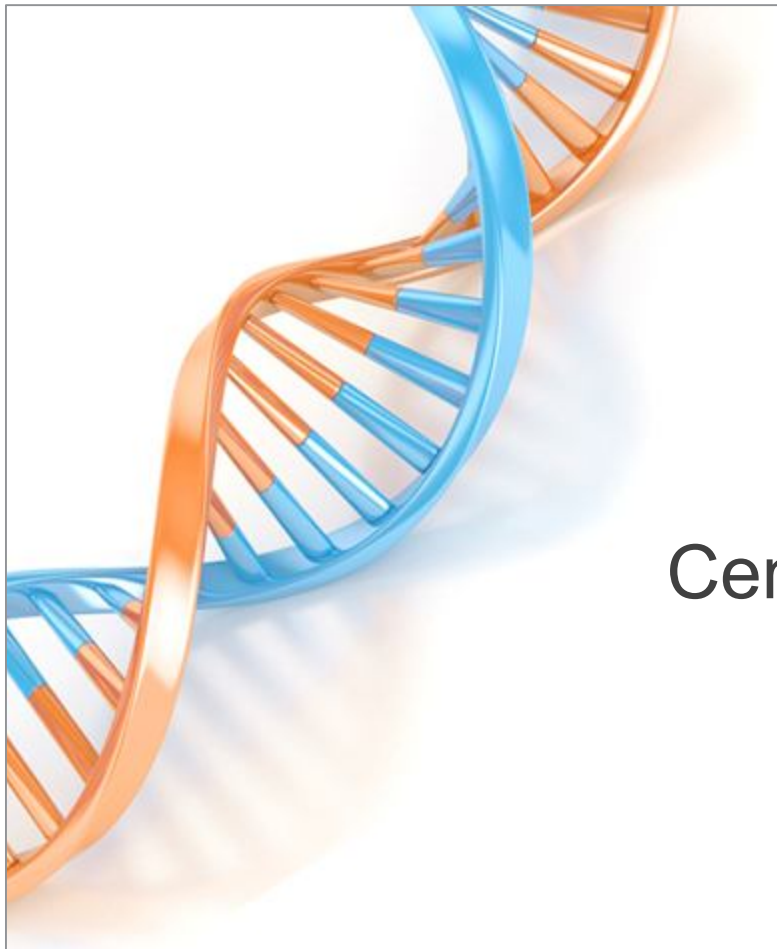


Overview of the situation in EU with focus on Central and Eastern Europe

April 2018

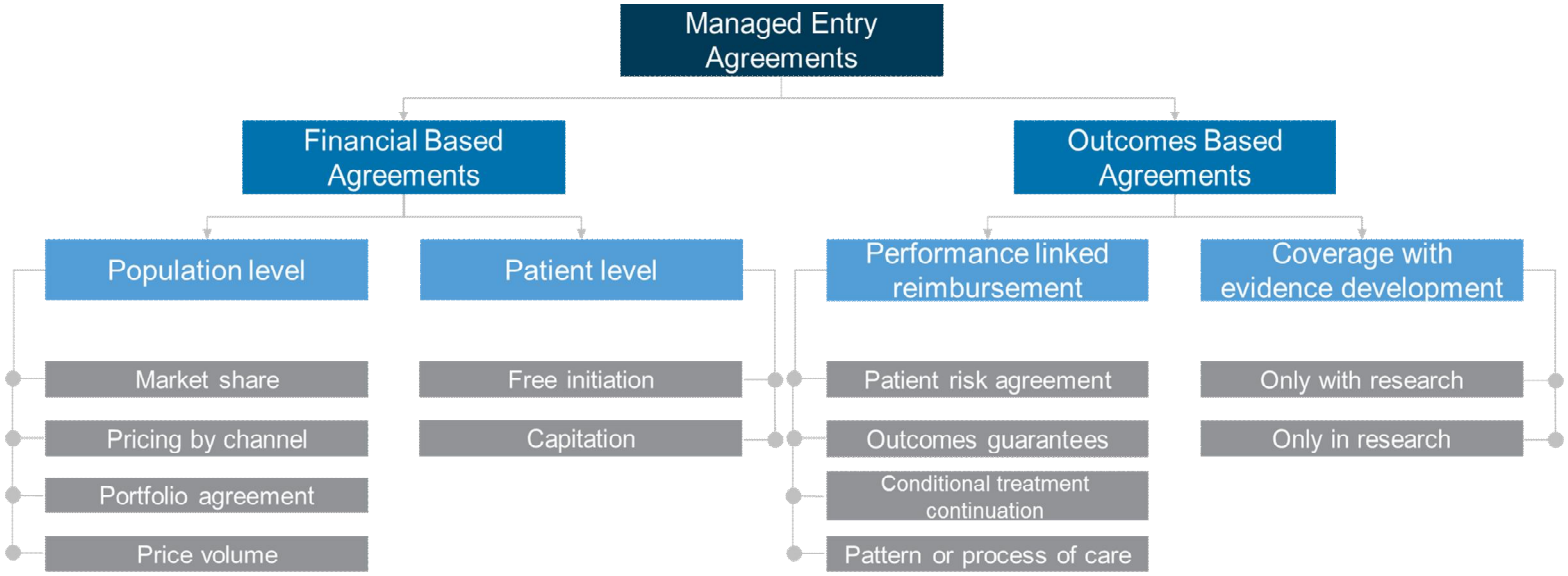
CRA Charles River Associates

Agenda

- Development of managed entry agreements
- The evolution of MEAs to reflect new challenges
- Potential solutions

The use of financial and outcomes based agreements has evolved considerably over the last five years

- Driven by concerns about **affordability of medicines** and whether the **evidence on value** warrants the price
