

Moving from a "single price mechanism" to an "indication-based mechanism":

Quo vadis?

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Introduction

Given its innovative nature and its potential to cure, innovative medical technologies provide a high added value to patients. It also causes a transformation pressure for payers and producers.

Advanced Therapy Medicine Products (ATMP) (but not only) are developed with the intention of treating multiple indications, reflecting a growing trend towards indication-based pricing (IBP). This approach is economically driven. Thus, IBP has received considerable attention due to the expected future growth in its use. The model has gained traction and is under debate in literature.

Indication-Based Pricing tailors drug prices based on the value the drug provides for each specific indication. The idea is that a drug might provide significantly different levels of benefit for different conditions, and the price should reflect this variability.

Evidence on how IBP is utilized in practice, its impact and consequences is still scarce. Thus, the aim of this paper is to discuss differential pricing per indication, describe the different types of IBP schemes and assess their attractiveness, barriers, challenges and opportunities.

Challenges with single pricing

As early as in 2014, Peter Bach, then Head of the Health Policy and Outcomes Center at Sloan Kettering, advocated for indication-based pricing, particularly in oncology, where drugs often have multiple indications but vary significantly in effectiveness across them. The rise of orphan drugs and personalized medicine has since amplified the need for differential pricing by indication, as the pressure to tailor costs to clinical value has grown considerably. In particular, the area of targeted and promising innovative technologies, where treatment is based on the genetic profile of the tumour rather than its origin, is increasingly coming to the fore for IBP.

The current pricing and reimbursement frameworks, which generally target a single indication per medication, are not adequately designed to address the complexities of multi-indication therapies. Consequently, countries are navigating the challenges of indication-based pricing through indirect methods, frequently relying on pragmatic negotiations and political discretion to determine value. This approach,

however, lacks the rigor of evidence-based decision-making and may result in suboptimal outcomes, both in terms of patient access and the efficient allocation of healthcare resources.

A single price policy refers to a traditional pharmaceutical pricing strategy where a drug is priced uniformly across all indications or therapeutic areas. While this approach is common, it poses challenges related to efficiency and equity.

Under this model, payers may be discouraged from covering lower-value indications if the uniform price is disproportionately high compared to the clinical benefit, potentially limiting patient access.

Additionally, manufacturers may be hesitant to invest in developing new indications, as the inability to adjust prices for different uses can lead to insufficient demand, making it difficult to recover fixed investment costs.

Indication-based pricing has been proposed as a more flexible alternative. This approach allows drug prices to vary by indication, ensuring closer alignment between the price and the value delivered in each therapeutic area.

Current best practices for IBP

Current best practices in key markets for pricing focus on finding the right approach for medicines that treat multiple conditions, especially in the case of rare diseases and cancer drugs. These drugs often provide different levels of benefit depending on the condition they treat, making it difficult to set a fair price.

The idea of pricing medicines differently based on the indication they treat, could help match the price of a drug more closely to its value for each indication. This could also make the pricing system more efficient, as each condition would be assessed separately, avoiding the influence of one indication's price on others. It could also help make these drugs available to patients more quickly.

Despite its potential, Indication-Based Pricing is not widely implemented in major markets. Instead, many countries opt for flexible solutions to manage the pricing of multi-indication drugs, typically through negotiations and adaptable agreements rather than a straightforward IBP approach.

Full adoption of IBP is often viewed by key stakeholders as complex, with significant challenges

that need to be addressed before it can be widely implemented, including:

1. **Regulatory barriers:** Current pricing systems are mostly set up to use a single price for a drug, making it hard to apply different prices for different indications and conditions.
2. **Administrative difficulties:** Tracking drug use by indication and managing different prices can create extra work and increase the administrative burden, often resulting in delay of access.
3. **Arbitrage risks:** There's a risk that some hospitals or organizations might buy the drug at a lower price intended for one condition but use it for a more expensive one.
4. **Constrained healthcare budgets:** Pressure on budgets are triggering greater scrutiny on the cost of multi-indications therapies.

In the literature on how IBP is applied in practice, the most common forms include:

- **Different brands for each indication**
 - This approach allows each brand to be assessed as a separate product. However, it can become complex when dealing with very similar indications, treatment lines, or patient groups.
 - It has enabled the application of different prices per brand in almost all major markets.
- **A single weighted average list price across indications**
 - This price reflects the weighted average of either the volume, value, or both for the various indications.
 - The volume can be estimated in advance (ex ante) or reconciled afterward (ex post) through rebates, based on the actual number of patients for each indication.
 - This is widely considered the simplest approach to implement, but it requires strong data collection systems, as patient-level information by indication is typically not tracked.
- **A single list price based on the highest-value indication or a cost-effectiveness threshold**
 - Net prices vary by indication according to their individual volume, value, or a combination of both.
 - These net prices are often managed through Managed Entry Agreements, which involve financial discounts or performance-based arrangements by indication.
 - A single list price with differential discounting per indication (often called "secret pricing") is widely used in countries that operate a

centralized healthcare system, e.g. UK, Germany, France, Italy or in markets with a fragmented healthcare system, e.g. USA or in country with a centralized reimbursement list e.g. Switzerland.

