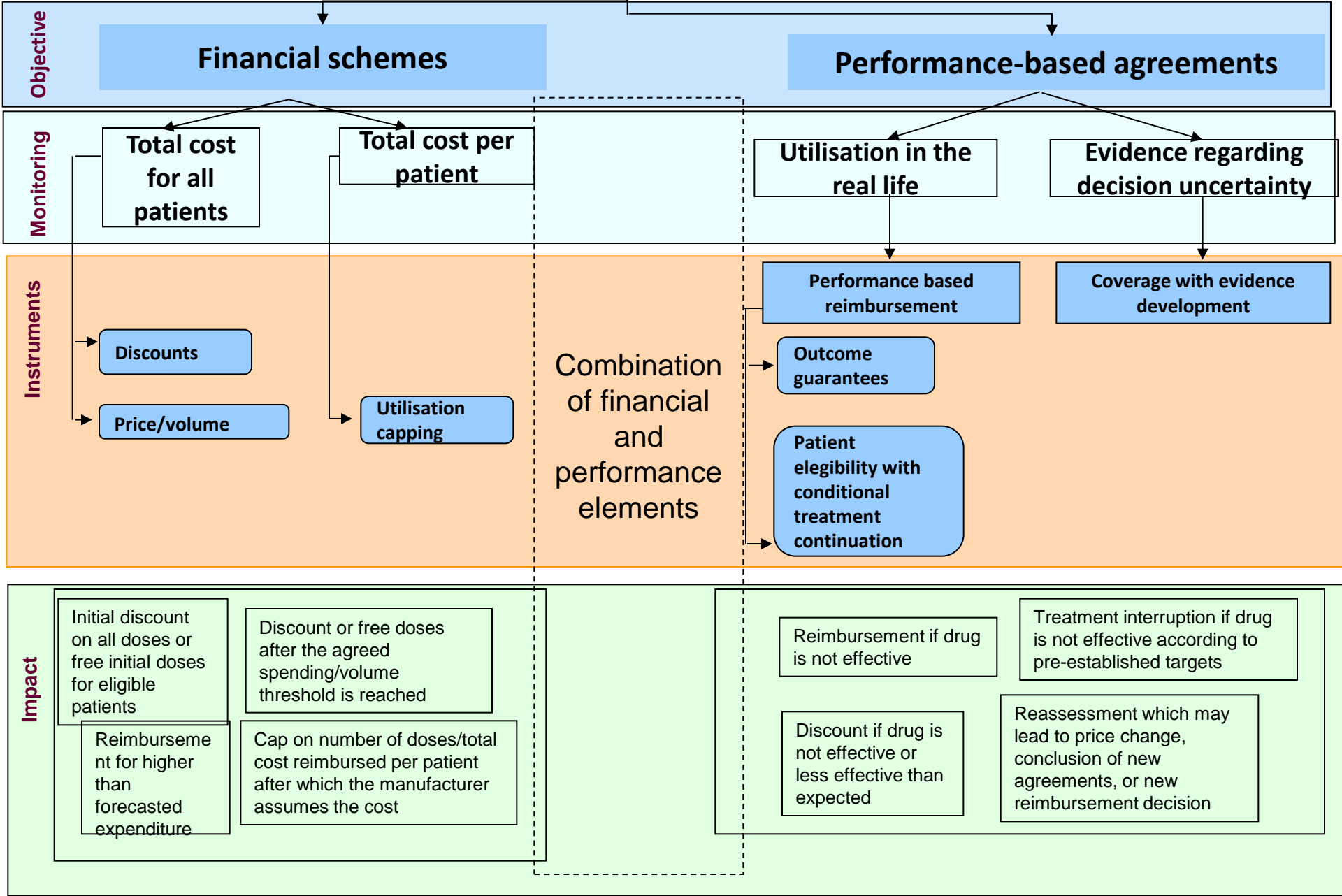
Examples of instruments used	
Sales and expenditure databases	Total: 198 <ul style="list-style-type: none">- Italy: 85- Portugal: 76- Lithuania: 35- Sweden 2
Patient registries	Total: 119 <ul style="list-style-type: none">- Italy: 78- Czech Republic: 21- Belgium: 13- Sweden: 7
Studies	Total: 64
Online systems for reimbursement	Total: 11 <ul style="list-style-type: none">- UK: 11

Actors involved in implementing MEAs

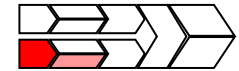
- Main stakeholders involved
 - Payers, drug assessment agencies, and physicians
- Responsibility for negotiating the agreement with the manufacturer
 - Payers (e.g. NIHDI in Belgium), drug assessment agencies (e.g. AIFA in Italy, TLV in Sweden) or DoH (UK)
- Responsibility for filling in the patient registries
 - Physicians usually in collaboration with other stakeholders (e.g. monitoring registries in Italy are managed by AIFA; an advisor physician from the National Health Insurer controls the implementation of MEAs in Belgium)
- Responsibility for data provision
 - Manufacturers

