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Pricing and reimbursement of multiple indication medicines: Can a balance be found between different stakeholder perspectives to optimise value and access for patients, while ensuring sustainable and affordable innovation?

ISPOR EUROPE 2024 Panel Report

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The Issue. Access to innovative multi-indication medicines is complex and suboptimal in Europe due to current pricing & reimbursement (P&R) regulations

Multi-indication medicines can bring value to society. They multiply the availability of treatment options for patients within or across disease areas[1 - 3] and have a mechanism of action and safety profile that are already well understood[4,5].

At the same time, the value of each indication may vary significantly due to differences in disease severity, therapeutic effect, and available therapeutic alternatives[1,6]. This presents a challenge for P&R, as a single, uniform price cannot adequately capture the value of individual indications[3,6].

European countries have different ways of managing multi-indication medicines, but in practice lengthy negotiations and price erosion are still common, which can lead to delayed or restricted patient access[1,3,5-7].

Shared Perspectives. Hundreds of stakeholders acknowledge that multi-indication medicines face multiple P&R challenges in Europe

During the ISPOR panel session, ~800 participants in the audience across industry, academia and public organisations agreed that P&R challenges for multi-indication medicines exist, in their responses to the following question:

When aiming to achieve optimal patient access, do you believe that multi-indication medicines present unique challenges in Europe for:

Response option (choose one or more of the following)	% that selected
Value assessment across indications	9.63%
Price setting across indications	22.46%
Budget impact / affordability due to increased no. of eligible patients	9.63%
Company revenue / sustainability due to price erosion of previous indications	11.76%
All of the above	45.45%
No – they are the same as any other medicine	1.07%

Where We Are Today. Given the increasing number of promising novel medicines with multiple indications, particularly in oncology, immunology & inflammation (I&I), it is essential to ensure P&R systems are well-adapted

Scientific advancements have enabled the development of novel therapies for various immune diseases, many in areas of unmet need.

These are exciting and needed advancements for several reasons:

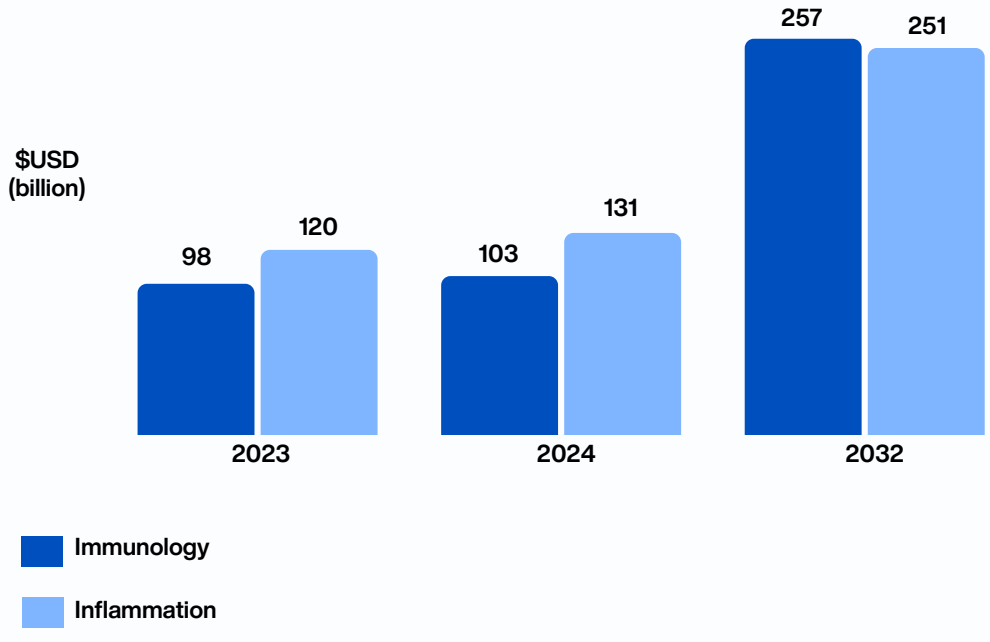
1. **Increased scientific understanding** of I&I has enabled better identification of therapeutic targets for potentially more effective treatments[8]
2. **Important new insights that certain diseases share common molecular pathways** has enabled the development of medicines, such as anti-TNFs or IL13s, which can target several indications[9,10]
3. **There is a need for these treatments**. I&I conditions affect a large and increasing number of people. E.g., Autoimmune disease affects 5-10% of the population[11,12], with a rising annual prevalence in recent decades of 12.5%[13]. The degree of unmet need across these diseases varies, so the number of patients and extent of clinical benefit from one therapeutic agent will differ[8]

As a result of this developing science, we are seeing an exciting surge of innovation in I&I, and many of these new medicines are for multiple indications.

In terms of multi-indication medicines, the scientific advancements listed above relate to:

- Multi-indication medicines becoming progressively common not just in oncology, but also in I&I, with an increase in the number of indications per drug across therapeutic areas in recent years[1,2]. E.g., targeted immunotherapies launched over the past 25 years have had an average of four indications per product[4].
- A substantial growth of innovation in I&I over the past decades, with several manufacturers investing in the development of new, promising therapies[14,15].

