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The Pricing and Market Access Landscape for Multi-Indication Products

Challenges and Opportunities in Europe

BioPharma companies are increasingly developing products with potential across multiple indications, particularly in oncology, with over two-thirds of cancer medicines approved for use in multiple indications in 2018.[1]

Conversely, securing reimbursement for new indications in many European markets can be challenging and lengthy[2]. The processes required for new indications are similar to those for new medicines and managing the different value of a drug in different indications makes utilising a single price difficult. This ultimately means patients may miss out on potential treatments through slow reimbursement of new indications, or lack of incentives to widen their use, and BioPharma companies forego the potential for greater revenue.

Whilst some notable therapies such as Keytruda and Dupixent have gained a foothold across numerous indications, this is in-spite of the structural challenges posed by payers in many markets. However, with potential for greater incentives for pursuing new indications under proposed EU rules[3], new models for reimbursing multi-indication therapies being used in Belgium and the Netherlands[4], and the advent of new modalities such as antibody-drug conjugates that target underlying disease mechanisms,[5] now is the time to consider how to navigate and shape the European landscape.

Table A: Key multi-indication assets and their therapeutic uses

Product	Manufacturer	First EMA Marketing Authorisation	Therapeutic Use
Humira (adalimumab)	AbbVie	2003	**More than 5 Indications,** including psoriatic arthritis, crohn's disease and hidradenitis suppurativa
Opdivo (nivolumab)	BMS	2015	**More than 15 Indications,** as a monotherapy, combination and adjuvant across a range of cancers inc. NSCLC, melanoma, renal cell carcinoma and classical hodgkin lymphoma
Keytruda (pembrolizumab)	MSD	2015	**More than 20 Indications,** as a monotherapy, combination and adjuvant across a range of cancers inc. NSCLC, melanoma, urothelial cancer and oesophageal cancer
Dupixent (dupilumab)	Sanofi/ Regeneron	2017	**More than 5 Indications,** including atopic dermatitis, asthma and chronic rhinosinusitis

Source: European Medicines Agency

In this paper we will set out the structural challenges for bringing multi-indication assets to market, and the commercial strategies that are available to BioPharma companies to mitigate these.

[1] Mills et al. Launch sequencing of pharmaceuticals with multiple therapeutic indications: evidence from seven countries. BMC Health Services Research 23:150 (2023)
[2] The root cause of unavailability and delay to innovative medicines, EFPIA, April 2022
[3] Reform of the EU pharmaceutical legislation, European Commission, 26 April 2023.
[4] Lawlor et al. Accelerating patient access to oncology medicines with multiple indications in Europe, Journal of Market Access & Health Policy. 9:1 (2021)
[5] Fu et al. Antibody drug conjugate: the "biological missile" for targeted cancer therapy. Sig Transduct Target Ther 7, 93 (2022).

1 Challenge

A lack of incentives to pursue new indications given costs and complexity

Varying European market approaches to multi-indication agreements increase the work required to bring new indications to market. Research by the European Federation of Pharmaceutical Industries and Associations found that evidence requirements, particularly for oncology treatments, varied across European markets, with little similarities in acceptance of surrogate endpoints other than progression-free survival[6]. This results in the requirement to develop specific dossiers for each country, combined with the expectation of volume discounts in many markets, making the pursuit of new indications economically challenging in some circumstances.

Table B: Pricing structures used for multi-indication products in key European markets

	Market	Approach to multi-indication products
	UK (England)	A single price is used, with the price needing to be cost effective for the lowest priced indication. Different prices for different indications are possible, via the use of Managed Entry Agreements (MEAs) such as through the Cancer Drugs Fund.
	France	Multiple models for multi-indication products are possible. Weighted-average prices are typically used for multi-indication products, with assessments for each indication, and prediction and tracking of volume weight used to set a single price.
	Germany	A single 'weighted average' price is used for multi-indication products, reflecting the value and volume of use for the different indications. Manufacturers can typically bring new indications to market quicker than other major European markets (in terms of time between marketing authorisation and patient access), with a temporary period of 6 months (recently reduced from 12 months) of free pricing ahead of negotiations.
	Italy	Multiple models for multi-indication products can be used. Performance-based MEAs have been used in Italy[7], as well as other forms of confidential MEAs which facilitate different net prices for different indications. Price decreases based on increased product volume are also agreed.[8]
	Spain	Typically, a single list price is agreed nationally, and is revised downwards for new indications based on the expected growth in volume. Net price can decrease at regional level, with Spain's 17 Autonomous Communities or local hospitals able to negotiate further discounts with manufacturers.

