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A RAPID REVIEW OF KEY CHALLENGES AND SUCCESS FACTORS IN IMPLEMENTING MANAGED ENTRY AGREEMENTS FOR PHARMACEUTICALS: LESSONS FOR GREECE

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Background & Objective

To explore utilization trends and to identify challenges and key factors for successful implementation of Managed Entry Agreements (MEAs) for pharmaceuticals, in order to inform local policy and decision-making.

Methods

A rapid evidence review was conducted. A systematic search was performed in April-May 2024 in PubMed/Medline and Scopus. The review included articles in English that discussed experience with MEAs internationally. Theoretical pieces and conference abstracts were excluded. The search was limited to articles published from 2014 onwards. Title, abstract and full text screening was performed by three researchers. Data on MEA types, barriers/challenges, success factors and advantages were extracted into standardized tables. A pilot test was conducted on a random sample of studies to ensure consistency in data collection.

Results

60 studies were included in the review. Various MEAs are used internationally which aim to mitigate budget impact, address uncertainties in clinical and cost-effectiveness, ensure appropriate clinical use, and enhance patient access to promising therapies. According to published data, MEAs are more frequently implemented in oncology, neurology, rheumatology, and endocrinology and also in the case of medicines for rare diseases and advanced therapies (Table 1).

Table 1. Most commonly implemented MEA types and therapeutic areas

Country	MEA Type	Therapeutic Areas
Spain	Risk-sharing agreements, Financial-based agreements	Oncology, Neurology, Rheumatology, Rare Diseases
Italy	Risk-sharing agreements, Performance-based reimbursement, Financial-based agreements	Oncology, Rare Diseases, Non-oncology
United Kingdom	Coverage with Evidence Development (CED), Performance-linked reimbursement, Financial-based agreements	Oncology
Belgium	Volume-price agreements, Discounts, Financial-based agreements	Oncology
Netherlands	Volume-price agreements, Performance-based agreements, Financial-based agreements	Oncology, Rare Diseases
Ireland, Austria, Norway	Performance-based reimbursement	Oncology, Rare Diseases, Advanced Therapies
Bulgaria	Volume-price agreements, Discounts	Inflammatory Diseases, Rare Diseases
Australia	PBRSA, CED, Volume-price agreements	Cancer, Rare diseases, Chronic diseases
Canada	Financial-based, Performance-based	Oncology, Rare diseases
South Korea	Expenditure caps, Utilization caps, CED	Cancer, Rare diseases
United States	Financial-based, Outcomes-based	Oncology, Rare diseases
Argentina	Financial-based	Oncology, Rare diseases
Saudi Arabia	Risk-sharing agreements	High-cost treatments
Iran	Financial-based	High-cost treatments
Malaysia	Financial-based, Outcomes-based	High-cost treatments

Key success factors include the development of a guidance framework; engagement and commitment of stakeholders; communication and transparency; reliable data collection methods and systems; and adjustment of the legal/regulatory framework.

Table 2. Key Success Factors for MEAs

Key Success Factors	Outcomes-Based Agreements (OBAs)	Performance-Based Risk-Sharing Agreements (PBRSAs)	Financial-Based Agreements	Coverage with Evidence Development (CEDs)
Regulatory Framework & Guidelines	Clear regulatory processes, guidelines, and alignment of contract timelines with outcomes.	Well-defined, measurable outcomes; regular reviews for payment adjustments.	Flexible legal frameworks; simplified negotiation processes.	Engagement of stakeholders; tailored duration of agreements.
Data Collection & Infrastructure	Robust infrastructure for tracking outcomes; risk-sharing models.	Strong information systems; real-time data collection and outcome analysis.	Predictable budgeting and transparent economic forecasting.	Clear data collection frameworks; use of international guidelines.
Stakeholder Collaboration & Trust	Transparency and trust via data sharing; collaboration with all parties involved.	Collaboration between payers, providers, and pharmaceutical companies.	Incentives for collaboration among stakeholders.	Structured stakeholder engagement; emphasis on long-term evaluations.
Outcome & Risk Management	Adequate risk-sharing between payer and producer.	Use of technological tools for patient-reported outcomes (PROs).	Alignment of pricing with international benchmarks.	Continuous evaluation of clinical effectiveness based on collected evidence.