Global market size of immunology and inflammation[14,15]



Pipeline review of the top 10 I&I pharmaceutical companies: a large portion of I&I pipeline products have multiple indications[16-26]

I&I medicines have distinct characteristics, which may exacerbate P&R challenges for multi-indication medicines

Many of the new innovations in I&I are expected to have multiple indications. Multi-indication medicines are not new; they are common in oncology but still face P&R hurdles that can inhibit development and access. Managing their P&R has not been fully solved for oncology, and now they are increasing in a disease area (I&I) in which there is need, but which will be more complex and challenging due to key differences:

- Oncology has distinct tumours, whereas immunology conditions may be overlapping / coexisting
- Oncology often has an acute treatment setting with short treatment durations, whereas immunology is typically a chronic treatment
- In oncology there is a common endpoint (survival, progression) that has typically been used for indication-based agreements – there is no such common endpoint in immunology as far as we know

There is significant potential value in the increased innovation in I&I for diseases with unmet need, and a need to revisit how P&R of multi-indication medicines is approached in terms of:

- **Current P&R approaches and challenges for multi-indication medicines:** what we can learn from past and existing approaches?
- **Forward looking solutions:** how we can go forward to support continued development and patient access for promising multi-indication medicines in I&I?

Current P&R Approaches. How multi-indication medicines are managed today, based on literature and empirical experience

A scoping literature review on P&R policies and regulations for multi-indication medicines was conducted:

- The focus was on EU4 + UK, but articles beyond this scope were also included to inform understanding of challenges and potential best practices

Review findings were rounded out with some product case studies and former payer interviews to validate the conclusions.

The ISPOR panel discussion provided further understanding from the international and country-specific perspectives.

To date, several European countries have employed blended (aka 'weighted-average') pricing, which results in a single price weighted across all indications by either volume alone (e.g., Spain), or volume and value (e.g., Germany, France)[1,3,27]. In the UK, differential discounting can be used, whereby confidential discounts to the list price can be negotiated for each indication, resulting in different net prices, but only under certain restrictive conditions[1,3].

In Italy, there has been a shift away from allowing different net prices per indication, relying on registries that allow tracking the use of drugs for each indication (indication-based pricing – IBP), to using a single weighted price across indications, in which discounts for new indications are applied to all indications[8].

IBP, which applies distinct prices for different indications for the same medicine[3], is recognised in the literature as having the potential to address the disconnect between the value and price of multi-indication products[3, 5, 6]. However, it is likely not a feasible solution in practice; a number of barriers to implementing pure IBP have been highlighted, such as issues with payment and distribution systems, or inadequate infrastructure for monitoring indication use[1, 3, 5].

Forward-Looking Solutions. Where do we go from here?

Existing solutions in the literature and practice were discussed among the ISPOR panelists, reflecting key considerations when identifying and implementing feasible solutions for a given country.

"*We need solutions. As a health economist, I do prefer that solution to be IBP. However, IBP is difficult to implement. We need to be pragmatic. IBP should be used in select cases when it is necessary (e.g., very different values across indications). A blended pricing approach is easier, but it should be transparently implemented with a role given to a value-based approach; IBP could be used in select cases when very necessary.*"
- Claudio Jommi

"*If we really want to implement value-based approaches within our health systems, we may need to see the current challenges as opportunities to improve our infrastructure, approaches and stakeholder collaboration"*
- Amanda Cole

"*It's an issue that many stakeholders do and will continue to face. We know country systems are different and while there may be no silver bullet, there are probably ways to optimize existing solutions and may be solutions that we haven't even thought about yet. It is important for all stakeholders to work together if we are going to find solutions to the challenge of multi-indication medicine P&R"*
- Julien Patris

Based on this information, ISPOR audience participants provided insight into what they saw as potential feasible ways forward, through their answers to the following question:

Reflecting on the solutions that were discussed, what do you think would be the most effective and feasible way forward?

Response option (choose one or more of the following)	% that selected
Implementation models w/ tailored minimum data requirements around usage & value by indication	12.04%
Optimisation of data infrastructure to support real-world evidence collection and tracking	17.13%
Confidential blended pricing model with explicit weights for different value indications	**28.24%**
'Pure' IBP (distinct prices for different indications for the same medicine), in exceptional cases	14.81%
Innovative payment models (e.g. multi-year, multi-indication agreements)	**27.78%**

While IBP might be the most ideal solution in theory that we should continue striving for, it is a practically challenging and long-term solution that requires time. In the meantime, pragmatic, short-term solutions are needed. The literature and experts suggest three key ideas as a starting point, based on the survey question above:

1. **Blended price 2.0:** a blended price solution, with confidentiality on the agreement, but with some transparency on the underlying mechanisms, and allowing for IBP in specific situations
2. **Portfolio deal:** a type of innovative payment model including coverage of an entire portfolio of medicines within the same disease area at one list price per patient (but different net prices)
3. **Multi Year, Multi Indication agreement (MYMI or Pipeline deal):** a predefined pricing arrangement covering upcoming indications to provide some predictability and incentives, an accelerated health technology assessment to ensure fast access, and some budgetary mechanisms

We are working to collaborate and understand from all stakeholders' perspectives what feasible solutions look like. If you would like to be kept updated and / or collaborate, please scan the QR code:

Conclusions

There is recognition of the need for novel solutions to manage the P&R of an increasing number of multi-indication products in a more optimal way for all stakeholders[2,28]. Stakeholder collaboration is essential to achieve this[2]. Such collaboration should focus on creating understanding between different stakeholder needs and perspectives, and finding a consensus on the best and most feasible ways forward. This requires striving toward co-creation with the health technology assessment (HTA) / P&R / Access community to test existing potential options and identify whether additional options exist. Whatever the solution, a key component will be ensuring that P&R processes allow for transparent and collaborative negotiations, to efficiently reach sustainable agreements and better ensure efficient patient access.

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