Taxonomy: A framework for analysing and evaluating MEAs

Managed entry schemes

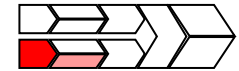


Value Proposition



- ❖ A strong Value Proposition will be payer-centric in nature, and will contain compelling evidence that
 - Showcases all dimensions of value (medical/therapeutic-, patient reported outcome- and economic benefits)
 - Reflects the full impact of the innovation to payers and HTAs and
 - Translates the clinical profile into a compelling cost/effectiveness ratio
- Using comprehensive and good quality evidence
- Leveraging critical value dimensions with a view to constructing *tailor-made* **RSA plans**

Payer-centric Value Proposition (1)

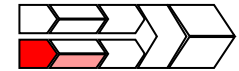


- Critical elements that payers may require include:
 - **Differentiation relative to standard of care**

Although superiority might be shown against BSC on all primary- and secondary endpoints, it may deter payers from considering the improvement as being major
 - **Relevant comparator (head-to-head)**

A placebo-controlled trial is often seen as a weakness. Payers prefer to see H2H trials. In the absence of H2H data payers would need to see data for detailed indirect comparison across the primary and secondary endpoints that incorporate any difference in trials.

Payer-centric Value Proposition (2)



- **Quality of evidence**

The non-significant claim on overall survival will negatively impact the value perception for payers. Without a clear statistical superiority claim for overall survival, payers will consider new therapies at most comparable to existing ones despite new therapies showing considerable additional benefits on other attributes

- **Data collection**

If time horizon is not long enough to capture full clinical- and economic impact of disease payers may demand long-term (real life) data

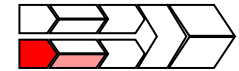
- **Comparative efficacy/effectiveness**

Measures of effect in “real-life” conditions: Clinical- and cost effectiveness data in real-world vs. a clinical setting

- **Cost effectiveness data**

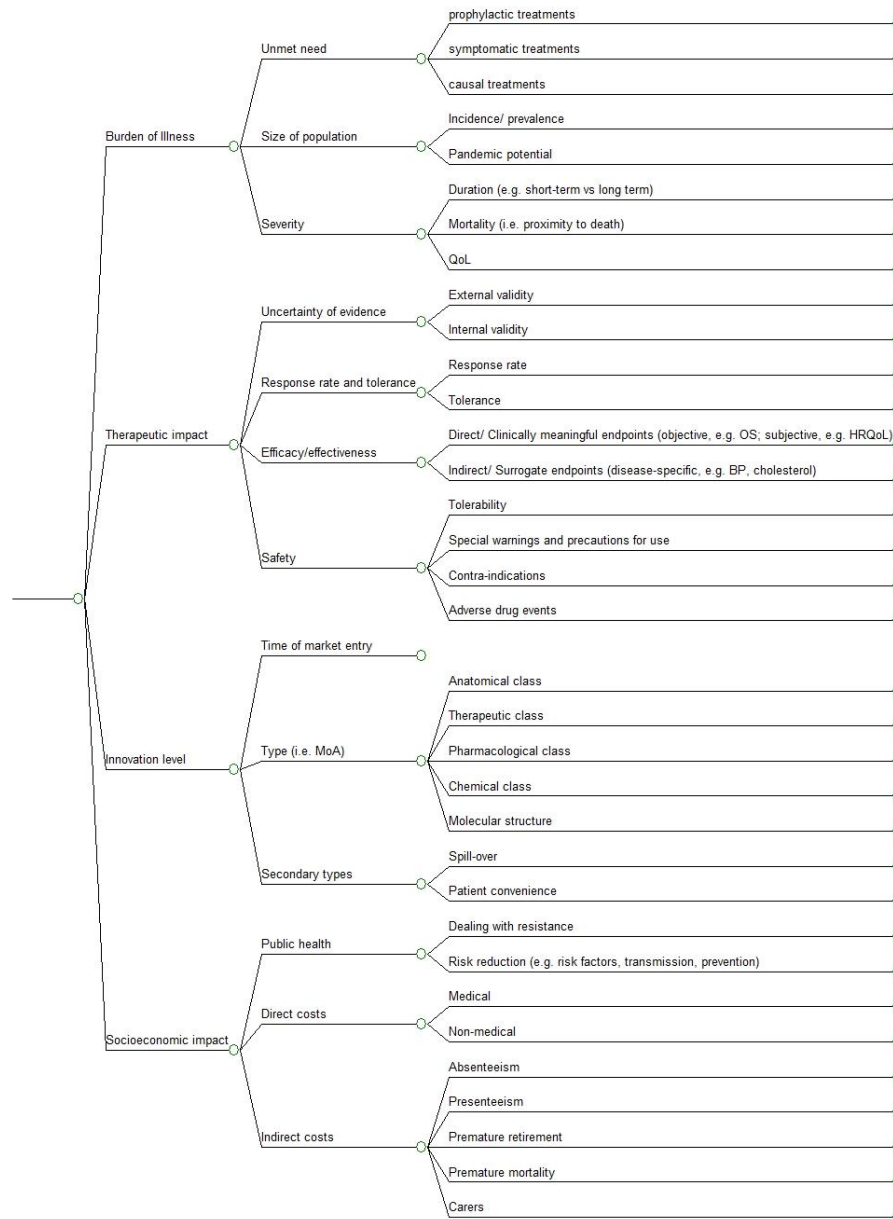
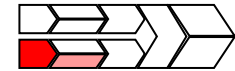
Evidence used for the NICE submission but possible other additional

