Launch prices of new drugs have increased substantially during the past decades, posing a challenge to health care and reimbursement systems. Prices of new drugs entering the market, especially for treatment of cancer disorders or rare diseases, often exceed $100,000 per patient and treatment year. Many more of these drugs have been approved via the accelerated approval pathway in the US or equivalent pathways in other countries, which has been followed by immature evidence with uncertainty about the drug’s actual therapeutic value. The combination of high prices and immature data poses challenges to payers. As a tool to achieve access for patients to new, high-priced drugs while managing uncertainty, so-called managed entry agreements (MEAs) have been implemented in many countries (eg, the United Kingdom, Italy, Switzerland, France, and Australia).

Based on the World Health Organization definition, MEAs are arrangements between a manufacturer and payer or clinician that enable access to (coverage/reimbursement of) a health technology that is subject to specified conditions. Several types of MEAs exist. The main types of MEAs are finance based, performance/outcome–based agreements, or a mix of both systems. Finance-based MEAs are characterized by their aim to contain costs and facilitate the affordability of a product irrespective of the patient’s health outcome (eg, by determining a price/volume cap or providing an often confidential discount). Outcomes-based MEAs aim at reducing uncertainties surrounding the therapeutic value of a drug and focus on the patient’s outcome. Examples are performance-linked reimbursement schemes in which the reimbursement of drugs is tied to the measure of treated patients’ health outcomes or to adjust the price dependent on additional evidence the manufacturer is mandated to provide (coverage with evidence development).

While the number of drugs with MEAs has increased during recent years, the financial effect of MEAs is not yet well understood, which is an important question for policymakers that is addressed in this issue of JAMA Health Forum in the study by Trotta et al. They demonstrated that 62 new drugs were granted an MEA and generated paybacks between 2019 and 2021 in Italy, one of the first countries that introduced MEAs. In approximately half of the cases, financial-based MEAs were applied and most of the drugs were for treatment of cancer disorders. A total payback amount of €327.5 million ($357.9 million) was collected, which corresponded to a median share of payback compared with the overall expenditure on the medicines included in the analysis of only 3.8% and only 0.8% of the overall expenditure for drugs purchased by public health institutions in Italy, suggesting that MEAs only have a modest budget association. Their findings are consistent with previous studies and policy reports that have suggested the limited budgetary effect of MEAs.

Why do MEAs not hold their promise? Trotta et al outlined that identifying clinical thresholds and measures of relevant health outcomes is challenging and established at market entry when uncertainties exist. The lack of clear definitions of the clinical threshold, the outcome measure, and the assessment time may contribute to the low financial association of MEAs. The authors further outline that MEAs are extended after expiration despite the lack of inclusion of additional evidence to resolve clinical uncertainties.

A further reason may contribute to the unsatisfactory financial association of MEAs: many countries with MEAs rely on external reference pricing as a major determinant in price negotiations. External reference pricing is the practice of benchmarking drug prices against those in other economically similar countries. This system has a major flaw. In general, the referenced prices are official list prices instead of actual net prices paid and determined in MEAs. Consequently, countries using external reference pricing systems overestimate actual prices, which is associated with
escalating drug prices across countries, an opaque upward spiral that cannot be successfully reversed by opaque MEAs.

What approaches can be taken to overcome the drawbacks? First, MEAs should be applied cautiously and with a clearly defined set of rules in terms of relevant health outcomes, compliance with a strict period during which new evidence must be provided, and there should be stricter monitoring. Ideally, this information would be shared publicly to also help other countries to make informed decisions. As outlined by Trotta et al, lack of compliance should not be associated with the extension of the MEAs under the same conditions, but should rather be followed by predefined consequences to discourage a delay in the submission of new evidence.

Second, countries that have incorporated MEAs should use the study of Trotta et al as a motivation to (regularly) analyze the financial effect of MEAs in their own country and share the results publicly. This is all the more crucial because many countries have introduced MEAs for an increasing number of drugs during the past years with only limited understanding of the actual financial effect. A periodic evaluation helps to make informed decisions on the application of well-designed MEAs for specific drugs with the goal to improve affordability for patients of drugs with (potentially) high therapeutic value.

Third, more transparency on the actual prices paid for drugs for which MEAs have been applied are indicated, as also outlined in the World Health Organization resolution in 2019. In the absence of transparency, countries should consider excluding external reference pricing as a price negotiation determinant.

In August 2022, the Inflation Reduction Act was signed into law, which will allow Medicare to negotiate the prices of a limited number of drugs from 2026 onwards. The US Centers for Medicare & Medicaid Services published information to provide more specific guidance on how they intend to do so. In sum, the starting point for an initial offer will be based on the net price of therapeutic alternatives, with a ceiling price based on the lower end of either a percentage of the nonfederal average manufacturer price or the average current net price to Part D plans. This initial offer can be adjusted upward or downward based on several factors, including the research and development costs or the federal support for the drug's discovery. MEAs have not been a specific discussion point in the recent memorandum, but may evolve in the future as a possible arrangements for price negotiations of drugs.

The introduction of MEAs across countries has proliferated in recent years, and this trend will likely continue in the future. Cautious application with a clearly defined set of rules, periodic assessment of the financial effect, and more transparency would be beneficial to improve access of patients to drugs with (potentially) high therapeutic value across countries.

ARTICLE INFORMATION

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REFERENCES