- European countries have **increasingly** used **contracting** (referred to as managed entry agreements - MEAs)
  - These take two main forms
  - The simplicity of financial agreements has meant most countries have focused on financial based agreements



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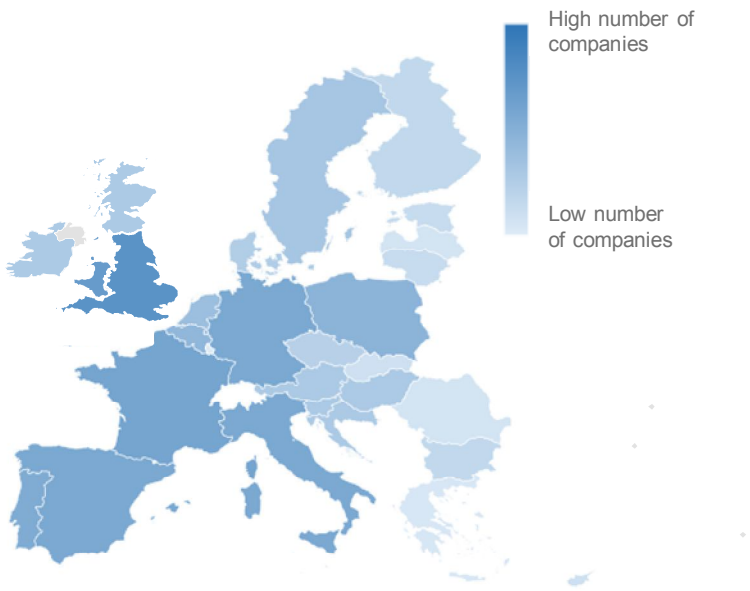
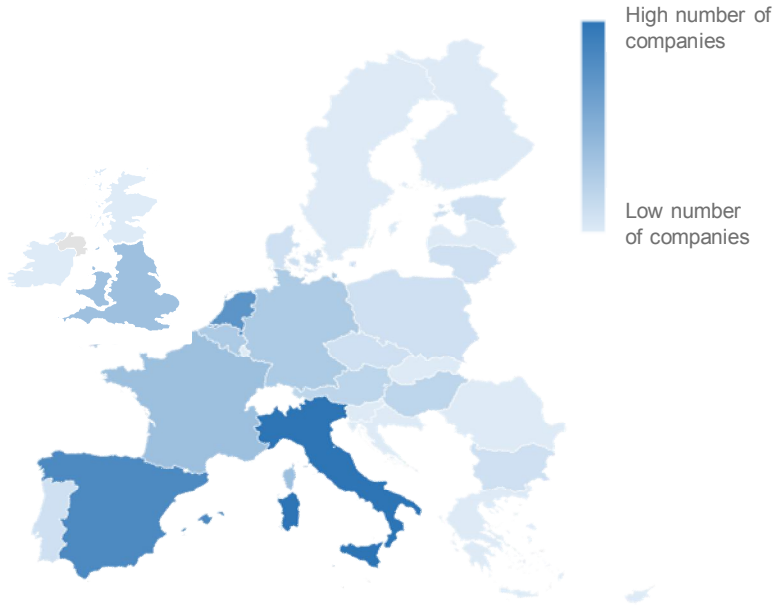
Use of MEAs is developing in many countries but focused primarily on Financial based MEAs

