European Access Hurdles Portal & the Root Causes Analysis **Smaller markets**

Revised Country Analysis

April 2025

efpia

CRA Charles River Associates

Approach: We have followed a multi-step approach to understand the root causes of unavailability and delay in smaller markets

Defining the question

- Establish what the expected challenges will be with the Portal 2025 data
- Draft hypotheses on how the data can be better explained, particularly for smaller markets

Literature review

- Conduct review of existing evidence in the public domain:
  - Academic publications
  - Grey literature (policy papers, industry publications, media, etc)

Country focus groups

- Collaborate with national trade associations to host focus groups and understand local access challenges and policy priorities

Company interviews

- Conduct 1:1 interviews between CRA team and company representatives
- Pressure-test how the identified challenges have impact on filing and access

Solutions and reporting

- Develop proposed policy solutions for overcoming the identified challenges
- Draft report on root causes in smaller markets
- Publish in April / May

Malta *Cyprus* *Latvia* *Lithuania* *Estonia* *Slovenia* *Croatia* *N. Macedonia* *Montenegro*

Approach: We have applied this framework to understand patterns of filing and availability in each smaller market

Why might there be delays in filing of a newly centrally approved medicine?

Hypotheses

1

…because it is unnecessary to file to obtain access

Examples:
- *Direct to tendering*
- *Class-level service lists*
- *Alternative access schemes that provide faster patient access*

2

…because local requirements make it difficult or impossible for the MAH to file

Examples:
- *Requirements for price or assessments in other markets*
- *Expectations of price or assessments in other markets*
- *Lack of necessary local data or expertise (low patient population)*

3

…because features of the local system make it impractical to file

Examples:
- *Non-transparent P&R criteria and methodologies*
- *Low likelihood of success*
- *Under-resourced HTAbs*
- *Waiting lists for reimbursement*

4

…because it is unsustainable (the business case cannot be made) for the MAH to do so

Examples:
- *Unsustainable pricing rules*
- *Unpredictable budget allocation decisions and use of clawbacks*

*If MAHs lack a local presence in a smaller market, this can make it **impossible**, impractical or **unsustainable** for them to file a new medicine for P&R, depending on the local context and P&R requirements*

Summary results: We find that the reasons for delays in filing in smaller markets are multi-faceted and driven by the local context

Why are there delays in filing of newly centrally approved medicines?

Relative importance of each factor in:	…because it is unnecessary to file to obtain access	…because local requirements make it difficult or impossible for the MAH to file	…because features of the local system make it impractical to file	…because it is unsustainable (the business case cannot be made) for the MAH to do so
Malta	●	◔	◕	◕
Cyprus	◕	◔	●	◑
Latvia	◔	◔	●	◕
Lithuania	◔	◑	◕	◕
Estonia	◔	◑	◕	◕
Slovenia	○	◔	◑	◑
Croatia	○	◑	◑	◑
N. Macedonia	◕	◔	●	●
Montenegro	◑	◔	◕	●

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: MAH = marketing authorization holder

Key: ◔ ◑ ◕ ●

Relative importance (in the local context) of each potential argument for explaining the filing data

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In Malta, there is a low reimbursement rate (2%) of innovative medicines and a low filing rate (9%)

P&R overview

- **Either MAHs or Medical Consultants can file** for inclusion on the Government Formulary List (GFL)
- Pharmacists within the **DPA** compile **HTAs** including **clinical and budget impact** assessments for review by the GFLAC
- The GFLAC and ACHCB review outputs from the DPA an issue both **technical and financial recommendations** to the **MoH** on whether an innovative product should be included on the GFL
- Along with the **Minister for Finance,** the **Chief Medical Officer** and **Senior Health Officials,** the **MoH** is responsible for **setting out prioritization** before the CPSU are responsible for **procurement, negotiating** with **MAHs** and **issuing tenders**

New perspective on Root Causes

1. There are no **direct barriers** impacting the timing of filing in Malta, but in practice, payers reference the completed assessments and decisions made in other European countries
2. The Maltese P&R system is chronically **under-resourced**, leading to **delays in decision-making,** budgetary constraints see **specific therapy areas prioritized** for procurement
3. There is a **significant lack of transparency** as to a **product's status** after filing and a significant backlog, discouraging filling
4. The tenders are largely **single-winner, price-only** and lasting **3-4 years**, meaning innovative medicines can be frozen out of the public reimbursement market

Alternative access (15%)

- It is **not necessary for medicines** to have **filed** and be listed on the GFL to bid for a tender, creating the possibility for reimbursed patient access **without filing** and going through the standard reimbursement system
- The **Maltese Community Chest Fund** offers public access for products which are not supplied via standard reimbursement route and **does not require filing**
- The **Exceptional Medicines Treatment Committee (EMTC)** assess and approve medicines on a named patient basis for rare disease medicines not currently on the GFL

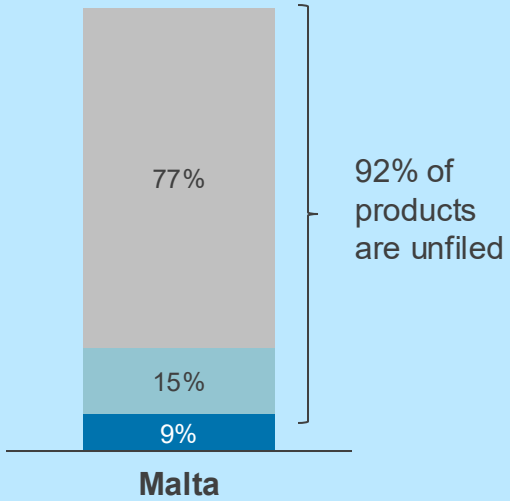
Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: ACHCB = Advisory Committee for Health Care Benefits; CPSU = Central Procurement Supply Unit; DPA = Directorate for Pharmaceutical Affairs; GFL = Government Formulary List; GFLAC = Government Formulary List Advisory Committee; HTA = health technology assessment

In Malta, it is not necessary to file a medicine for P&R in order to achieve broad patient access

What does the Portal data tell us?

Status of filing and reimbursement



How can we interpret this considering our understanding of the market?

1 …because it is unnecessary to file to obtain access

2 3 4

9%

- 9% of products have been filed for inclusion on the Government Formulary List (which doesn't necessarily guarantee patient access)
- **Patients may have access** to many of the 92% of unfiled products, as products can be directly tendered and procured from wholesalers

15% ⬆

  - 15% availability through an alternative public channel **is likely an underrepresentation** of company willingness to provide access; it partially represents the difficulty for innovative medicines to win tenders (class level, winner-takes-all, price criterion, can be competing against generics)
  - It seems likely that some of the remaining 77% have been submitted to tenders upon request from the CPSU and not succeeded; **the Portal is not set up to capture this nuance**

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: CPSU = Central Procurement Supply Unit; P&R = pricing and reimbursement

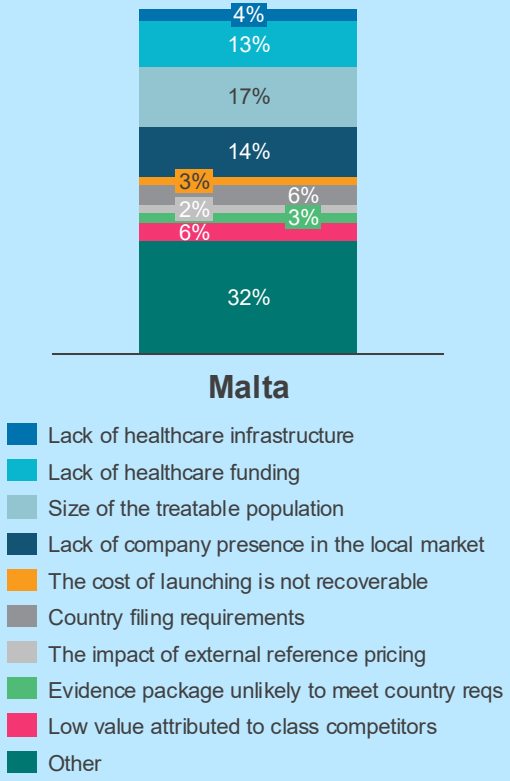
Key: ⬆ = underrepresented in Portal data

<> = fairly reflected in Portal data

We expect that the impact of local filing requirements is underrepresented in the Portal data for Malta

What does the Portal data tell us?

Reasons provided for non-filing



How can we interpret this considering our understanding of the market?

