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BLOG NOTE

MULTI-INDICATION DRUGS: CAN ONE PRICE FIT ALL?

Multi-indication drugs: Can one price fit all?

Key factors to consider when defining the market access plan of a medicine for multiple indications

Highlights

- An increasingly number of medicines have shown to be effective in more than one indication, which leads to several price setting and reimbursement challenges
- Prices of multi-indication drugs in Europe are adjusted downward to a single price based on competitive dynamics of the highest budget impact indication
- Indication-based pricing could solve some of the challenges of the current uniform price system, increase patients' access and provide incentives for research and development in certain lower-value indications. However, its implementation in Europe is still associated with major operational hurdles
- The manufacturer must perform indication launch sequencing to optimize the reimbursement of a product in multiple indications and maximize its revenues

The number of medicines marketed for multiple indications has increased considerably in recent years. In oncology, an increase from approximately 50% to 75% in multi-indication drugs was observed between 2014 and 2020[1], with specific oncology drugs being developed for multiple cancer types or for several lines of therapy within each cancer. In countries where a formal health technology assessment (HTA) is conducted, medicines are usually assessed individually for each indication before receiving positive reimbursement, but existing indications are open for discussion when a new indication is presented, especially if the new indication is associated with an increased budget impact.

The HTA evaluation of multi-indication therapies is linked to critical challenges that impact several stakeholders along the process and ultimately lead to access delays to many life-saving medicines. Apart from the administrative burden and budget pressure it poses to payers, a key challenge to reimbursing these medicines is setting a price that reflects the therapeutic value and willingness to pay for each approved indication. Although indication-based pricing (IBP) seems the most intuitive approach to establish the price of multi-indication drugs, this process is not widely implemented in the current European reimbursement landscape. Instead, prices are adjusted downward to a single price based on competitive dynamics of the highest budget impact indication. Indeed, any experienced EU access leader will tell you to choose your first indication wisely, as the price will only go down from there.

[1] Lawlor et al. Accelerating patient access to oncology medicines with multiple indications in Europe. J Mark Access Health Policy. 2021

Main factors influencing the market access of multi-indication drugs

01

The implied therapeutic value of a medicine to patients and healthcare systems varies between indications. Each indication likely demonstrates a distinct clinical and cost-effectiveness versus the original label, which would allow for price discrimination according to the indication. This concept is known as indication-based pricing (IBP), which is linked with two key issues:

- **Increased administrative burden:** each indication receives an HTA assessment in Europe, thus multi-indication drugs drastically increase the administrative burden of appraisal and many national and regional systems do not have the infrastructure, headcount or time to track individual products with indication-based prices.
- **Expansion of patient access:** additional indications expand the potential patient population, and therefore, the product sales volume. In countries that are budget impact focused (e.g., Italy, Spain), a new indication with a large population size might not receive a positive reimbursement decision without a high-risk of price erosion for all indications.

How economically attractive is IBP for both payers and manufacturers?

02

In value-based pricing markets, allowing the price to vary between indications could lead to the positive reimbursement of lower value indications at a lower, cost-effective price, and to the recognition of higher value indications with a higher price. Undoubtably, IBP would be beneficial to manufacturers as it would increase the price of higher value indications, but it would also incentivize the development and launch of the product for lower value indications without impacting the "anchor price" of the revenue-driving indication. So while IBP, and the possibility of lower healthcare budget pressure, is attractive to payers and espoused by some HTA authorities, history shows that most health systems do not have the infrastructure to implement and track a large volume of indication-based medicines for the entire drug budget[1,2] :

- Main European countries (e.g., France, Germany, and UK) currently lack data capabilities to accurately support IBP (e.g., collection of both hospital and outpatient prescription data) and would require an extensive transformation of the price-setting system, hence why products with multiple indications continue to be attributed a single-weighted-average price across indications in these countries
- Price discrimination per indication is even harder in Spain due to its current legal framework and decentralized healthcare system, which precludes the adoption of IBP and value-based reimbursement

For the majority of medicines, the largest indication and, ideally, competition will drive the price down to a single price. Without significant investments in the healthcare system, IBP will not be achievable on a large-scale basis on the payer.

That said, there are select, successful IBP cases in Europe:

- In Italy, indication-specific patient registries can lead to several discounting methods (e.g., payment by results, cost-sharing, risk-sharing, volume discounts), which allow for the significant variation of net prices across all indications. If we consider the oncology medicine Avastin® (bevacizumab), the implementation of patients registries for the 7 approved indications allowed the collection of efficacy data in different contexts, and the definition of risk-sharing agreements that vary by indication

On the drug developer side, multiple-indication products are planned using a real options approach: given the high-risk of failure, smaller indications are generally planned first and larger indications afterwards ("fail quickly; fail cheaply"). What that means from a market access perspective is that smaller, and often lower budget impact indications with relatively high prices, will launch first. As noted above, given the volume expansion expected and the inability to achieve IBP in many countries, the manufacturer will need to maximize this first-indication price. If the initial expected price is too low, the manufacturer may choose to not seek regulatory approval, or not reach a negotiated price in certain countries, thus denying patient access.