Although these mechanisms are evolving towards models that partially align with IBP principles, they are still largely designed around the current pricing framework, which typically focuses on single-indication medicines. A pure IBP system would resolve some critical issues, particularly regarding the definition of the relevant market for each indication. By applying this concept, pricing could become more efficient, with each indication being evaluated independently, preventing one indication's price from influencing the others.

National pricing regulations used for multi-indication medicine

Since pricing and reimbursement decisions are made at the national level, there is great methodological variability in terms of addressing the challenge of IBP. Information is provided for the following countries, resp. entities:

1. France
2. Germany
3. Japan
4. Italy
5. Spain
6. The Netherlands
7. Switzerland
8. UK
9. USA
10. European Union

1. France

Current status

Several models in use: single volume- and value-weighted average price; possible post-launch price revision based on real-world evidence (RWE), different prices for different brands of the same molecule possible; for expensive drugs, e.g. gene therapy and oncology, different prices for different indications through (not published) rebates possible.

Challenges

Mainly the strict cost-effectiveness and HTA processes, which could make it difficult to implement IBP on a large scale. In addition, there are concerns about the complexity and cost of managing multiple prices for the same drug, especially when trying to balance

affordability and innovation in a government-controlled system.

2. Germany

Current status

A single weighted average price is used, reflecting the value and volume of use for different products.

Regional discounts can be applied by health plans to the national negotiated price. Manufacturers can keep the net price secret in exchange for a regulated rebate.

Challenges

While IBP is not yet explicitly part of the price negotiations, the AMNOG framework has the flexibility to incorporate such models. Given that drug prices are reassessed based on therapeutic benefit for different patient populations.

3. Japan

Current status

Japan assesses the effectiveness of a drug for different indications. If a drug is more effective for one indication than another, the pricing may be adjusted to reflect the value provided for that particular condition. After launch, if the drug is approved for a new indication, the price may be reviewed and adjusted depending on the incremental benefit or reduced efficacy for that new indication. This process ensures that prices reflect the drug's performance for each specific use case.

Challenges

Implementing multiple prices for the same drug across different indications is complex. It requires robust monitoring and data collection systems to track usage and outcomes. Additionally, negotiations between pharmaceutical companies and regulatory authorities over price adjustments can be intricate and time-consuming.

4. Italy

Current status

Single national list price, but net prices can vary across indications using Managing Entry Agreements (MEAs). Performance-based MEAs, as well as other forms of confidential MEAs, allowing different net prices for different indications. Well-developed registries owned by national regulatory authorities, which allow the application of different types of value-based pricing and financial discounts.

Challenges

Limited transparency on the agreement and value attribution criteria for each indication.

5. Spain

Current status

A single price list is agreed nationally and revised downwards for new indications based on expected volumes. However, confidential discounts can be applied at regional level.

Challenges

Decentralized system leads to lack of homogeneity in data quality and collection across regions. Data are not consolidated at national level in a timely manner.

6. The Netherlands

Current status

There is a mechanism in place that directly addresses the issue of IBP, the multi-year, multi-indication (MYMI) agreements between payers and manufacturers to ensure both rapid and broad patient access. The agreement spans multiple indications and years. Rather than treating each new indication differently, the agency designs a comprehensive framework that covers multiple indications in terms of value assessment, pricing and reimbursement. MYMI programs can include a variety of components, such as a pricing agreement that covers upcoming indications; an abbreviated upfront value assessment or no assessment for new indications; pre-launch agreements to reimburse new indications over a period of time.

Challenges

Focus primarily on high-cost drugs, such as oncology. Each manufacturer has a separate MYMI contract, the terms of which are confidential. All contracts are price-volume agreements and are reviewed annually.

7. Switzerland

Current status

The list price of an active ingredient remains the same, but the agency allows manufacturers to apply indication-based discounts (mostly confidential) to bring the net price in line with the value of the active ingredient.

This approach reduces the risk of list price erosion when a new indication is introduced. As of December 2022, there were 20 drugs listed with indication-based discounts, all for high-cost cancer products.

Challenges

Switzerland has been defined in the literature as the country where IBP is most feasible, but the number of drugs with differential indications and net prices is still limited. Widespread adoption of IBP may be difficult. There is still a lack of transparency about the relationship between price and value.