Total number of companies initiating Financial Based MEAs in 2015 to 2017*



Total number of companies initiating Outcomes based MEAs 2015 to 2017*



- Companies initiate financial based MEAs widely across the EU.
- However, in the last three years (2015-2017), outcomes based MEAs have been initiated in many markets across the EU with a focus on Italy and Spain in a few regions

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Most MEAs are aimed at managing budgets by creating predictability

- There are significant differences in the use of MEAs by country
  - Outcome based agreements: Italy, the Netherlands Spain
  - Financial based agreements: France, England

- Most countries have focused on simpler, financial based agreements
  - But this reflects faster growth in financial agreements (rather than slow down in outcomes based agreements)
  - Use of MEAs is still a minority of products in most countries

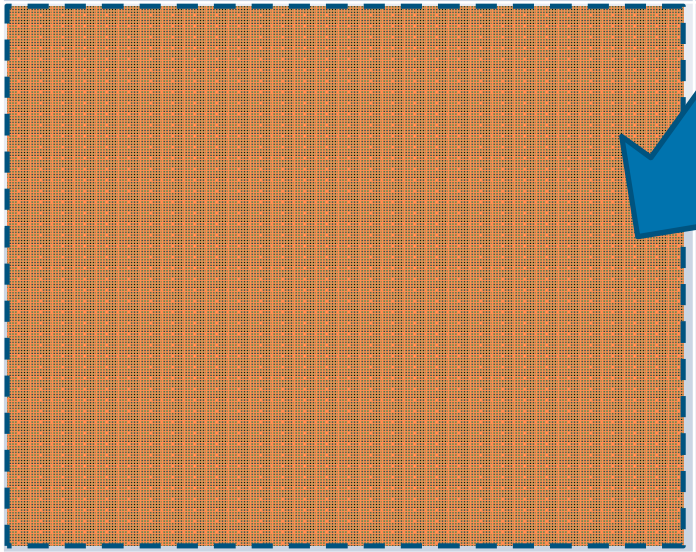
- Most MEAs are designed to reduce uncertainty
  - Budgetary
  - Usage
  - Clinical performance
  - Alignment of prices with value

The relationship between underlying cause and type of MEA

Issue	MEA solution
Budget Uncertainty: Management of budget impact	**Financial agreements:** PVAs, budget caps, dose caps, discounts, and price-match with comparator, free initiation
Value Uncertainty: Management of value for money (utilisation to optimize performance)	**Outcomes agreements:** Performance linked agreements, Conditional reimbursement for limited time with parallel collection of additional evidence on drug effectiveness, Reimbursement decisions updated post assessment of new evidence
Clinical Uncertainty: Management of uncertain or unacceptable clinical and or cost-effectiveness	

The relationship between underlying cause and type of MEA

Issue	MEA solution
Budget Uncertainty: Management of budget impact	**Financial agreements:** PVAs, budget caps, dose caps, discounts, and price-match with comparator, free initiation
	C omes agreements: ormance linked agreements, onditional reimbursement for limited time with parallel collection of additional evidence on drug effectiveness, Reimbursement decisions updated post assessment of new evidence



New medicines are leading to a range of new challenges

Multi indication/combination based products

- Number of assessment/agreements
- Different value per indication
- Tracking usage