1 | **2** | 3 | 4

because local requirements make it difficult or impossible to file

6% ↑

- **Country filing requirements** is likely to be **under-represented** in the Portal results
  - Whilst there is no ***formal*** requirement that makes it impossible to file, there are ***informal*** preferences. As a country of only 500,000 people, payers would prefer to leverage assessments from other countries for efficiency

17% <>

- **Budget impact models** mean that the **size of the treatable population** impacts feasibility of filing in Malta as it can be difficult or impossible to source local data; we see this represented in the Portal results

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Key: ↑ = underrepresented in Portal data
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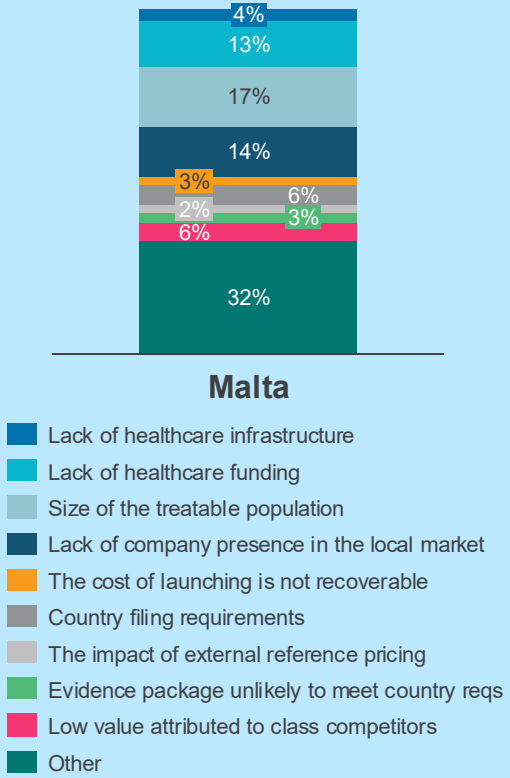
A major issue impacting filing decisions in Malta is likely not being fully captured by the current options in the Portal

What does the Portal data tell us?

Reasons provided for non-filing



How can we interpret this considering our understanding of the market?

1 | 2 | **3** | 4

…because features of the local system make it impractical to file

Missing

- **Lack of transparency of the P&R process** after filing is a major concern in Malta, and deters companies from filing because they aren't then able to track the status of their product or enter into reasonable dialogue or negotiation with authorities
  - **32%** ○ Our hypothesis is that this issue cannot be picked up by the Portal's current reasons for non-filing, and may in part explain some of the **high proportion of 'Other'** responses that are consistently picked up in the data
- **14% <>** **Lack of company presence** can exacerbate the difficulties that companies experience in navigating the unconventional Maltese P&R system; we see this reflected in the Portal data

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: P&R = pricing and reimbursement

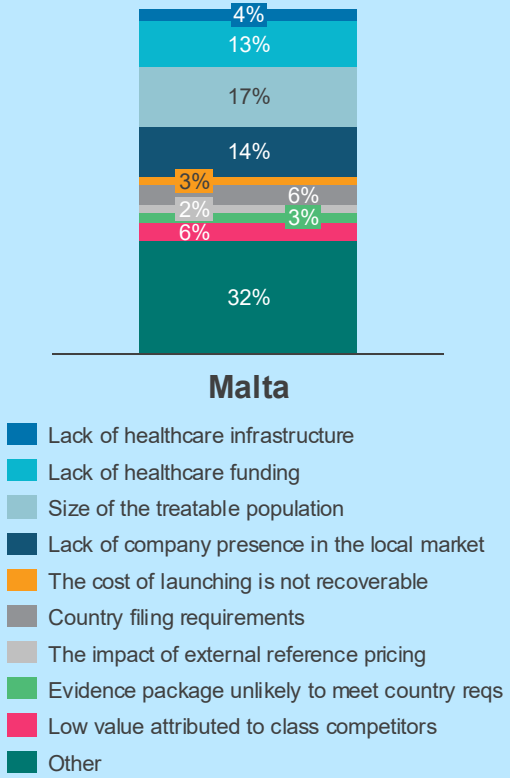
Key: ⬆ = underrepresented in Portal data

<> = fairly reflected in Portal data

It is challenging for companies to make a reasonable business case to launch in Malta as a result of significant budget constraints

What does the Portal data tell us?

Reasons provided for non-filing



How can we interpret this considering our understanding of the market?

1 2 3 **4**

…because it is unsustainable (the business case cannot be made) for the MAH to do so

- **13%** • **Lack of healthcare funding** means that even products that have had a positive HTA decision may not have had budget allocated to enable their reimbursement
- **6%** • This is exacerbated by the use of tenders as a budget management tool, often at a class-level (single winner, price based). This challenge is most likely **underrepresented** in the Portal data as the role of tenders is not specifically captured. We hypothesise that some companies may also have categorised this issue as **'Low value attributed to class competitors'**
- **17%** • **The small size of the treatable population** compounds the impact of budgetary restrictions and price-based tenders on making a reasonable business case to launch a new medicine; **some of the 17% represented in the Portal data** is likely due to this challenge

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: MAH = marketing authorization holder

Key: ⬆ = underrepresented in Portal data

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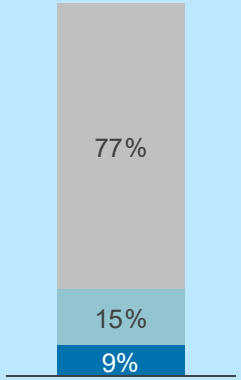
The raw Portal results for Malta will therefore need to be framed with a more nuanced description of the complex barriers to filing

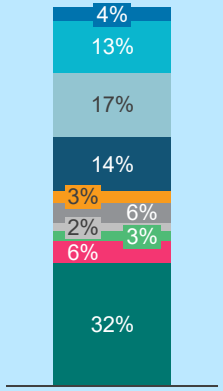
What does the Portal data tell us?

Status of P&R



- Reimbursed or filed for P&R
- Not yet filed for P&R (available through other public channel)
- Not yet filed for P&R (unavailable)

Reasons for non-filing



- Lack of healthcare infrastructure
- Lack of healthcare funding
- Size of the treatable population
- Lack of company presence in the local market
- The cost of launching is not recoverable
- Country filing requirements
- The impact of external reference pricing
- Evidence package unlikely to meet country reqs
- Low value attributed to class competitors
- Other

	Relative importance in Malta:	***Summary***
1 …because it is <u>unnecessary</u> to file to obtain access	●	15% availability through an alternative scheme is likely an **under-representation** of company willingness to provide access (through tenders, Community Chest Fund).
2 …because local requirements make it <u>difficult or impossible</u> for the MAH to file	◔	17% 'size of treatable population' needs to be put in context of **difficulties for BI modelling**; 6% country filing requirements depends on definition of '**requirements**'
3 …because features of the local system make it <u>impractical</u> to file	◑	Suggests potential need to add new reason related to '**lack of transparent P&R process**'; difficulties exacerbated by lack of company presence appear **fairly reflected** (14%)
4 …because it is <u>unsustainable</u> (the business case cannot be made) for the MAH to do so	◕	**Budgetary constraints** and the small potential market size in Malta are major challenges for making a viable business case; we see this reflected in the Portal data

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: BI = budget impact; MAH = marketing authorization holder; P&R = pricing and reimbursement

Key: ◔ → ◑ → ◕ → ●

Relative importance (in the local context) of each potential argument for explaining the filing data

In Cyprus, there is a low reimbursement rate (1%) of innovative medicines and a low filing rate (20%)

P&R overview

- Manufacturers **must file for inclusion** in the positive reimbursement list of the **National Health System (GESY)**
- The **Medicines Advisory Committee (MAC)** are then responsible for assessing the submissions; although clinical best practices are considered, the main focus is on **the budget impact** of the innovative product
- If the MAC recommends inclusion, the Medicines Reimbursement Advisory Committee (MRAC) will **negotiate an acceptable price** with the manufacturer for inclusion in the positive reimbursement list

New perspective on Root Causes

1. There are no **direct barriers** impacting the timing of filing in Cyprus, but in practice, payers reference the completed assessments and decisions made in other European countries
2. The MAC are **under-capacity** and have **complex guidelines**, including the need to develop Cyprus-specific therapeutic protocols for each product, contributing to **significant delays,** discouraging filling
3. There is a **lack of transparency** for MAHs on the progress of their product submission and indirect reference to reimbursement and HTA in other jurisdictions (the use of **Greece** as a key reference market results in **downward price pressure**)
4. Budget pressures are intense, the pharmaceutical expenditure budget **has not risen in line with a memorandum of understanding** with the industry, nor in line with the growth of GESY's total budget
5. Budget impact analyses are difficult to achieve **without access to local epidemiological data,** discouraging filing for orphan products

Alternative access (27%)

