Blueprint for a multi-year, multi-indication-inspired access framework

Definition of the MYMI-inspired access framework

The multi-year, multi-indication (MYMI)-inspired framework is a holistic approach to facilitate agreements between manufacturers and payers for the reimbursement of medicines across multiple indications and over several years. It provides a comprehensive structure for assessing therapeutic benefit and managing pricing and reimbursement (P&R) for both current and future indications. By enabling long-term, multi-indication agreements, this model offers an innovative way to improve access and support sustainable management of multi-indication medicines.

Context

There is increasing knowledge and understanding of common pathophysiological mechanisms of phenotypically different diseases, such as in oncology and in immunology and inflammation. These insights have led to the development of so-called multi-indication medicines.

While promising benefits for different diseases that share the same aetiology, multi-indication medicines continue to face significant challenges across the development and access pathway, from regulatory reviews to payer assessments and clinical adoption.

Timely and coordinated solutions will be essential to ensure patients in need have access to all licensed and effective uses of such multi-indication medicines. A proactive, multi-stakeholder response – in which payers, policymakers, physicians, patients and pharmaceutical companies are all involved in the development of novel approaches – is necessary to ensure that these innovations can deliver maximum value for patients, healthcare systems, and society.

MYMI agreements have been highlighted briefly in the literature as having high potential, and have been used in some European countries (e.g., Belgium, the Netherlands). However, further investigation is required to understand if MYMI agreements can offer additional benefits over existing approaches.

Furthermore, the MYMI agreement has generally been characterised as a pure financial approach that impacts P&R, and contrasted to other P&R approaches such as blended or indication-based pricing (IBP). The blueprint below seeks to go beyond the concept of a MYMI agreement as a solely financial approach. Instead, it outlines a more holistic framework for therapeutic benefit assessment and P&R. This framework may include certain alternative pricing arrangements, but offers a broader structure that enables payers and manufacturers to reach comprehensive agreements for products covering multiple indications over several years.

This MYMI-inspired framework includes several key pillars and elements to guide the assessment and reimbursement of multi-indication medicines. Rather than suggesting a strict process, these pillars and elements offer a flexible menu of options that can be applied in different ways (whether fully or partially) and in various combinations, depending on the specific disease or product context, as well as country-specific systems and priorities. Importantly, the MYMI-inspired framework encapsulates various dimensions, including

broader financial mechanisms beyond pricing, adjustment of health technology assessment (HTA) processes, and early access.

Key principles of the framework

The application of this holistic framework to achieve agreements on multi-indication medicines is guided by four fundamental principles.

1. **Scope / eligibility assessment**
    - Application of the framework will not be relevant for all multi-indication medicines but rather restricted to certain products. Potential eligibility criteria include (*note: these criteria may be used in combination, and they may not be mutually exclusive; each country can set their specific eligibility criteria according to their needs*):
        - Products with major added therapeutic value for current and future indications
        - Products with more than two indications expected to launch over a certain number of years
        - Products with different formulations, dosage regimens and/or treatment durations
        - Diseases with high unmet need
        - Products that have a certain level of robustness in clinical development (i.e., are supported by strong trial methodology that is appropriate for the disease context)
        - Products that have undergone specific regulatory procedures (e.g., PRIME, accelerated approval)
2. **Mutual commitment**
    - Successful implementation of the framework will require mutual commitment between manufacturers and authorities, as well as clearly defined shared goals.
3. **Patient and key opinion leader (KOL) involvement**
    - All stakeholders should be consulted when devising agreements under this framework, including patients and KOLs, to ensure their voices are included in assessment and/or decision-making processes.
4. **Flexibility for country implementation**
    - The MYMI-inspired framework can encompass various elements and processes. It may be the case that not all of these elements and processes are relevant for a given country system / context or a given product or disease area – they do not need to be.
    - The framework therefore provides flexibility for individual countries to adapt the approach and implement the framework according to their local needs and product / disease-specific requirements, by working with what is relevant from the menu of options.
        - E.g., in some countries, the final agreement for a multi-indication medicine may include no upfront assessment of the value for money in new indications, while in others, an upfront assessment may be legally required and should therefore be applied, albeit using an abbreviated approach.

Overarching components of the framework

The framework itself encompasses three overarching key components:

I. **Establishing the agreement**

II. **Scope and application of the agreement**

III. **The infrastructure needed for implementation**

Each component is comprised of key pillars, and each pillar includes a set of elements. For each element, users must 1) consider its applicability in their country and, where relevant, 2) define and agree on the parameters for implementation.

Overarching component I: Establishing the agreement

The process of establishing an agreement is comprised of three key pillars: 1) horizon scanning and early dialogue, 2) agreement negotiation and establishment, 3) agreement lifecycle management. The pillars and their elements for selection / consideration are listed and explained below.

