MANAGED ENTRY AGREEMENTS (MEA)

Perspective

Challenges

Potential Solutions
Managed Entry Agreements (MEAs) are classified into financial or outcomes-based agreements

**FINANCIAL BASED AGREEMENTS**

- Price-volume agreements - Price discount (rebates/discounts over a pre-agreed % of sales)
- Cost capitation (per patient) - Portfolio agreement (discounts based on manufacturer’s portfolio)
- Discounted initiation (free/discounted product during initial treatment phase)
- Pricing by channel (discount on certain products/channels e.g., hospital vs. retail)
- Cost spreading or annuity-based (payment spread across a period of time)

**OUTCOMES BASED AGREEMENTS**

- Performance-linked agreements (e.g. where companies provide a refund or provide free goods if the desired clinical outcomes are not reached)
- Coverage with evidence development or conditional reimbursement (reimbursement linked to the development of additional clinical value and cost-effectiveness evidence that can be re-submitted by the manufacturer after a few years for re-evaluation)

Managed Entry Agreements – Arrangement between a manufacturer and payer/provider that enables access to a health technology subject to specified conditions
Both financial and performance-based arrangements have their specific advantages and disadvantages.

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<tr>
<th>FINANCIAL BASED AGREEMENTS</th>
<th>OUTCOMES BASED AGREEMENTS</th>
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<tbody>
<tr>
<td>▪ Reduce budget impact uncertainty and average cost per patient</td>
<td>▪ Show manufacturer’s trust in the product and solves uncertainty around efficacy results</td>
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<td>▪ Support list visible price for international referencing</td>
<td>▪ Help maximize access and revenue/price potential</td>
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<tr>
<td>▪ Do not require sophisticated infrastructure</td>
<td>▪ Protect visible price for international referencing</td>
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<td>▪ Do not address concerns on product-specific performance issues</td>
<td>▪ Low effect on budget impact uncertainty and limited support in reducing the average cost per patient</td>
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<tr>
<td>▪ Do not avoid risk of access restrictions</td>
<td>▪ Require a sophisticated infrastructure</td>
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<tr>
<td>▪ Can reduce the potential for maximizing revenues/price</td>
<td>▪ Risk of potential revenue loss if efficacy is not finally proven in real-life experience</td>
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Usually, financial arrangements are preferred over performance-based arrangements as first negotiation options, unless products are submitted with immature data or have uncertainty around real-life results.
Outcome-based agreements (MEAs) have historically presented stakeholders with multiple challenges

Challenges in measuring, tracking and assigning causality to outcomes:

1. Hard to define and measure specific outcomes of interest
2. Difficult to assign causality to the treatment subject to the MEA (OS in cancer, people could die because another treatment did not function well, etc...)

Requires sufficient infrastructure: data systems, analytics and related infrastructure are complicated, and necessitate meaningful investments

Monitoring and management of burdens: many deals impose transaction costs, and payers may not have sufficient resources to devote to tracking and adjudicating multiple MEAs across TAs

Privacy issues: data and patient privacy rules create substantial operational challenges – while some MEAs in small populations can unintentionally identify a patient

Too many customized deals: multiple manufacturers pursuing different MEAs requiring different infrastructure, outcomes and monitoring
As a result, most markets have favored financial deals, impeding a move towards outcomes-focused health care systems.
However, recent and expected market evolutions are driving a renewed interest in traditional and novel MEAs.

1. Market evolutions are renewing interest in traditional outcomes-based MEAs and making novel agreements possible, like pricing by indication, annuity-based agreements for novel therapies such as cell and gene therapies, special agreements for combination therapies, etc...

2. Novel MEAs can either fall in the two broad buckets of financial or outcomes-based, or be a combination of financial-and outcome-based

3. This renewed interest is being driven by the need to incentivize innovation, facilitate earlier access to valuable medicines (while managing risk) and optimize the use of combination regimens.
And while barriers to change, such as faster innovation cycle and increased RWE generation, exist...

Innovation cycle is becoming faster:
1. Competition enters the market quicker e.g. Hepatitis C, IOs, CDK4/6, etc...
2. Resulting in earlier competitive pressures on prices and reduced need for MEAs to manage

Faster innovation cycle means Standard of Care (SOC) changes faster leading to traditional long-term MEA designs do not account for this

Changing power of payers and physicians leading to the implementation of clinical pathways, reducing the ability of pharmaceutical companies to inform product access / uptake through MEAs

Increasing generation of RWE means that manufacturers can use RWE to differentiate and it does not need to be in the form of a MEA