- **Until Jan 2025**, a large proportion of innovative medicines were made available via the named-patient basis route at the MoH, which had funding of ~€100mn, **did not require manufacturer filing**, allowed **higher prices** and saw a **shorter delay to patient access**
- However, this route is **now under the control of GESY**, leaving the future uncertain

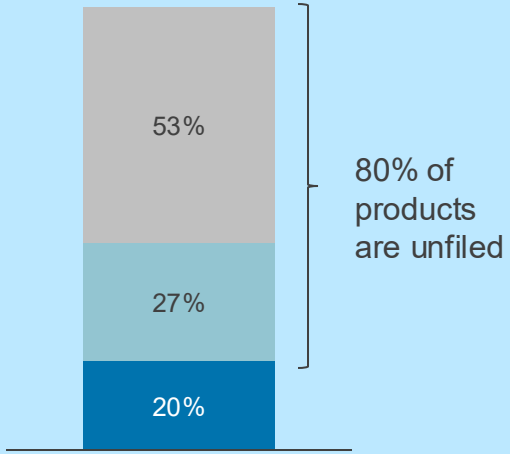
Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: GESY = National Health System; HTA = health technology assessment; MAC = Medicines Advisory Committee; MAH = marketing authorization holder; MoH = Ministry of Health; MRAC = Medicines Reimbursement Advisory Committee; P&R = pricing and reimbursement

Patients have access to more Portal products through alternative access schemes than products that have been formally filed for P&R

What does the Portal data tell us?

Status of filing and reimbursement



How can we interpret this considering our understanding of the market?

1 …because it is unnecessary to file to obtain access

2 3 4

20% • 20% of products have been filed for inclusion in the **positive reimbursement list** of the National Health System (GESY)

- Only 1% are actually reimbursed and hence available in Cyprus

27% • A greater proportion of Portal products (27%) have not been filed for reimbursement through GESY **but are accessible to patients** through an alternative access scheme funded by the Ministry of Health; this process generally works faster than the process for listing on the positive reimbursement list

- For the remaining 53% of products, it is not be necessary for all of them to be filed for reimbursement in the future in order for patients in Cyprus to have access, as some products will be better suited to the named patient route*

*As of January 2025, the named patient programme is now under the remit of GESY (rather than the Ministry of Health). It is uncertain what types of medicines will be eligible if GESY alter the existing inclusion criteria and process

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: GESY = National Health System

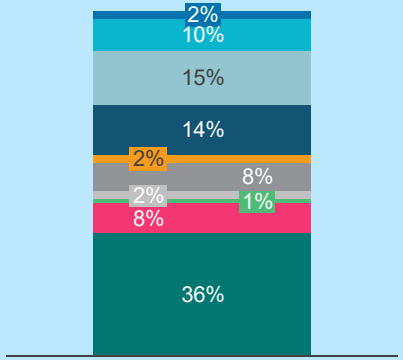
Key: ⬆ = underrepresented in Portal data

<> = fairly reflected in Portal data

Informal filing requirements and small patient numbers can impact the speed of filing of new medicines

What does the Portal data tell us?

Reasons provided for non-filing



Cyprus

- Lack of healthcare infrastructure
- Lack of healthcare funding
- Size of the treatable population
- Lack of company presence in the local market
- The cost of launching is not recoverable
- Country filing requirements
- The impact of external reference pricing
- Evidence package unlikely to meet country reqs
- Low value attributed to class competitors
- Other

How can we interpret this considering our understanding of the market?

1 | **2** | 3 | 4

because local requirements make it difficult or impossible to file

8% ↑ • **Country filing requirements** is likely to be **under-represented** in the Portal results as whilst there is no formal restriction, Cypriot health authorities do consider how many countries a new medicine has been evaluated in and the outcome of those evaluations

+ 2% ↑ ○ List price setting is based on IRP with a basket of 10 reference countries; in practice, much focus is placed on the Greek price. This may impact speed of filing and P&R decision making in Cyprus

15% <> • **Budget impact models** mean that the **size of the treatable population** impacts feasibility of filing in Cyprus; we see this represented in the Portal results

○ In some cases, the data exists (held by the HIO) but is not accessible for companies to use in their submission

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: HIO = Health Insurance Organisation; IRP = international reference pricing; P&R = pricing and reimbursement

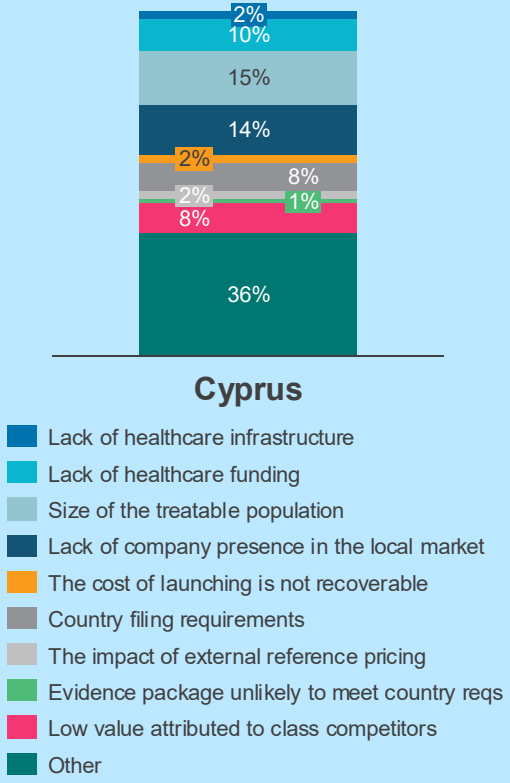
Key: ↑ = underrepresented in Portal data

<> = fairly reflected in Portal data

Introduction of the new P&R system has been a huge achievement, but initial backlogs may have disincentivised filing of new medicines

What does the Portal data tell us?

Reasons provided for non-filing



How can we interpret this considering our understanding of the market?

1 | 2 | **3** | 4

…because features of the local system make it impractical to file

Missing

- The National Health System was only introduced in 2019, resulting in an initial backlog of products that needed to be filed for P&R. During this transition period (2019-2024), companies may have **been deterred from filing new medicines until the backlog had been cleared** and the agency had capacity to review new submissions
  - **36%** This is a nuanced challenge that is not picked up by the nine generalised response options in the Portal. It is reasonable to assume a high proportion of **'Other' responses** may be linked to this situation
  - Compounding this, and likely also captured in the 'Other category' is the **complexity and lack of transparency of the P&R process**, which discourages companies from filing additional products when they remain uncertain about the status of previously submitted medicines

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: P&R = pricing and reimbursement

Key: ⬆ = underrepresented in Portal data

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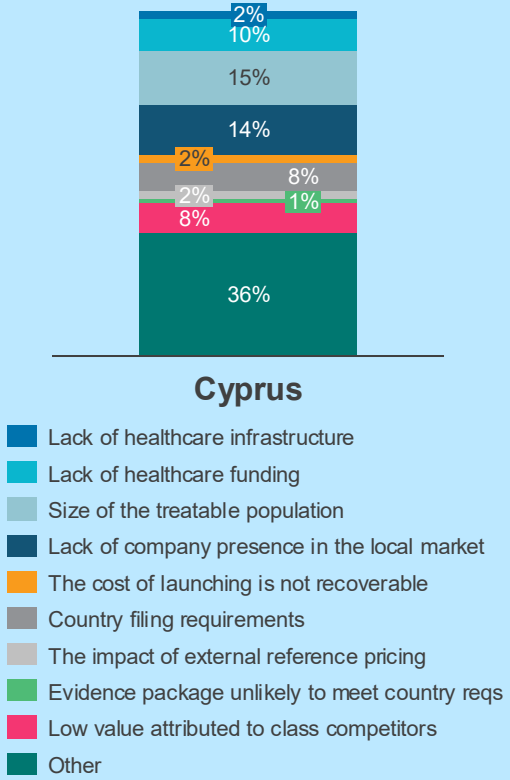
The pharmaceutical budget has not grown in line with the growth of GESY's total healthcare budget

What does the Portal data tell us?

Reasons provided for non-filing



How can we interpret this considering our understanding of the market?