Pillar 1: Horizon scanning & early dialogue

Elements:

- **Horizon scanning on indication therapeutic benefit and volume:** Horizon scanning should be conducted on the estimated therapeutic benefit and volume of current and future indications, to inform pricing and budget.
- **Horizon scanning on future competitive landscape:** Horizon scanning should be conducted on the future competitive landscape, to better understand the future standards of care in the upcoming indications and inform volume estimates.
- **Multiple early dialogues:** Multiple early dialogues between manufacturers and payers should take place to manage uncertainty around current and future indications, align on certain elements (e.g., relative emphasis of therapeutic benefit vs. volume) and ensure efficient agreement development.
- **Defined timepoints for initiation:** Horizon scanning and early dialogue can be commenced at certain timepoints, and these time points should be decided upon as soon as possible.
    - It may be beneficial to initiate dialogue before evidence generation.
    - Discussions can also occur just ahead of first product launch, and / or following initial or subsequent launches.
        - While post-launch engagement may help address uncertainties around therapeutic benefit and volume estimates, in many cases it may come too late to fully mitigate these challenges.

Pillar 2: Agreement negotiation & establishment

Elements:

Negotiations between manufacturers and payers must determine key points for the agreement, including:

- **Criteria and consequences of triggering assumption of similar therapeutic benefit**
    - Rules should be set for considering whether new upcoming indications trigger the assumption of similar therapeutic benefit relative to previous indications, and whether this results in no vs. abbreviated vs. full upfront assessment.

- **Reassessment criteria**
    - Clear criteria for reassessment need to be set in advance, and can be based on:
        - Setting minimum thresholds of clinical benefit for future indications (based on those of previous indications) with reassessments if the thresholds are not met, and / or
        - Pre-planned timepoints for reassessments

- **Contract duration**
    - The agreement should be for a set number of years, therefore, there is a need to define the specific duration that the agreement would apply for

- **Time horizon for prospective assessment**
    - A specific time horizon for considering future indications should be agreed, such that prospective assessments are conducted for indications expected to launch during the defined time period

- **Uncertainty management**
    - Budget concerns should be discussed, with potential requirements for certain financial commitments from both authorities and manufacturers
        - More adaptive budgeting solutions can be considered rather than budget caps and clawbacks (e.g., the agreement is renegotiated if the volume is too low or too high) – this is particularly important for rare diseases where epidemiology is not well established, as misestimating the threshold could have a substantial negative impact
    - Risk-sharing mechanisms should be discussed to help mitigate financial and evidential uncertainty, e.g., outcomes-based managed entry agreements, price-volume agreements

- **Data requirements**
    - The need for and type of data tracking of the product's use will vary and should be carefully considered. Depending on the pricing component of the agreement, different data requirements will apply:
        - Indication Based Pricing (IBP)– setting different prices for the same medicine by indication or eligible subpopulation so that price reflects indication-specific therapeutic benefit; this requires usage tracking by indication
        - Blended price – a single price for a multi-indication product calculated as a weighted average across indications, typically using therapeutic benefit and volume weights, with potential periodic adjustment as real-world use evolves; weights can be based on either estimated (e.g., informed by prospective epidemiological data) or actual data (e.g., informed by current and historic real-world evidence data)
        - Two-part tariff – a pricing scheme composed of a lump-sum or access fee plus a per-unit usage charge; only product tracking required.

    - In the absence of robust data infrastructure, alternative approaches should be considered, such as:
        - Product-specific solution involving a (private) third party
        - Patient support programme data
        - Data from a single expert centre with a significant patient cohort
    - The need for data tracking of patient outcomes in clinical practice should be considered
    - Data can also be collected to define epidemiology and the eligible population, e.g., natural history data

- **Confidentiality**
    - The need for the agreement to be kept confidential (discounts and pricing models) while at the same time ensuring basic transparency laws are in place (e.g., transparency and clarity regarding the process, including timelines, criteria, opportunities for stakeholder engagement, etc.)

- **Scope and application of agreement**
    - See Overarching component II below

Pillar 3: Agreement lifecycle management

Elements:

- **Process for agreement implementation and renewal:** A clear and transparent process is needed to implement, negotiate and renew agreement terms
- **Rules for agreement renegotiation and management:** Clear rules and mechanisms should be defined for renegotiation, exit clauses and dispute resolution
- **Agreed roles and responsibilities:** Roles and responsibilities for performance monitoring should be transparent and mutually agreed
- **Dynamic consideration of information:** There should be the possibility for dynamic consideration of information over time, which may trigger reassessment or application of pre-agreed rules (e.g., further evidence generation), and clearly defined criteria for how that should be implemented
- **Dynamic adjustments for combination therapies:** There should be the possibility of dynamic adjustments if combinations with external products emerge, and clearly defined criteria for how that should be implemented

Overarching component II: Scope and application of the agreement

The holistic framework enables the application of an agreement with a scope across various aspects of the assessment and reimbursement process, including: 1) expedited access, 2) adapted HTA, 3) comprehensive P&R, and 4) comprehensive contracting. These pillars and their elements for selection / consideration are listed and explained below.