Sources: Office of Health Economics, OECD

[6] The root cause of unavailability and delay to innovative medicines, EFPIA, April 2022
[7] Goodman et al. Potential approaches for the pricing of cancer medicines across Europe to enhance the sustainability of healthcare systems and the implications, Expert Review of Pharmacoeconomics & Outcomes Research, 21:4 (2021)
[8] Pani et al. Pricing for multi-indication medicines, Pharma Advances 4:2 (2022)
[9] Chapman, S., V. Paris and R. Lopert, Challenges in access to oncology medicines, OECD Health Working Papers, No. 123 (2020)

2 Challenge

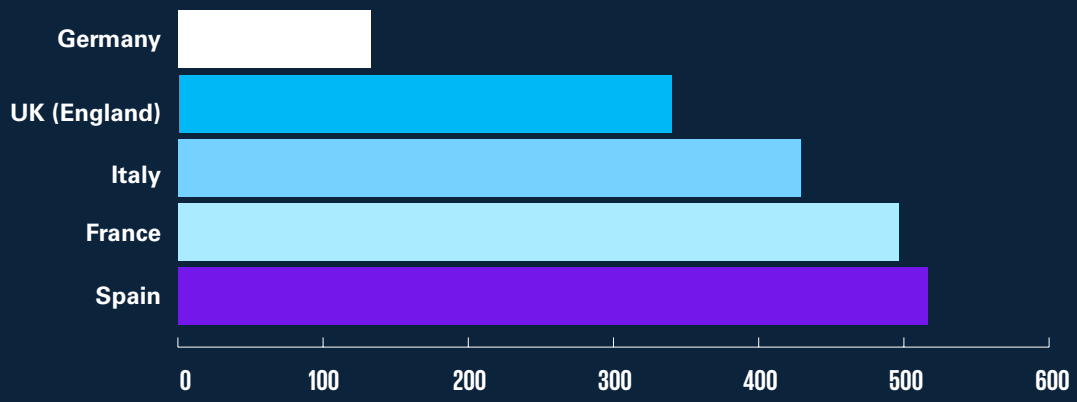
Limitations in national data infrastructure reduce the pricing agreement types for BioPharma companies

National data infrastructure in many European countries limits the types of multi-indication agreements that are possible. Italy is the only major market with the ability to track use by indication, with tracking possible in some circumstances in France and Belgium.[9] Where other major markets lack the data infrastructure for different prices for different indications to be feasible, there is generally less willingness to absorb the administrative burden of recording the indications for each prescription. Even in markets where sophisticated data tracking is in place, systems are not configured to manage tracking of use by indication. In Spain, despite establishing VALTERMED in 2019[10] , a national system to collect real world evidence, tracking of indications is not routine. Beyond the data infrastructure other factors may be limiting the types of agreements that are possible in Spain including regional approaches to setting price and varying budgets at the regional and hospital level.[11]

3 Challenge

Slow speed of authorisation for new indications

The length of Health Technology Assessment (HTA) processes and reimbursement negotiations can mean that patients' access to innovative products are delayed. Speed of access to new treatments varies across Europe, with research by European Federation of Pharmaceutical Industries and Associations showing that on average it took more than 500 days for new medicines to be reimbursed following marketing authorisation, with new indications of existing medicines facing similar hurdles.[12] The number of new indications is challenging for authorities to manage, with other factors like regional bodies conducting HTAs and lengthy negotiations to manage finite budgets.[13] Differences in speed of access across Europe stem from different approaches to assessment and reimbursement. Germany's temporary free pricing period (6 months) and approach to reviewing manufacturer submissions enables faster access, contrasts with the more fragmented process in Spain, with separation between clinical evaluation and reimbursement discussions.



Median time between marketing authorisation and availability on the market (Days)

4 Challenge

Constrained healthcare budgets are triggering greater scrutiny on the cost of multi-indication therapies

Recent fiscal challenges and ageing populations are stretching European healthcare budgets, with payers seeking to control spend on medicines, and negotiate steeper discounts on high volume products. Germany's 'Financial Stabilisation of the Statutory Health Insurance System' Act in 2022 brought increases in mandatory rebates and restrictions to the length of free pricing[14]. Similarly, in the UK the 'Voluntary scheme for branded medicines pricing and access' (VPAS), established in 2019 to manage national spending on innovative medicines has met increasing resistance from industry players[15]. Revenue clawback levels under the scheme have ballooned to 26.5% for 2023 as part of the measures designed to limit NHS spending.[16] Reforms in the UK and Germany reflect the budgetary pressures payers are seeking to manage across Europe. That said, there is the potential to explore whether budgetary pressures could be used to form longer term, innovative agreements that protect value while managing costs.