1 2 3 **4**

…because it is unsustainable (the business case cannot be made) for the MAH to do so

- There is some evidence to support that MAHs can struggle to make the necessary business case to file a new medicine in Cyprus:
  - 10% <> **'Lack of healthcare funding'** constitutes 10% of reasons for non-filing. Since the introduction of the NHS, whilst the total budget for financing the health system has increased (from 900m EUR in 2019 to 1.76bn in 2024), the amount of **the budget allocated towards medicines is expected to remain stagnant**
  - 21% <> **'Lack of company presence'** in Cyprus may be adding to this commercial hurdle, as companies need to invest in local consultants, distributors and/or wholesalers

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: GESY = National Health Service; MAH = marketing authorization holder

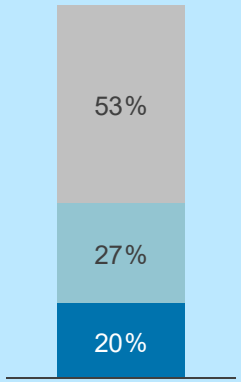
Key: ⬆ = underrepresented in Portal data

<> = fairly reflected in Portal data

The Portal data support that whilst navigating the new P&R process is challenging, many products are accessible through other means

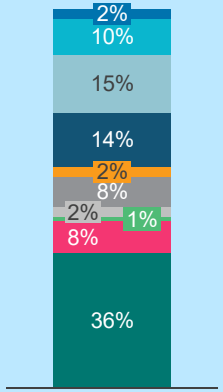
What does the Portal data tell us?

Status of P&R



- Reimbursed or filed for P&R
- Not yet filed for P&R (available through other public channel)
- Not yet filed for P&R (unavailable)

Reasons for non-filing



- Lack of healthcare infrastructure
- Lack of healthcare funding
- Size of the treatable population
- Lack of company presence in the local market
- The cost of launching is not recoverable
- Country filing requirements
- The impact of external reference pricing
- Evidence package unlikely to meet country reqs
- Low value attributed to class competitors
- Other

Relative importance in Cyprus:

Summary

1. **…because it is unnecessary to file to obtain access**

   Very few products in the Portal that are filed have been reimbursed (1%); as an alternative, many products (27%) are accessible through a **robust named patient programme**

2. **…because local requirements make it difficult or impossible for the MAH to file**

   8% ‘country filing requirements’ plus 2% ‘impact of ERP’ may be underrepresenting the **role of reliance on other countries’ evaluations** / decisions in the P&R process

3. **…because features of the local system make it impractical to file**

   Until the P&R system matures, and the backlog is cleared, MAHs are discouraged from filing new medicines as there are **delays and no transparency on previously filed medicines**

4. **…because it is unsustainable (the business case cannot be made) for the MAH to do so**

   The **pharmaceutical budget has not grown** in line with the overall healthcare budget, and many companies **lack an affiliated presence** in Cyprus

Key:

Relative importance (in the local context) of each potential argument for explaining the filing data

In Latvia, there is a low reimbursement rate (10%) of innovative medicines and a low filing rate (29%)

P&R overview

- Any of the NHS*, the MAH, a wholesaler or a legal representative can **file an innovative product for reimbursement**
- The State Medicines Agency (SMA) are responsible for conducting HTA, which includes a **clinical evaluation** and a **cost-effectiveness evaluation**
- Following a SMA recommendation, the NHS are responsible for determining whether a product is **included in the positive reimbursement list** following application of **prioritization criteria** and **negotiated price discounts**

New perspective on Root Causes

1. An inherent challenge in Latvia is the **insufficient (and fluctuating) healthcare budget** to procure all innovative medicines that the SMA recommends; as a result, there is a **permanent queue** of innovative products waiting to receive reimbursement, which have had a **positive assessment from the SMA** for many years
2. There are defined criteria for prioritizing **which medicines in the queue to reimburse**, but decisions can be politically driven in practice and prioritise certain therapy areas over others
3. The lack of **epidemiological information** in some therapy areas makes it difficult to conduct **budget impact analyses** when preparing a new dossier, or introduce **innovative contracting** beyond basic volume/price caps during negotiations
4. There are **poorly developed alternative access schemes** for highly specialized, orphan and/or high-cost medicines

Alternative access (6%)

- Although a **named patient reimbursement** programme is available in Latvia for patients to access innovative products which are not yet reimbursement, this is a small pathway (although budget is increasing) and is **inefficiently designed**, requiring approval by **both the SMA and MoH** with **separate contracts negotiated per hospital**

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

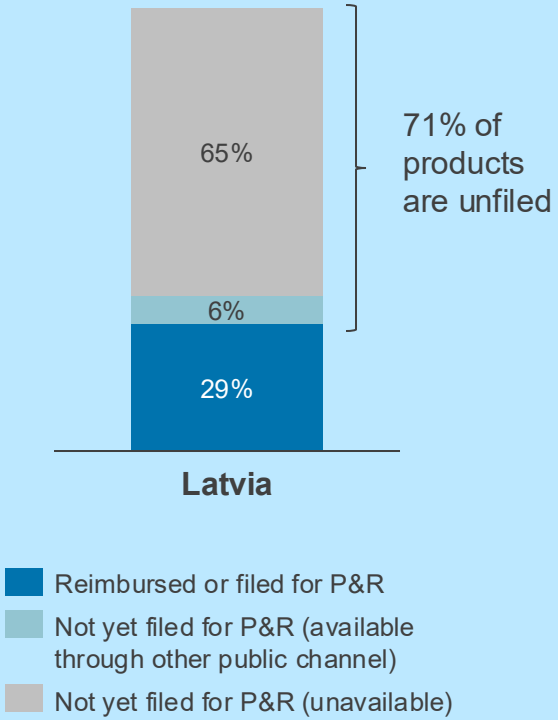
Abbreviations: HTA = health technology assessment; MAH = marketing authorization holder; MoH = Ministry of Health; NHS = National Health System; P&R = pricing and reimbursement; SMA = State Medicines Agency

*The NHS can propose the reimbursement of older medicines that are deemed highly necessary by preparing a simplified dossier that does not require review by the SMA

In absence of substantive alternative access schemes to bridge the gap to patient access, filing for P&R is necessary for new medicines

What does the Portal data tell us?

Status of filing and reimbursement



How can we interpret this considering our understanding of the market?

1 …because it is unnecessary to file to obtain access

2 3 4

29% • 29% of products have been filed for inclusion in the **positive reimbursement list**

- Only 10% are actually reimbursed and hence available to patients in Latvia
- This results from the constrained healthcare budget and the corresponding decision to manage this by putting medicines into a queue for reimbursement following a positive HTA decision

6% • An additional 6% of products are not yet filed but available through **named patient reimbursement**

- Given that only 6% of products have been able to reach patients through this route, filing for reimbursement is necessary in Latvia in absence of substantive alternative access schemes

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: HTA = health technology assessment; P&R = pricing and reimbursement

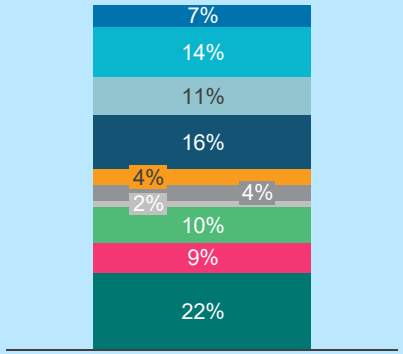
Key: ⬆ = underrepresented in Portal data

<> = fairly reflected in Portal data

For certain medicines, some companies may find it impossible to file if there are no useable local registries in that indication

What does the Portal data tell us?

Reasons provided for non-filing



Latvia

- Lack of healthcare infrastructure
- Lack of healthcare funding
- Size of the treatable population
- Lack of company presence in the local market
- The cost of launching is not recoverable
- Country filing requirements
- The impact of external reference pricing
- Evidence package unlikely to meet country reqs
- Low value attributed to class competitors
- Other

How can we interpret this considering our understanding of the market?

1 | **2** | 3 | 4

because local requirements make it difficult or impossible to file

4% <> 2% <>

- The impact of **country filing requirements appears fairly reflected in the Portal results**; whilst the P&R process involves **IRP**, filing is still possible if no prices are available in the reference countries. SMA also accept submissions made in English if necessary
- Poor quality registries in some therapy areas mean that it is not always possible to prepare the required dossier

11% <>
  - This is in part an effect of the **size of the treatable population** in Latvia; we see this represented in the Portal results and should consider population size as a factor affecting the possibility of filing (rather than just attractiveness of filing)

22%
  - In absence of a specific category for this issue in the Portal, we also assume some companies have recorded this challenge under **'Other'**

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: IRP = international reference pricing; P&R = pricing and reimbursement

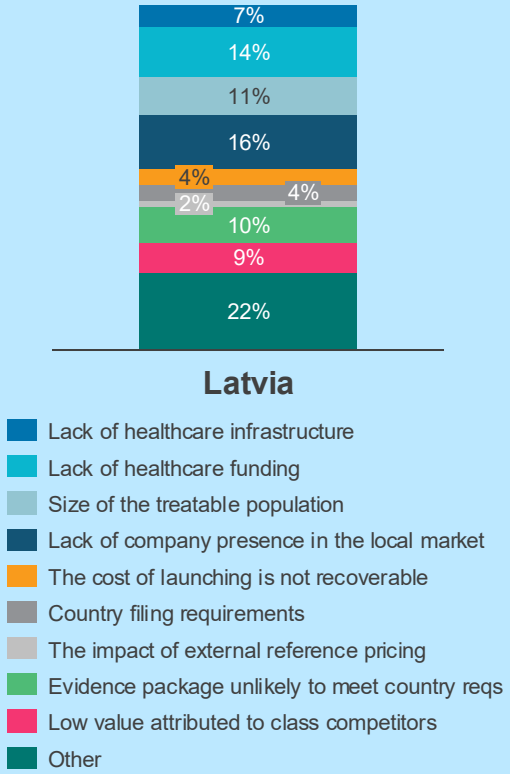
Key: ⬆ = underrepresented in Portal data

<> = fairly reflected in Portal data

The disconnect between positive HTA and timely reimbursement make it impractical for new medicines to be added to the queue

What does the Portal data tell us?