New therapies, such as cell therapies present a new barrier given that treatment is a process that can continuously improve; this means that MEA design would need to account for this
<table>
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<tr>
<th>Challenges</th>
<th>Description</th>
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<tbody>
<tr>
<td>Uncertainty about clinical impact or value</td>
<td>Stakeholders question whether products will work as shown in trials – especially for shorter and / or smaller trials. Avoid paying for or prescribing ineffective therapies.</td>
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<tr>
<td>Uncertainty about budget impact, cost or affordability</td>
<td>Still scarred from HCV, payers worry that treatment volume will exceed expectations. Limit exposure to unanticipated costs and keep expenditure below certain levels.</td>
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<tr>
<td>Uncertainty about patients</td>
<td>Physicians and payers want to know which patients to treat, and in which a response is most likely. Expect a defined benefit in a defined population.</td>
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<tr>
<td>Transaction and monitoring cost</td>
<td>Resources (including time) are scarce. Products or contracts that impose substantial monitoring requirements may be met with skepticism.</td>
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...and stakeholders have already begun to look for ways to support novel MEAs / innovative pricing models

### INNOVATIVE FINANCING MECHANISMS

- European financing mechanisms are evolving to allow for the incorporation of outcomes:
  - UK Cancer Drugs Fund (CDF) – allows early access while further data is being collected
  - Pan-KK Insurance Fund, Germany – allows for performance-based agreements to provide rebates to a central fund overcoming issue of switching insurers during treatment

### DATA COLLECTION ANALYSIS ADVANCES

- Collaborative efforts to improve data collection have started to see results in terms of tracking patient outcomes:
  - Collaboration for Oncology Data in Europe (CODE)
  - European anti-cancer medicines usage data network established by Quintiles IMS with support from leading pharmaceutical companies:
    - EuResist Network
  - Among the largest HIV databases; collaboration between manufacturers, HC systems and research groups

### NEW INNOVATIVE MEA PROPOSALS

- Industry working increasingly closely with stakeholders to generate MEAs that are mutually beneficial:
  - Amgen and Celgene jointly agreed with Swiss payers a combination regimen price that a) allowed access to an important regimen of 2L MM; and b) shielded both from large, referenceable price decreases, thus preserving incentives to innovate
  - CEPS (France) secured a money-back guarantee as an MEA with Gilead for Sovaldi in case of treatment failure

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**External stakeholder driven**

**Pharmaceutical industry driven**
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<tr>
<th>Policy Environment</th>
<th>Unreasonable expectations on who owns the risk</th>
<th>Can fall overly on the manufacturer (also the payer, provider or patient)</th>
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<td>Pile-on</td>
<td></td>
<td>When multiple controls are layered on top of each other: HTA, Budget Impact, Reference Pricing and… MEA.</td>
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<td>Procurement system challenge</td>
<td></td>
<td>Bids and tenders based systems are not suitable for MEA as seeking a race to the bottom only</td>
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<tr>
<td><strong>Data and infrastructure</strong></td>
<td>Administrative challenges</td>
<td>Costs and practicalities of administrating a complex agreement can be high</td>
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<td>(barriers to all stakeholders)</td>
<td>Poor data</td>
<td>Where access to data is limited, or quality is poor or if there is an inability to measure the results</td>
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Success by design: policy framework is key…

- VOLUNTARY
- CLEARLY DEFINED MEASURES
- CLEARLY DEFINED TIMELINE
- CLEARLY DEFINED ADMINISTRATION AND GOVERNANCE
- IMPACT ON ACCESS AGREED
- CONFIDENTIAL

POLICY REQUIREMENTS
Data must be sound and well managed...

<table>
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<tr>
<th>ACCESSABILITY</th>
<th>ORIGIN</th>
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<td>DATA AND SITE MANAGEMENT</td>
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<table>
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<tr>
<th>RELIABLE AND CREDIBLE VALIDITY</th>
<th>QUALITY</th>
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<tr>
<th>GENERALIZABLE AND REPRESENTATIVE TIMELY UTILITY TO SPECIFIC OBJECTIVES SUFFICIENCY (COMPLETE, SAMPLE SIZE, ETC...)</th>
<th>RELEVANCE</th>
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Managed Entry Agreements represent an approach to allow patient access in an environment of financial and/or clinical uncertainty. Such agreements can be complex and are often tailored to the specifics of the uncertainty, payer and environment.

Ensuring a fair policy environment can reduce barriers to company engagement in such agreements. Many forms of these agreements also require sound, well-managed data.

Adding another measure to existing cost control solutions (International Price Referencing, HTA, PVA, discounts, etc...)
Challenge:
A company presents for HTA approval an oncology product (riccumab) that has a one month survival rate. The cancer type has typically poor survival (e.g., average 1 month from diagnosis). This introduces the concept of relative benefit (i.e., +one month is meaningful if a person has only one month to live, not so much if the person has 48 months).

The product also has a poorly defined tail (i.e., while the average is one month, a few will survive many months and maybe even a year). The point here is also 1) to show that decisions are not simple, 2) to show there are limitations of an average value, and 3) to help justify why a payer might consider one month as worth considering for reimbursement.

The HTA believes overall that this product falls short of the QALY and requests a risk sharing agreement.

How would the group design it? What would be their considerations for the MEA?