MEAs (especially performance-based ones) face significant challenges including, but not limited to, methodological adaptation for real-world outcomes assessment, transparency and data collection issues, streamlining administrative processes, infrastructure issues, and engaging healthcare professionals effectively. Integrating patient-reported outcomes (PROs) and navigating data collection issues further complicate MEA effectiveness.

Table 3. Barriers and Challenges per type of MEA

MEA Type	Key Barriers/Challenges
Outcomes-Based Agreements (OBAs)	- Difficulty in selecting appropriate outcomes and managing confounding factors. - Infrastructure requirements for data collection and analysis. - Limited transparency and trust among stakeholders. - Financial risks due to outcome uncertainty.
Performance-Based Risk-Sharing Agreements (PBRSAs)	- Data collection complexity, particularly for real-world outcomes. - High administrative burden and resource needs. - Long-term financial sustainability challenges. - Legal and confidentiality issues.
Financial-Based Agreements	- Economic uncertainty and pricing negotiation challenges. - Market fluctuation risks (e.g., introduction of new competitors). - High administrative costs and lack of transparency in financial data. - Limited regulatory frameworks for effective implementation.
Risk-Sharing Agreements (General)	- Methodological challenges (e.g., defining clinical outcomes). - Fragmented health data systems impacting evidence generation. - Limited human resources and technical expertise. - Unclear legal frameworks for innovative contracting.

MEAs improve patient access to new therapies by aligning reimbursement with treatment effectiveness and managing healthcare costs. Through real-world data collection, cost-sharing, and performance-based metrics, MEAs reduce clinical uncertainties and ensure financial sustainability. This approach balances innovation, cost control, and patient-centered outcomes, supporting effective and efficient healthcare delivery.

Table 4. Advantages of MEAs

MEA Type	Advantages/Benefits
Outcome-Based Agreements (OBA)	- Mitigates uncertainty on clinical and economic outcomes by aligning reimbursement with real-world value. - Valuable for disease-modifying therapies, though implementation faces challenges. - Improves healthcare outcomes and budget management. - Enables early patient access and price predictability. - Focus on effectiveness incentivizes R&D for new therapies.
Coverage with Evidence Development (CED)	- Facilitates early access to innovative therapies while collecting real-world evidence on effectiveness and safety. - Reduces uncertainties by evaluating clinical and cost-effectiveness under real-world conditions, allowing for better-informed decisions on long-term funding. - Supports adaptive approaches, enabling iterative assessments as more data becomes available.
Financial-Based Agreements (e.g., Cost-Sharing)	- Helps manage budget impact by setting financial caps, rebates, or shared costs between payers and manufacturers. - Improves affordability and access by focusing resource use on patients most likely to benefit. - Increases predictability of healthcare expenditures, as agreements often define maximum spending limits or cost thresholds.
Performance-Based Risk Sharing Agreements (PBRSA)	- Links reimbursement to defined performance metrics, such as patient adherence, health outcomes, or biomarker improvements. - Encourages efficient resource allocation by tying payment to treatment success or predefined clinical benchmarks. - Enhances transparency and accountability by using measurable, agreed-upon outcomes, which can guide future reimbursement decisions and policy adaptations.

Conclusions

MEAs have emerged as a means for payers to address issues of affordability, uncertainty and access to new medicines; their successful implementation depends on overcoming multiple challenges. Greece has some experience with financial-based MEAs, but has not yet exploited the potential of performance-based MEAs for managing access to new medicines. Lessons learned from international experience can support decision-making on the introduction of such schemes.

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