Reasons provided for non-filing



How can we interpret this considering our understanding of the market?

1 | 2 | **3** | 4

3: …because features of the local system make it impractical to file

14% ⬆

- It is impractical to file all EMA-approved medicines in Latvia within a fixed time period as the constrained healthcare budget has made it impossible for all drugs to be reimbursed (even with a positive HTA decision); the impact of **'lack of healthcare funding' has likely been under-represented** in the Portal data as separate (public) data shows over 80 medicines currently in the queue
  - This will affect different medicines to different extents as **certain therapy areas are prioritised over others**. If a company has recently received EMA approval for a new medicine in an indication that is not a government priority, it would be impractical to file it for reimbursement and add a lower-priority medicine to an already long queue

16% <>

- Navigating this process system **without a local presence** is also challenging, particularly for smaller companies

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025); Evaluation of applications for inclusion of new drugs in the List of Reimbursable Drugs or expansion of reimbursement conditions (as of October 1, 2024)

Abbreviations: EMA = European Medicines Agency; HTA = health technology assessment

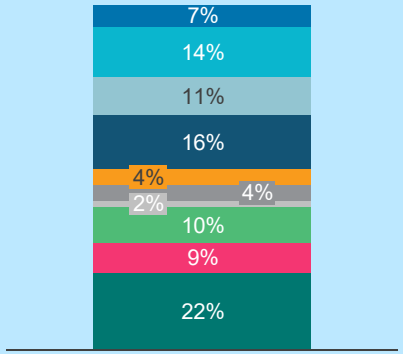
Key: ⬆ = underrepresented in Portal data

<> = fairly reflected in Portal data

The multi-faceted reasons for delays in filing in Latvia result in challenging commercial conditions for launching new medicines

What does the Portal data tell us?

Reasons provided for non-filing



Latvia

- Lack of healthcare infrastructure
- Lack of healthcare funding
- Size of the treatable population
- Lack of company presence in the local market
- The cost of launching is not recoverable
- Country filing requirements
- The impact of external reference pricing
- Evidence package unlikely to meet country reqs
- Low value attributed to class competitors
- Other

How can we interpret this considering our understanding of the market?

1 2 3 **4**

…because it is unsustainable (the business case cannot be made) for the MAH to do so

- The interaction between different reasons for non-filing suggest that in some instances this results in a challenging business case for filing a new medicine:
  - 11% ○ **The small treatable population** (which can make it difficult to prepare a dossier for filing), and
  - 14% ○ **The lack of healthcare funding** (which can make it impractical to file a new medicine given the existing queue),
  - 16% ○ Can be exacerbated by **lack of company presence**, resulting in the need to invest in local consultants and distributors
- **The cumulative effect is not possible to measure in the Portal data**, but logically these factors in combination result in concerns around sustainability of investing in a new product launch

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: MAH = marketing authorization holder

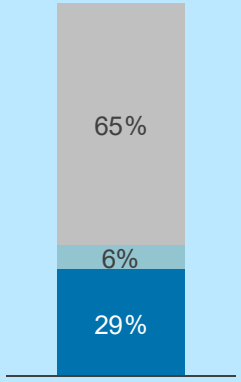
Key: ⬆ = underrepresented in Portal data

<> = fairly reflected in Portal data

The practicality of filing new medicines in Latvia is often a concern, particularly in therapy areas that are not prioritised by the government

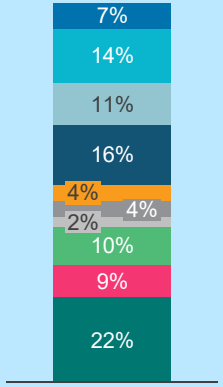
What does the Portal data tell us?

Status of P&R



- Reimbursed or filed for P&R
- Not yet filed for P&R (available through other public channel)
- Not yet filed for P&R (unavailable)

Reasons for non-filing



- Lack of healthcare infrastructure
- Lack of healthcare funding
- Size of the treatable population
- Lack of company presence in the local market
- The cost of launching is not recoverable
- Country filing requirements
- The impact of external reference pricing
- Evidence package unlikely to meet country reqs
- Low value attributed to class competitors
- Other

	Relative importance in Latvia:	***Summary***
1 **…because it is <u>unnecessary</u> to file to obtain access**		The named patient reimbursement scheme does not support widespread access to many products, so **filing for P&R is necessary** (although the NPP budget has grown in 2025)
2 **…because local requirements make it <u>difficult or impossible</u> for the MAH to file**		Payers are open to receiving new dossiers, but some companies may find it impossible to **file if there are no useable local registries** in that indication
3 **…because features of the local system make it <u>impractical</u> to file**		The disconnect between positive HTA and timely reimbursement (resulting from **lack of healthcare funding**) make it impractical for new medicines to be added to the existing queue
4 **…because it is <u>unsustainable</u> (the business case cannot be made) for the MAH to do so**		The **interaction between different reasons** for non-filing suggest that in many instances this results in a challenging business case for filing a new medicine

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: HTA = health technology assessment; MAH = marketing authorization holder; NPP = named patient programme; P&R = pricing and reimbursement

Key: 

Relative importance (in the local context) of each potential argument for explaining the filing data

In Lithuania, for products included in the Portal, there is a low reimbursement rate (7%) and a low filing rate (26%)

P&R overview

- MAHs file for reimbursement with the **State Medicine Control Agency** of Lithuania, who conduct an HTA by investigating comparative efficacy, comparative effectiveness and cost-effectiveness and produce a **public assessment report**
- The **NHIF** negotiate with manufacturers on the final price of innovative products and **conduct budget impact analyses**
- The Reimbursement Committee assess these reports and make a final decision on the outcome of a product; if successful a product moves to the **positive-waiting list where it remains until budget becomes available** to move to the positive list

New perspective on Root Causes

1. The current value assessment system is **complex**, leading to a lower likelihood of success if companies do not have **sufficient internal expertise** to navigate the system
2. It can be difficult for companies to prepare submissions for filing due to a **lack of available data** (e.g., epidemiological data), and because comparators used in pivotal trials may not reflect the Lithuanian SoC, contributing to low likelihood of success
   a) As a result, medicines are often deemed not to be adding additional therapeutic value, in which case there are **strict pricing rules applied** (average of existing alternatives in that indication, **including generics**)
3. There is a **lack of flexibility** in the P&R system for companies and a lack of willingness from payers for companies to propose innovative access solutions to **deal with data immaturity or uncertainty** in the evidence package, leading to high likelihood of rejection for many drugs
4. There is an **insufficient budget to implement positive HTA decisions**, leading to products remaining on the positive-waiting list for years

Alternative access (9%)

- There is an **ultra-rare pathway**, whereby patients can receive access to drugs that treat diseases with an incidence of 1 per 200,000 on a named-patient basis following a request by the physician/PAG and an assessment by the Committee for the reimbursement of ultra-rare diseases
- The **methodology for this assessment is not transparent** and decisions can often be **politically influenced**, leading to unpredictability for companies

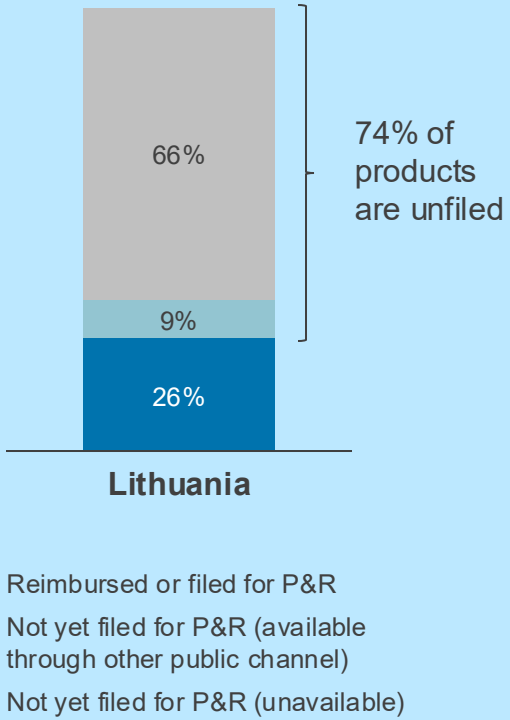
Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: HTA = health technology assessment; MAH = marketing authorization holder; NHIF = National Health Insurance Fund; PAG = patient advocacy group; P&R = pricing and reimbursement; SoC = standard of care

Filing for the standard pricing and reimbursement evaluation is necessary for most medicines to obtain patient access

What does the Portal data tell us?