Pillar 1: Expedited access

Elements:

- The agreement can enable expedited access for new indications, leveraging the initial early access assessment. This can take different forms and be inspired by the approaches of existing early access mechanisms, such as:
    - Deferred HTA (e.g., free pricing in Germany)

    - Commercial agreement with *a posteriori* P&R reconciliation (e.g., L'accès précoce in France)

- The agreement can also incentivise access by extending the price of current indications to new ones temporarily (until the new indication undergoes value assessment)

Pillar 2: Adapted HTA

Elements:

- There may be an abbreviated upfront value assessment for new indications, leveraging the full upfront assessment for initial indication(s) and horizon scanning, and assuming an agreed threshold of therapeutic benefit relative to previous indications is met

- There may no upfront value assessment for new indications, leveraging the full upfront assessment for initial indication(s) and horizon scanning, and assuming an agreed threshold of therapeutic benefit relative to previous indications is met
    - Reconciliation and or/ post-reimbursement retrospective assessment may be required

- HTA processes may need to be adjusted to reflect additional differences between a product's indications, such as differences in comparators or endpoints

Pillar 3: Comprehensive P&R

Elements:

- A pricing agreement is reached that covers current and future indications based on expected therapeutic benefit (compared to existing alternatives and / or previous indications) and volume, which can be structured using different pricing mechanisms, e.g. (see also above):
    - IBP – setting different prices for the same medicine by indication or eligible subpopulation so that price reflects indication-specific therapeutic benefit
    - Blended price – a single price for a multi-indication product calculated as a weighted average across indications, typically using therapeutic benefit and volume weights, with potential periodic adjustment as real-world use evolves
    - Two-part tariff – a pricing scheme composed of a lump-sum or access fee plus a per-unit usage charge

- The agreement can have flexibility in its pricing approach in cases with particularly high uncertainty, e.g., integrating with risk-sharing agreements

- The agreement makes possible accelerated reimbursement for new indications, OR the agreement makes possible immediate reimbursement for new indications

Pillar 4: Comprehensive contracting

Elements:

- One contract is established per product, for a number of current and expected indications over several years

Overarching component III: The infrastructure needed for implementation

In order for the framework to be implemented in practice, countries may require certain infrastructure and system elements to be in place. These are centred around the following pillars: 1) legal frameworks, 2) budgeting mechanisms, 3) data infrastructure, 4) HTA capability and 5) policy alignment. The pillars and their elements for selection/consideration are listed and explained below.

Pillar 1: Legal frameworks

Elements:

- A legal basis for alternatives to the standard P&R process to be possible
    - E.g. legal ability to utilize flexible P&R processes to enable rapid or no therapeutic benefit assessments for subsequent indications
- GDPR-compliant data sharing mechanisms
    - Secure systems are needed for exchanging and analysing indication-level data to track usage/outcomes and support decision-making
- A legal basis for implementing outcomes-based payment models
    - Legal ability to set payment models based on patient outcomes may be needed, as this is often an aspect of agreements spanning multiple indications and years

Pillar 2: Budgeting mechanisms

Elements:

- Flexible accounting systems
    - These can ensure aspects such as budget caps are flexible, to mitigate the risk of preventing therapies from reaching patients who may benefit
- Budget mechanisms allowing for payment deferral and multi-year commitments
    - Financing solutions that allow costs to be spread over several years can minimize upfront budgetary issues

Pillar 3: Data infrastructure

Elements:

- Ability to track usage (see also above)
    - Infrastructure to track treatment usage and reimbursement when needed; whether per-indication tracking is required depends on individual markets and agreements
- Ability to collect and analyse outcome data
    - Centralized systems involving national electronic health records and linked datasets may be needed to track patient outcomes in clinical practice
- Disease-specific registries
    - Targeted registries could be adapted for tracking in certain disease areas

Pillar 4: HTA capability

Elements:

- Ability to apply the agreements dynamically as new unexpected indications are added
    - There must be a defined process to apply or update agreement terms when new indications are approved, supporting timely patient access

    - A process should also exist to update the terms of the agreement in instances when the competitive landscape changes in one or more of the indications
- Alternative approaches to traditional per-indication therapeutic benefit assessment
    - P&R processes that support rapid or no upfront therapeutic benefit assessment for subsequent indications, if the new indication meets an agreed threshold of therapeutic benefit, can allow for more efficient assessment of new indications
- Methods to aggregate or compare therapeutic benefit across indications
    - Specific methodologies may be needed to evaluate the individual therapeutic benefit of each product indication

Pillar 5: Policy alignment

Elements:

- National policy support for value-based agreements
    - Legislative or regulatory support could better enable implementation of innovative agreements
- Alignment with broader policy goals
    - Synergies of agreements with national health priorities (e.g., cancer plans, rare disease strategies) could maximize impact
- Resources to manage agreements
    - Ensure ring-fenced budgets and resources to establish and operate the agreements