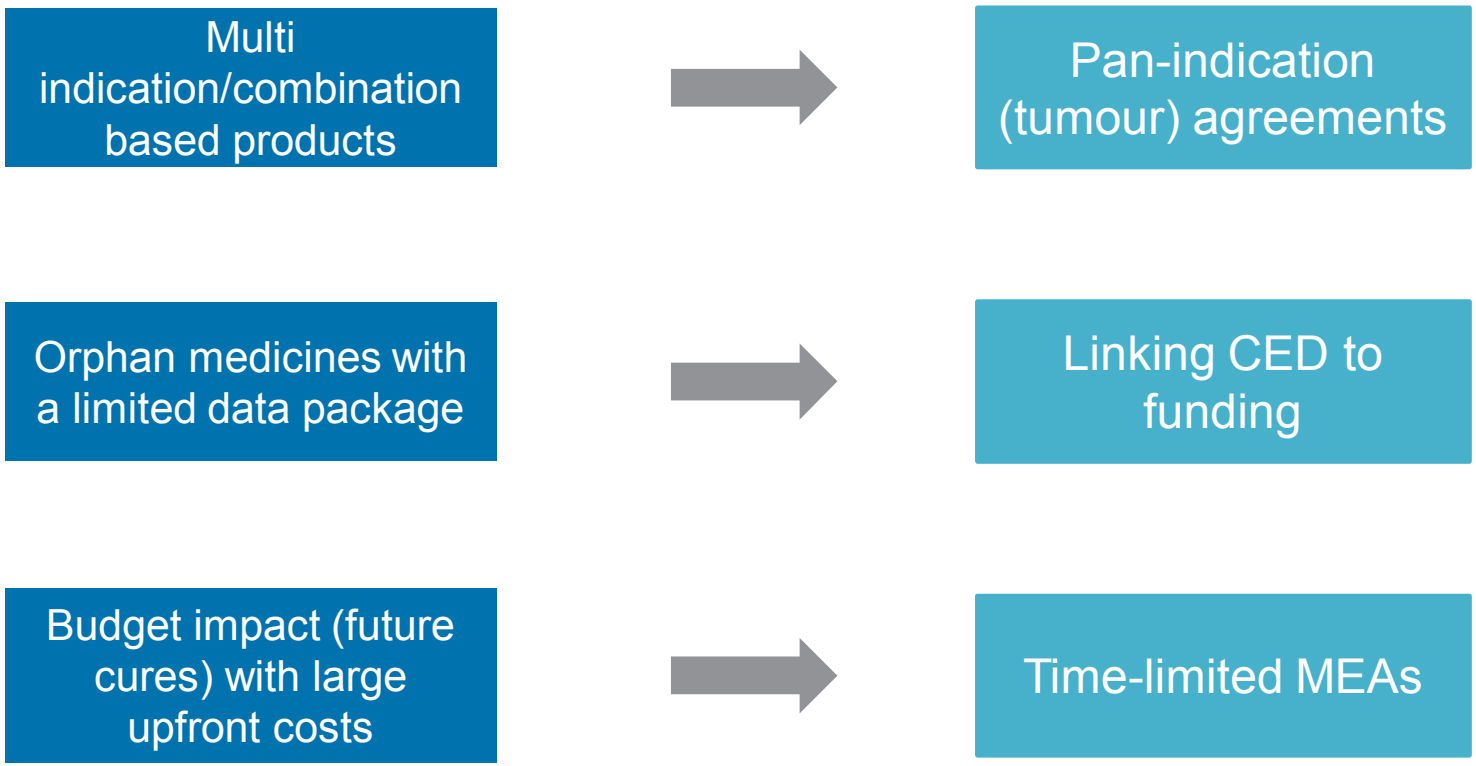
Orphan medicines with a limited data package

- Requirement of evidence development
- Reassessment

Budget impact (future cures) with large upfront costs

- Limiting budgets
- Maintaining competition

Changing nature of innovation is leading to MEAs evolving to reflect challenges to payer



Novel agreements allocating spending to new medicines has accelerated access

- On 1 January 2017, Belgium implemented a **new reimbursement system** for all PDx immuno-oncology products with a **segregated and capped budget**.