Status of filing and reimbursement



How can we interpret this considering our understanding of the market?

1 …because it is unnecessary to file to obtain access

2 **3** **4**

26% • 26% of products have been filed for inclusion in the **positive reimbursement list**

- Only 7% are actually reimbursed and hence available to patients in Lithuania
- This results from the constrained healthcare budget and the corresponding decision to manage this by putting medicines into a queue for reimbursement following a positive HTA decision and agreement on price and reimbursement conditions

9% • An additional 9% of products are not yet filed but available through alternative access schemes such as **the physician/PAG-request ultra-rare disease pathway** (which functions like an NPP)

- Filing for reimbursement is there not necessary for certain rare disease medicines

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: HTA = health technology assessment; NPP = named patient reimbursement; PAG = patient advocacy group; P&R = pricing and reimbursement

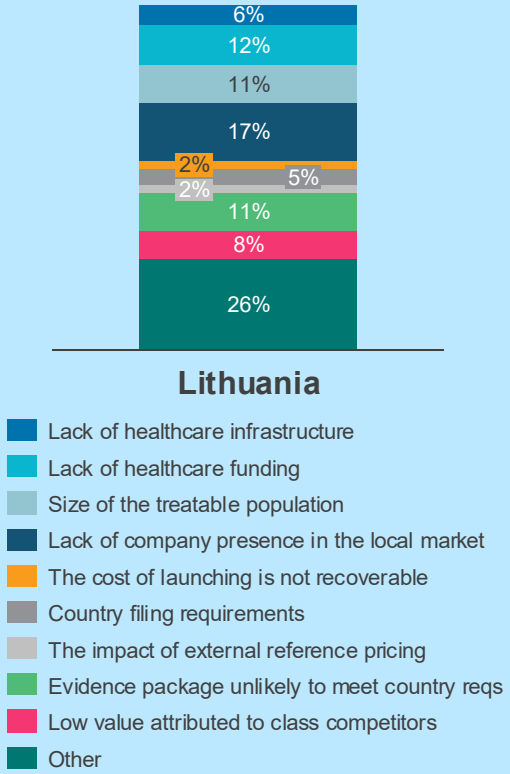
Key: ⬆ = underrepresented in Portal data

<> = fairly reflected in Portal data

Filing can be delayed as a result of MAHs not being able to access data or because of payer preference to reference completed HTAs

What does the Portal data tell us?

Reasons provided for non-filing



How can we interpret this considering our understanding of the market?

1 | **2** | 3 | 4

because local requirements make it difficult or impossible to file

5% ↑
- **Country filing requirements** is likely to be **under-represented** in the Portal results; whilst there is no formal requirement that makes it impossible to file, in practice payers reference the clinical assessments from other countries (particularly English-speaking)

11% <>
- **Budget impact models** mean that the **size of the treatable population** impacts feasibility of filing in Lithuania as it can be difficult or impossible to source the required local data

Missing
- The Portal results likely underrepresent this challenge as small patient population size is not the primary driver; instead, **lack of access to data** makes budget impact modelling challenging. Cost data maintained by the health insurance fund **is not accessible for companies to use in their filings**

26%
- Some of the 26% of **'Other'** responses may be associated with this data access barrier

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

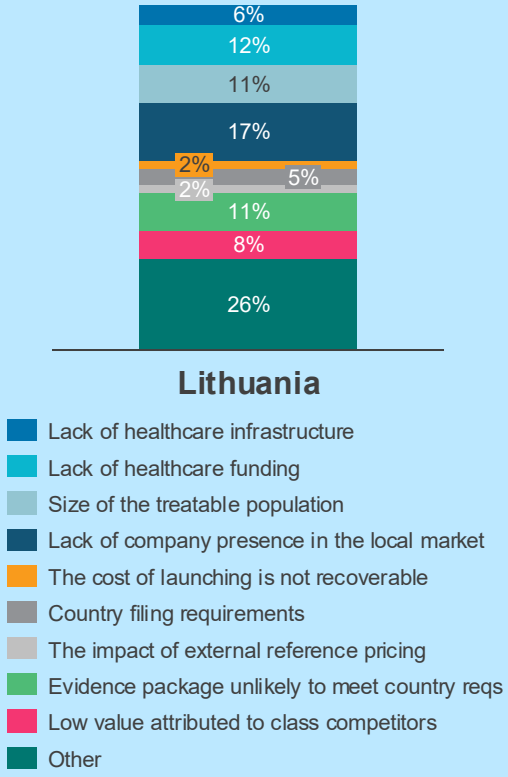
Abbreviations: HTA = health technology assessment; MAH = marketing authorization holder

Key: ↑ = underrepresented in Portal data
<> = fairly reflected in Portal data

The major barrier to filing in Lithuania is practicality; the P&R system is highly complex, and it is challenging to achieve reimbursement

What does the Portal data tell us?

Reasons provided for non-filing



How can we interpret this considering our understanding of the market?

1 | 2 | **3** | 4

3 …because features of the local system make it impractical to file

Missing

- The **complexity of the P&R system** in Lithuania results in high evidence requirements for companies and delays due to lack of capacity or expertise within the SMCA; **this challenge cannot be succinctly captured in the Portal data** as it does not align with any of the pre-set reasons
  - **17%** ⬆ Data on **'lack of local presence'** may be capturing some of this challenge, as it exacerbates the difficult of navigating the system
- **26%** <> Also missing from the Portal results (and likely captured under **'Other'**) is the effect of **lack of ICER flexibility** for specialist drugs and lack of processes for managing evidence uncertainty, resulting in a high likelihood of rejection for many medicines
  - **10%** ⬆ Given the low reimbursement rate of new medicines, there is also often **misalignment on the clinical comparator** as what was used in clinical trials does not reflect the Lithuanian SoC
- **12%** <> **'Lack of healthcare funding'** may reflect that medicines must enter a subsequent 'positive-waiting list' to wait for budget to be allocated for reimbursement

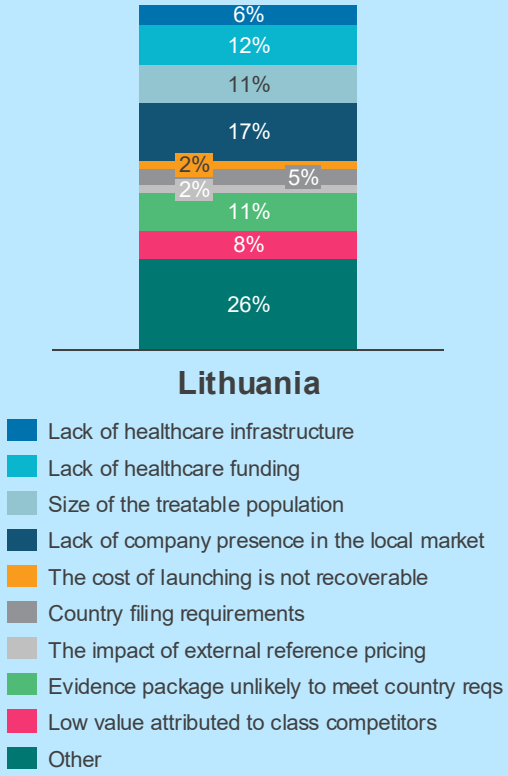
Key: ⬆ = underrepresented in Portal data

<> = fairly reflected in Portal data

Regulations and requirements of the P&R system can make it challenging to develop a viable business case to launch

What does the Portal data tell us?

Reasons provided for non-filing



How can we interpret this considering our understanding of the market?