8. UK

Current status

While the NHS still largely follows a single price model, there are some opportunities to apply differential net pricing per indication, particularly in oncology and rare diseases. This is done either through the Patient Access Scheme (PAS) or the Cancer Drug Fund, or through a secret discount based on a cost-effectiveness threshold.

Challenges

Although PAS theoretically provides some pricing flexibility, it does not support IBP because only one agreement per drug (i.e., across all indications) is allowed. Due to confidentiality clauses, it is not clear whether other existing models offer a real possibility to implement IBP.

9. USA

Current status

The US largely follows a single price model. IBP is not yet widely implemented, but there is interest from certain insurers, particularly in the context of oncology drugs and multi-indication biologics. Commercial payers are open to the idea of adjusting the price of a drug based on the value it provides for each indication.

Some pharmaceutical companies have entered into pay-for-performance contracts for certain gene therapies or oncology drugs, where rebates are tied to clinical outcomes. While these agreements are still limited in number, they represent a shift toward pricing models that take into account patient outcomes and indications.

Challenges

IBP faces significant regulatory hurdles, particularly related to Medicare and Medicaid, which have complex pricing frameworks. In addition, the fragmented payer system makes it difficult to implement a consistent IBP approach. There are also concerns about the potential administrative burden associated with tracking drug utilization by indication and negotiating different prices for the same drug across multiple insurers.

10. European Union

Current status

IBP is gaining attention in the EU market, especially in light of the ongoing reforms of pharmaceutical legislation. One of the key aspects of the IBP reform is that each indication for a drug could be evaluated separately for its clinical and cost effectiveness, leading to a separate pricing agreement per indication. The

reform encourages the use of MEAs to treat IBP. There is an emphasis on the collection of real-world evidence. Pharmaceutical companies will have to demonstrate outcomes for each indication, and pricing could be adjusted in each case.

Challenges

Complexity of implementation. IBP requires sophisticated systems to track and assign prices based on use and outcomes. As pricing and reimbursement decisions are made at the national level, there is a need for better harmonization across the EU to ensure that IBP can be implemented consistently across member states.

Conclusion

Despite the significant shift and the enormous challenges associated with IBP, there are no substantial efforts being made toward a sustainable solution, neither from the demand nor the supply side. The approach is limited and aligned with a "second best" solution: optimizing as much as possible within the constraints of the existing regulatory framework.

Sources on single price policy and indication pricing

This article makes no claim to completeness and is not a scientific treatise - nor is it intended to be. Rather, the focus is on the entrepreneurial perspective. The most important literature sources used for support are:

Single Price Policy

1. Danzon, P. M., & Towse, A. (2003). "**Differential pricing for pharmaceuticals: Reconciling access, R&D, and patents.**" *International Journal of Health Care Finance and Economics*
This paper examines the rationale for differential pricing across countries and populations, but it also discusses the single-price model's implications for developed and developing markets.
2. Murphy, K. M., & Topel, R. H. (2006). "**The value of health and longevity.**" *Journal of Political Economy*
While not directly about single-price policy, this paper explores how pricing strategies can align with health benefits and innovation incentives, key considerations when moving away from single pricing models.
3. Frank, R. G., & Zeckhauser, R. (2007). "**Custom-made versus ready-to-wear treatments: Behavioral propensities in physicians' choices.**" *Journal of Health Economics*
This study explores the limitations of a one-size-fits-all approach, relevant to the single-price model in

pharmaceuticals, especially in cases where drugs have multiple indications.

Indication-Based Pricing (IBP)

4. Towse, A., & Garau, M. (2019). "**Indication-based pricing (IBP): is there a role in the UK?**"
Pharmacoeconomics

This paper examines the potential for indication-based pricing in the UK, discussing the pros and cons, especially in the context of the NHS and value-based pricing schemes.

5. Bach, P. B. (2014). "**Indication-specific pricing for cancer drugs.**" JAMA

In this influential article, Bach advocates for indication-based pricing, particularly in oncology, where drugs often have multiple uses but vary widely in their effectiveness across indications.

6. Lakdawalla, D. N., & Phelps, C. E. (2020). "**Indication-based pricing for pharmaceuticals in the US healthcare system.**" Journal of Health Economics

This paper looks at the economic and policy implications of moving towards an IBP model in the U.S. It highlights the efficiency gains but also explores the challenges in terms of implementation.

7. Garrison, L. P., & Towse, A. (2017). "**Value-based pricing and reimbursement in personalised healthcare: Introduction to the basic health economics.**" Journal of Personalized Medicine

Discusses the theoretical foundation for indication-based pricing, especially in light of value-based healthcare and personalized medicine.

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