[1] Campillo-Artero et al. Price Models for Multi-indication Drugs: A Systematic Review. Appl Health Econ Health Policy. 2020

[2] Cole et al. Economics of innovative payment models compared with single pricing of pharmaceuticals. OHE Research Paper. 2018

This happens because the manufacturer would need to protect the price level for future indications where a higher value-based price would be justified. Indeed, the company would likely reduce or eliminate any additional R&D investments in the disease area given low price expectations, whereas indication-based pricing would have allowed a reasonable price to be achieved without creating risk to future value-based prices in additional indications. The patient is caught in the middle.

Which mechanisms are in place in Europe to minimize multi-indication pricing challenges and facilitate patient access?

03

Launching the same product under different brands for different indications could be an opportunity for indication-based pricing and, therefore, for differential pricing between indications. Other alternatives to IBP[1,2] are:

- **Multi-year-multi-indication (MYMI) agreements:** agreements between payers and manufacturers that cover multiple indication and years, allowing for faster patient access, reduced uncertainty, and improved predictability for manufacturers and payers as prices are not negotiated after launching a new indication (e.g., pricing arrangements covering multiple indications; lighter HTA process or no assessment for new indications; individual product or product-class budget with reference to horizon scanning)
- **Volume-weighted average price:** single price calculated as the average between indications, and weighted by the expected volumes of use for each indication
- **Differential discounts based on volume or value:** single price indicative of the indication with greatest value, with differential discounts (i.e., in some cases provided by financial or outcomes-based risk-sharing agreements) for indications with lesser value. Venclyxto® is approved as combination therapy with rituximab for the treatment of chronic lymphocytic leukemia (CLL) patients who have received at least one prior therapy, and as monotherapy for the treatment of chronic lymphocytic leukemia (CLL) patients who have a 17p deletion or TP53 mutation and who have experienced treatment failure with a B-cell receptor pathway inhibitor. In Switzerland, Venclyxto® is provided for the latter indication with a small discount to the ex-factory price (4.2%) due to the chronic nature of the treatment, as opposed to the limited treatment period for the first indication[3]
- **Patient-population restrictions:** the proposed indication can be restricted if the product is not considered cost-effective and the subpopulation restriction can be leveraged during pricing negotiations
- **Bundled assessments:** In Germany, the assessment of successive indications by G-BA can be "bundled" if they are expected to be approved 6 months apart[4]

[1] Lawlor et al. Accelerating patient access to oncology medicines with multiple indications in Europe. J Mark Access Health Policy. 2021

[2] Campillo-Artero et al. Price Models for Multi-indication Drugs: A Systematic Review. Appl Health Econ Health Policy. 2019

[3] http://www.xn--spezialittenliste-yqb.ch/ShowPreparations.aspx

[4] https://www.aokbv.de/hintergrund/gesetze/index_16946.html

Takeaways for Manufacturers

04

Unfortunately, optimizing all indications at once is not always feasible when commercializing your medicine. Multi-indication products risk mitigation should consist of the following steps:

- Perform indication sequencing early on the development process by evaluating and prioritizing the indications that will contribute the most to product lifecycle revenue, and sequence the indications to support pricing across future indications
- Be prepared to deprioritize the launch or the price of certain indications that create too much pricing and/or technical risk to the anchor indication's value. Fighting for an Orphan-like price in a low-revenue indication may create risk to a high-value, anchor indication and may not be worth the time
- Investigate which countries are open to IBP at the national, regional and local/hospital level. While IBP is still limited, there are a variety of examples where it can be implemented; local knowledge is key
- If you have multiple indications with dramatically different price levels, and they have high-revenue contribution levels, examine manufacturing solutions that may allow multiple products to be created

A robust indication sequencing approach to multi-indication products will allow the manufacturer to not only optimize the reimbursement outcomes in the different countries of the market access plan, but also the profits of its pharmaceutical product.

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About LatticePoint Consulting:

LatticePoint is a boutique consulting firm that focuses on pricing and market access for innovative medicines and medical devices. LatticePoint is led by former industry market access leaders who understand how to plan for the political, scientific, and financial realities that will be pivotal in negotiating product access. We work with biopharma companies and investors to help define, negotiate, and defend the value of their products in key markets around the world. The LatticePoint team has over 40 years of pharmaceutical and biotechnology industry experience. Led by former industry market access leaders and a high-caliber team with significant experience in the sciences, licensing, M&A due diligence and integration, venture capital and international affiliate operations, we have a depth of experience, both at the global and regional levels. Our multilingual staff of native German, French, Italian, Spanish, Portuguese and English speakers is experienced at handling negotiations in many key countries while keeping an eye on cross-border implications. We engage with payers, providers, hospitals, HTA bodies and EMA for early access, give feedback on clinical program design, and create and execute in-country reimbursement strategy negotiations in key markets around the world. We retain a Global Payer Panel for market research interviews.