[10] Tania Rodrigues. How to democratize access and prevent the next supermodel medicine, Pharmaceutical Technology, 11 December 2019
[11] Flume et al. Feasibility and attractiveness of indication value-based pricing in key EU countries. Journal of Market Access and Health Policy. 10:4 (2016)
[12] The root cause of unavailability and delay to innovative medicines, EFPIA, April 2022
[13] Kamphuis et al. Access to medicines in Europe. LSE Consulting (2021)
[14] Francesca Bruce. Germany's New Government Will Maintain Price Freeze And Slash Free Pricing Period, Scrip Pharma, 2 December 2021
[15] Janet Beal. Pharma sector reels as UK Government doubles VPAS payback rate on NHS drugs. Pharmaceutical Technology, 30 January 2023
[16] Big Pharma has harsh words for UK's ballooning voluntary reimbursement agreement. Endpoints News, 21 February 2023.

The Commercial Options for Multi-Indication Pricing

	What is it?	Benefits	Drawbacks
Indication-based pricing	Seeking to align the price of each indication to its perceived value. It means establishing different prices for each new indication, through different list prices per indication, or via indication specific rebates.	Avoids potential price erosion when bringing new indications to market with higher forecasted patient volumes.	Difficult to implement in practice. Some payers will not accept different prices for a single product. This is often due to the administrative burden or lack of data infrastructure to track prescriptions/ patient volumes across different indications.
Price volume agreements or tiered rebates	Emphasis is on volume over value for new indications. They involve setting up thresholds on the volume of use, with rebates or decreases in the list price when volume reaches the agreed threshold.	Preferential for BioPharmas looking to increase market share as they incentivise prescribers towards high volume. Can be complex to implement and forecast multiple tiered thresholds.	Payers tend to prefer simpler agreements and may be less inclined towards tiered rebates. Forecasts need to be robust and validated to inspire confidence that agreed volume thresholds will be met.
Weighted average price or 'blended price'	Relies on assessing the value and volume of each indication to create a single price to reflect the overall value of the product.	Preferential for BioPharmas, by enabling lower value indications to be introduced without undercutting the revenue of earlier, higher value indications Generally preferred by payers due to the simplicity of achieving a single price.	Payers can be reluctant to agree a single price before other indications are launched. May prefer to agree retrospective weighted average prices, when real world data and a significant number of indications have been approved.
Multi-Year, Multi-Indication Agreements (MYMI)	Involve agreeing reimbursement across current and future indications with the aim to accelerate access to new indications. They create a comprehensive framework which covers multiple indications in terms of value assessment, pricing and reimbursement to enable faster access to new indications.	Cited as a factor in improving the speed of access to new indications across some EU markets. In Belgium and the Netherlands, use of MYMI agreements has been recognised as key in reducing delays in the approval of new indications following marketing authorisation. Time to patient access was reduced in Belgium from 395 days to 30 days, and from 220 days to 120 days in the Netherlands.[17]	The prospect of these types of agreements is distant in many European markets, due to payer reticence to agree to long term agreements without sight of clinical data. There would likely need to be significant change in many HTA processes to allow for multi-year-multi-indication agreements.

[17]Lawlor et al. Accelerating patient access to oncology medicines with multiple indications in Europe, Journal of Market Access & Health Policy. 9:1 (2021)

Key Questions for BioPharma Companies

Do you understand payer receptivity to forms of multi-indication pricing across European markets?

In the short-term, significant changes to how multi-indication drugs are reimbursed are unlikely, but market teams can take smaller steps to improve negotiations, like combining negotiations of new indications to make discussions more efficient. To understand where this might be possible, market teams should remain up to date with developments from payers, monitoring what types of agreements competitors have agreed, and the different options for accelerating access to new indications.

Do you have tools and processes that help you plan negotiations?

Commercial teams need the right tools and support to engage in market access negotiations with payers across European markets. Being able to plan different pricing scenarios based on changes to the eligible population or price changes associated with new indications can help market teams plan their negotiation strategy, particularly in markets focused on budget impact. Where forecasts and data inputs can be validated by third party experts, this may increase payer confidence during negotiations.

Are you shaping the debate on multi-indication pricing across the EU?

Collaborating with third parties like PAGs and industry associations can help to illustrate the patient access issues caused by current approaches to multi-indication pricing, whether by illustrating the costs of slower access to innovation for patients or demonstrating that off-label use is already occurring under the status-quo. By showing that dysfunctions are occurring under the status-quo to the detriment of patients, BioPharma companies can make the case for systemic reform to improve outcomes for patients.

Talk to our experts

KPMG is helping BioPharma companies to:

- Evaluate payer receptivity towards innovative multi-indication agreements
- Design commercial playbooks including commercial constructs and agreements to consider while preparing for negotiations
- Create 'what if' scenarios to test the commercial impact of various scenario models to support negotiations

Our team of healthcare and life sciences and pricing/ market access experts combine their deep sector knowledge, with our analytical capability to create future proof and practical solutions for multi-indication assets during launch preparation.

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