1 2 3 **4**

…because it is unsustainable (the business case cannot be made) for the MAH to do so

2% ↑

- 2% of responses citing **'the cost of launching is not recoverable'** under-represents the compounding effect of the complexity of the P&R system: to navigate the process and source the necessary local data, companies frequently hire external support**. This investment is risky** given the difficulties in achieving successful reimbursement, budget driven reimbursement decisions, and the uncertainty of being on the positive-waiting list

8% <>

- The business case for launching a **"me-too" medicine** is different; these medicines have simplified evidence requirements, but **very restrictive pricing policies;** Portal responses citing **'low value attributed to class competitors'** may represent these types of innovative medicine

Key: ↑ = underrepresented in Portal data

<> = fairly reflected in Portal data

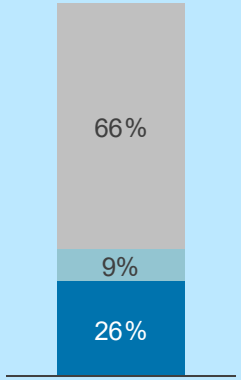
efpia

CRA Charles River Associates

The Lithuanian P&R system is complex and requires the Portal data to be interpreted with a nuanced, country-specific approach

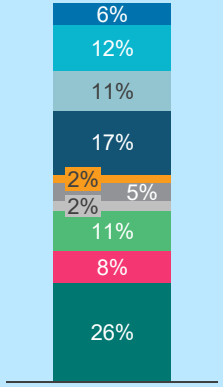
What does the Portal data tell us?

Status of P&R



- Reimbursed or filed for P&R
- Not yet filed for P&R (available through other public channel)
- Not yet filed for P&R (unavailable)

Reasons for non-filing



- Lack of healthcare infrastructure
- Lack of healthcare funding
- Size of the treatable population
- Lack of company presence in the local market
- The cost of launching is not recoverable
- Country filing requirements
- The impact of external reference pricing
- Evidence package unlikely to meet country reqs
- Low value attributed to class competitors
- Other

	Relative importance in Lithuania:	***Summary***
1 **…because it is unnecessary to file to obtain access**		Filing for the standard P&R evaluation is necessary for most medicines to obtain patient access, but **not for orphan medicines** (given the physician-led access channel)
2 **…because local requirements make it difficult or impossible for the MAH to file**		Filing can be delayed as a result of MAHs not being able to access data or because of payer preference to reference completed HTAs; **the Portal data cannot capture these challenges**
3 **…because features of the local system make it impractical to file**		The major barrier to filing is **practicality**; the P&R system is highly complex, and it is **challenging to achieve reimbursement**. The Portal options do not capture this complexity
4 **…because it is unsustainable (the business case cannot be made) for the MAH to do so**		**Regulations and requirements of the P&R system** can make it challenging to develop a viable business case to launch; this is multi-faceted and hard to quantify in the Portal data

Key: 

Relative importance (in the local context) of each potential argument for explaining the filing data

In Estonia, for products included in the Portal, there is a moderately low reimbursement rate (25%) and filing rate (38%)

P&R overview

- The **EHIF** manages reimbursement of new medicines through a **positive list** of medicines and healthcare services. The list is **updated 4x per year**, although applications for the list of services can be submitted 1x per year
- **MAHs or HCP associations** can file for inclusion of a product on this list, following which HTA is carried out
- There are **service lists** which set price and reimbursement conditions for classes of drugs; generic and biosimilar products can be included in these lists **without filing for P&R**. Innovative products part of the same class can achieve reimbursement through an abridged process, whereby they do not need to submit CEA and it is **sufficient to show budget neutrality**

New perspective on Root Causes

1. The **ICER thresholds applied to innovative medicines are low** compared to other countries (including neighboring Baltic countries) and are challenging for innovative medicines to meet (exacerbated by VAT rate being considered in the calculation)
   a) Strict reimbursement restrictions are frequently applied to medicines as a result of the ICER thresholds
2. After a positive HTA and reimbursement decision, medicines are **included quarterly into the positive reimbursement list**
3. Estonia has the smallest population size of the Baltic states (1.3 million people); combined with the challenging pricing conditions, this makes it **challenging to make a viable business case** to launch a new medicine in certain contexts (e.g. for rare diseases, or for smaller companies)
4. There are **limited alternative access schemes**, with individual patient-based reimbursement available only for non-registered medicines following a HCP application. In practice, this is rarely used

Alternative access (4%)

- Outside of the standard process, there are **no alternative routes for widespread patient access**
- **Charity Estonian Children's Funds** offer privately initiated cancer treatment for infants via private charity funds (i.e., 'The Gift of Life')
- Named patient reimbursement is possible mainly for non-registered medicines if HCPs can make a case to the EHIF, although **criteria is clear** for acceptance, the decision on reimbursement may vary

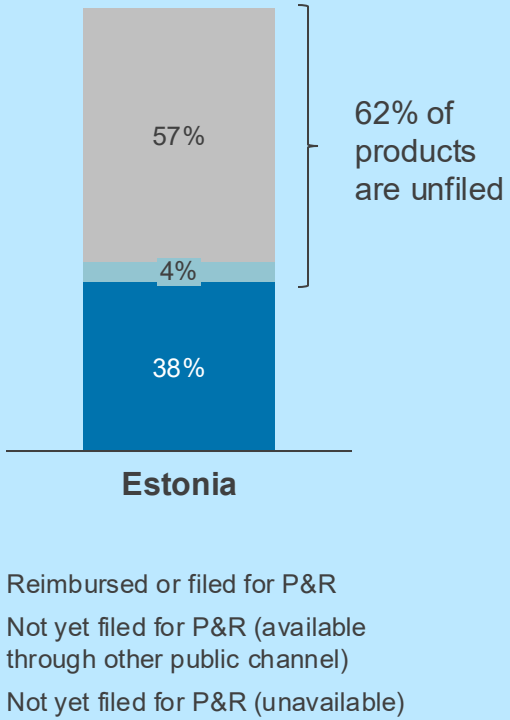
Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: EHIF = Estonian Health Insurance Fund; HCP = healthcare professional; HTA = health technology assessment; ICER = incremental cost effectiveness ratio; MAH = marketing authorization holder; P&R = pricing and reimbursement; VAT = value added tax

It is not necessary for MAHs to file all new medicines for P&R evaluation in Estonia in order to achieve reimbursement

What does the Portal data tell us?

Status of filing and reimbursement



How can we interpret this considering our understanding of the market?

1 …because it is unnecessary to file to obtain access

2 **3** **4**

38% ↑ • 38% of medicines in the Portal have been **filed for inclusion on the EHIF's positive list**

- Only 24% are actually reimbursed and hence available to patients in Lithuania
- Although it is **not necessary for biosimilars and generics to file** for reimbursement**, all innovative products must file** to be included on the positive list. This can be an abridged process if manufacturers are happy to accept the current P&R conditions of the class of drugs
- Filing can also be initiated by HCPs rather than the MAH

4% • 4% of medicines are available through named patient reimbursement (i.e., via private charity funds); a process that is **initiated by HCPs** rather than by MAHs filing for P&R

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: EHIF = Estonian Health Insurance Fund; HCP = healthcare professional; MAH = marketing authorization holder; P&R = pricing and reimbursement

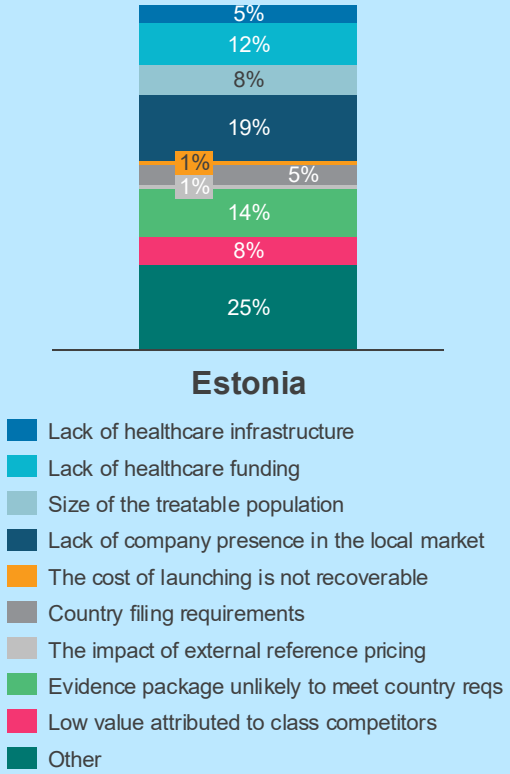
Key: ↑ = underrepresented in Portal data

<> = fairly reflected in Portal data

Historically it has not always been possible for MAHs to file for P&R, which has likely affected some medicines in the Portal

What does the Portal data tell us?