A full price-and-reimbursement process is only **required for the first indication**.

All **subsequent indications** are **automatically reimbursed**, once approved by the EMA, in line with the EMA label and without restrictions.

One **master MEA contract** for all IOs and all indications within the class.

List prices can **remain different** and do not change with new indications.

Accelerated **time to patient**

A **budget cap** is set based on budget estimates by the Belgian Sick Insurance Agency and revised every 3 years.

If the **cap** is **exceeded** – companies are required to make a refund, based on respective market share (net turnover).

Time-limited managed entry agreements

MEAs and competition

- There is a tension between MEAs negotiated at launch and exploiting competition of new entrants into therapeutic classes
- This is particularly evident for hepatitis C (HCV) where multiple competitors were anticipated
- This lead to evolution in the use of MEAs in a number of EU markets

Price negotiation for anti-HCV

The agreements reached were innovative for the Italian system:

- Listed a set of **criteria** for types of **patients** to be reimbursed
- Included a **procedure of de-listing** of drugs that share similar indications, when **higher efficacy drugs** are available ensuring continuity of care.

Mandatory **renegotiation** of listed drugs within specified time periods occurs to ensure treatment with drugs with increased efficacy and the best cost-benefit ratio.

Linking agreements on evidence development to funding

MEAs and dedicated funds

- Over the last few years, many countries have developed ring-fenced funds for innovative medicines.
- There vary in terms of focus
  - Innovative medicines
  - Orphan medicines
  - Therapy areas specific funds: Oncology, HCV medicines
- Increasingly eligibility for funding depends on HTA appraisal and MEA

Cancer Drug Fund (CDF)

- All cancer drugs/indications appraised by HTA body (NICE)
- **Early funding option** available, through new interim funding arrangements and clear entry and exit points for drugs in the CDF
- **Managed Access Scheme (MAS)** between NHS England and pharmaceutical companies, setting out the terms of a drug's entry into the CDF, and the means for data collection necessary to resolve uncertainty relating to clinical and cost-effectiveness over a 2-year period
- **Fund pays for medicines** where **evidence is not robust enough.** To allow for a final decision to be made, the drug could be recommended for the CDF

The use of MEAs in CEE markets

- Use of MEAs has increased in CEE countries since the mid-2000s
  - This reflects change to legal framework (Bulgaria, Croatia, Hungary, Latvia, Poland, Romania and Slovenia)
  - Evolution in the process of price negotiation (Estonia)

- The majority of MEAs are financial, but there is growing number of performance-based MEAs
  - Addressing uncertainty in clinical effectiveness and/or cost-effectiveness and appropriate utilisation were identified as policy goals, as well as limiting budget impact

MEAs are not a panacea: there can be advantages and disadvantages depending on where and how they are used

	Advantages	Disadvantages
Patients	• Greater access to promising treatments • Further innovation promoted • Potential for future influential involvement in design • Possible greater influence as reimbursement no longer binary	• Administrative burden • Possible withdrawal at the end • Data protection issues • More robust research not done • Limited engagement opportunities
Payers / Providers	• Encourages products to show value • Avoid trade-off between spending and access • Build evidence base • Limit total budget impact • More cost effectiveness: VBP	• Costs & bureaucracy • Uncertain accuracy of reporting system • Difficult to withdraw technologies if ultimately fail • Limited ability to assess and implement evidence • Uncertainty in expenditure
Manufacturers	• Access for new therapies • Best product performance through targeted use • Mitigation pricing spillovers • Better public image	• Costs & bureaucracy • Lost price / volumes if targets are not reached • Challenge to business model if use increases

Source: CRA (2014)

Conclusions

- The use of MEAs varies from country to country reflecting the needs of health care system, the infrastructure, experience

- There are a range of different types of MEA that can be useful – both financial and outcome based MEAs can be used to manage budgetary and clinical uncertainty
  - No single solution
  - Simple solution are usually preferred
  - Some confidentiality is an important pre-requisite for use of MEA

- It takes time to for the use of MEAs to develop

- MEAs can offer win-win solution benefiting patients, healthcare system and innovators
  - Predictability, value for money and money for value, timely access