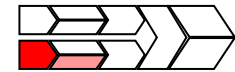
Additional evidence requirements



- Payers may require additional data besides the pivotal trial results through follow up studies or registries in order to reduce uncertainties including
 - Collect H2H comparative data that demonstrate better any treatment differences
 - Provide data that reflect (more) statistically significant outcomes (e.g. in OS or PFS)
 - Address uncertainties in clinical-and cost effectiveness in real world (e.g. PRO metrics)
 - Collect real world (effectiveness) data

Value is multi-dimensional...





...a practical and necessary set of dimensions should be considered

Efficacy
Direct endpoints
Survival
Disease progression
Disease recovery
Clinical events
Symptoms scores
HRQoL
Indirect endpoints
Validated endpoints
Non-validated endpoints
Safety
Adverse drug events
Tolerability
Contraindications and special warnings
Innovation
Mechanism of Action (MoA)
Patient convenience
Socioeconomic
Public health
Direct costs
Indirect costs

Comparative presentation of value drivers



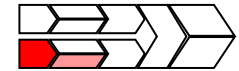
Value drivers		GRECOTINIB vs. HELLASOMAB		
		Inferior	Not stat. dif.	Superior
Efficacy				
Overall Survival (OS)	Median			
Overall Survival (OS)	Mean			
Skeletal Related Effects (SRE)	Time to first			
Skeletal Related Effects (SRE)	Incidence			
Objective Response Rate (ORR)				
Radiographic Progression Free Survival (rPFS)	Median time to			
Modified Progression Free Survival (mPFS)	Median time to			
Biomarker Response				
Time to treatment discontinuation (TTTD)	Patients proportion			
Radiographic Progression Free Survival (rPFS)	Patient proportion free of progression			?
Biomarker Progression	Patient proportion free of progression			?
Skeletal Related Effects (SRE)	Rate	?		
Biomarker Progression	Median time to	?		
Safety				
Adverse events	Hypokalemia			
Tolerability	Hepatotoxicity			
Adverse events	Bone pain	?		
Innovation				
Mechanism of Action (MoA)				
Patient convenience	Special instructions			
Socioeconomic				
Direct medical costs	Outpatient visits			
Value for money	Cost effectiveness			
Value for money	Cost minimisation			

Health Insurer's Point of View



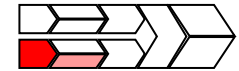
- ❖ Health Insurers might be willing to confirm the content of the Value Proposition or willing to build their own version reflecting or adjusting for their own perspective.
- Most of the data should be available through the peer review literature
 - -If not published their credibility might be questioned
 - -Insurers might conduct their own systematic literature review(s) to
 - ensure all critical evidence is incorporated
- Other sources might be required for the collection of real world effectiveness data and resource use (cost of illness) data
 - -Registries and observational studies

Constructing RSAs



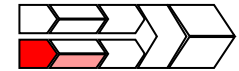
- The content of the value proposition can then inform the discussions surrounding the development of potential RSA options.
- Aim is to leverage Uncertainties (clinical, cost-effectiveness, other) of the technology in order to decrease the risk of a worst-off clinical benefit-risk ratio (BRR) or incremental cost effectiveness ratio (ICER) in real settings.
- Need to make a series of hypothetical scenarios on expected volumes and expected prices.

Volume expectations



- ❖ Expectations on volume are needed to inform RSAs.
- Follow-on products: epidemiological data on disease prevalence should be available
 - -WHO, CDC, national databases, peer review literature
- First-in-class: data on disease prevalence might not be available
 - -Conduct primary data collection activities such as
 - observational and descriptive studies, e.g. national registries

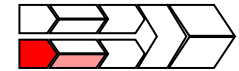
Performance based RSAs



- ❖ Choose clinically meaningful endpoints that are
 - Objective
 - Patient/disease relevant
 - Operational (i.e. practical and measurable)
 - “Cheap” to monitor
 - Can be monitored within a specified amount of time

- Potential endpoints include biomarker response to treatment (i.e. response rate), biomarker progression following treatment (i.e. disease progression), radiographic exams, etc.

Financial based RSAs



- ❖ Simpler than performance based agreements
 - ❖ Make use of confidential discounts between the manufacturer and the payer
 - ❖ Sales cap based on price-volume agreement
 - ❖ Based on the grounds of budget impact
-
- Potential options include the application of single discounts, multiple discounts (e.g. 100% discount for the first 3 mo, 50% discount for the next 3 mo, ending up paying full price), and revenue or sales caps