Reasons provided for non-filing



How can we interpret this considering our understanding of the market?

1 | **2** | 3 | 4

2 because local requirements make it difficult or impossible to file

5% ↑

- Historically, it has **not always been possible for MAHs to initiate the process** for inclusion of a new medicine on the reimbursement list; '**country filing requirements**' may have affected some of the earliest products in the Portal
  - Additionally, country filing requirements is likely to be **under-represented** in the Portal results; whilst there is no formal requirement that makes it impossible to file, in practice payers reference the clinical assessments from other countries (particularly English-speaking) to help mitigate uncertainty

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: MAH = marketing authorization holder; P&R = pricing and reimbursement

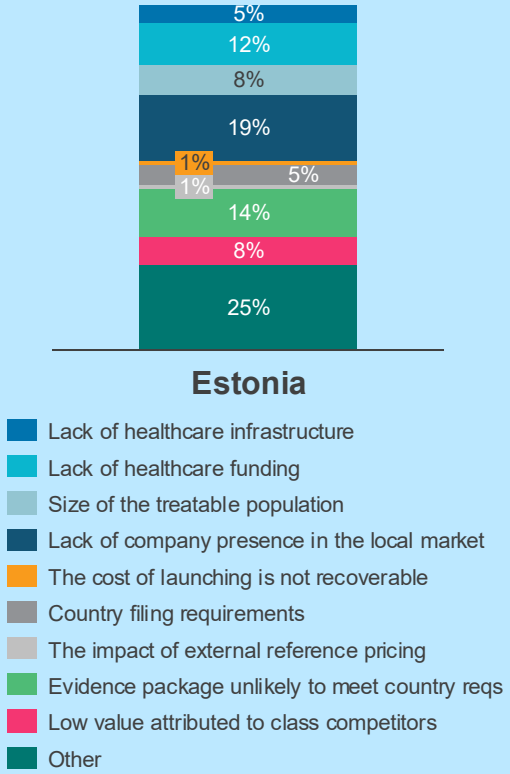
Key: ↑ = underrepresented in Portal data

<> = fairly reflected in Portal data

Many medicines cannot meet the ICER thresholds; this makes it impractical to waste MAH and EHIF resources on a lengthy evaluation

What does the Portal data tell us?

Reasons provided for non-filing



How can we interpret this considering our understanding of the market?

1 | 2 | **3** | 4

3 …because features of the local system make it impractical to file

14% ↑

- The **ability for manufacturers to meet local P&R requirements is likely under-represented** in the Portal results, as the challenge in Estonia is not primarily driven by evidentiary barriers (as worded in the Portal response options) but in the **low ICER thresholds** and the way these are calculated
  - Companies report that new medicines that have demonstrated cost-effective in other European countries can struggle to meet ICER thresholds in Estonia; it can be unpractical to go through the long filing and P&R evaluation process **if there is no possibility of meeting the ICER threshold**
  - 8% ↑ Some companies using the Portal may have reflected this under '**low value attributed to class competitors**'; the EHIF select the comparator product at a late stage in the P&R process, so it is not always feasible for companies to prepare their analysis accordingly

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: EHIF = Estonian Health Insurance Fund; ICER = incremental cost-effectiveness ratio; MAH = marketing authorization holder; P&R = pricing and reimbursement

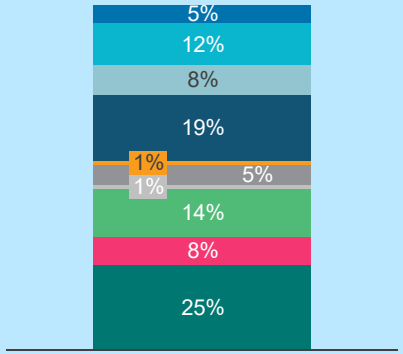
Key: ↑ = underrepresented in Portal data

<> = fairly reflected in Portal data

The small size of Estonia and the low per capita spend on healthcare makes it a challenging commercial environment for companies

What does the Portal data tell us?

Reasons provided for non-filing



Estonia

- Lack of healthcare infrastructure
- Lack of healthcare funding
- Size of the treatable population
- Lack of company presence in the local market
- The cost of launching is not recoverable
- Country filing requirements
- The impact of external reference pricing
- Evidence package unlikely to meet country reqs
- Low value attributed to class competitors
- Other

How can we interpret this considering our understanding of the market?

1 2 3 **4**

…because it is unsustainable (the business case cannot be made) for the MAH to do so

12% ↑ • Estonia has the **lowest per capita spend on pharmaceuticals** of the EU markets included in this analysis; this results in **budget-driven reimbursement decisions** by the EHIF, affecting the commercial viability of MAH decisions to invest in launching in Estonia

- 8% <> Compounding this is the **small total population size** (1.3 million people), which we see impacting filing decisions for several products in the Portal
- 19% <> **For smaller companies in particular**, the combined effect of a small pharmaceutical budget, small treatable population size, and the need to invest in local vendor and distributor support can make it commercially inviable to launch a new medicine in Estonia

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: EHIF = Estonian Health Insurance Fund; MAH = marketing authorization holder; P&R = pricing and reimbursement

Key: ↑ = underrepresented in Portal data

<> = fairly reflected in Portal data

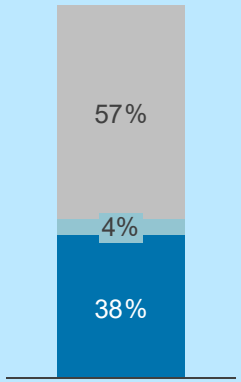
efpia

CRA Charles River Associates

It is not necessary for all medicines to file for P&R to achieve reimbursement; where it is necessary, it is often not practical to file

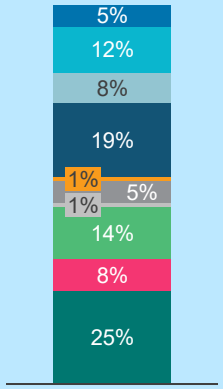
What does the Portal data tell us?

Status of P&R



- Reimbursed or filed for P&R
- Not yet filed for P&R (available through other public channel)
- Not yet filed for P&R (unavailable)

Reasons for non-filing



- Lack of healthcare infrastructure
- Lack of healthcare funding
- Size of the treatable population
- Lack of company presence in the local market
- The cost of launching is not recoverable
- Country filing requirements
- The impact of external reference pricing
- Evidence package unlikely to meet country reqs
- Low value attributed to class competitors
- Other

	Relative importance in Estonia:	***Summary***
1 …because it is <u>unnecessary</u> to file to obtain access		**Filing for the standard P&R evaluation is necessary** for innovative medicines to obtain patient access, with minimal alternative options
2 …because local requirements make it <u>difficult or impossible</u> for the MAH to file		Historically it has not always been possible for MAHs to file; now there are no prohibitive rules, but an assumption that some **HTA results from other countries have been published**
3 …because features of the local system make it <u>impractical</u> to file		Many medicines cannot meet the **low ICER thresholds**, making it impractical for MAHs to expend internal and EHIF resources on an evaluation that will not end with patient access
4 …because it is <u>unsustainable</u> (the business case cannot be made) for the MAH to do so		The small size of Estonia and the **low per capita spend on healthcare** makes it a challenging commercial environment for companies, particularly smaller companies

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: EHIF = Estonian Health Insurance Fund; HTA = health technology assessment; ICER = incremental cost-effectiveness ratio; MAH = marketing authorization holder; P&R = pricing and reimbursement

Key:

Relative importance (in the local context) of each potential argument for explaining the filing data

In Slovenia, for products included in the Portal, there is a moderate filing rate overall (56%), but this is lower for OMPs and ATMPs

P&R overview

- After MA, the manufacturer applies to the JAZMP to determine its **Maximum Allowed Price (MAP)** via **international reference pricing** where the MAP cannot exceed the lowest price of a product in Austria, France or Germany
- The ZZZS will conduct a **clinical assessment** and, if successful, will enter into **negotiations** with the manufacturer. ZZZS will use **the current cost of drugs** in the **respective therapeutic area** as a starting point and **MEAs** are common for oncology, orphan and ATMP medicines. If successful a product will be places on a **positive list for reimbursement**

New perspective on Root Causes

1. Although the requirements for local BI and CE analysis in P&R dossiers are clear, the dossier development can be challenging, especially for small affiliate teams and companies without a local presence, due to difficulties **sourcing local data** and the possible need to hire a local vendor
2. Historically, the ZZZS have **lacked sufficient resources** for timely assessment and negotiations, leading to some **delays** (e.g. months between a positive reimbursement decision and the beginning of price negotiations). However, ZZZS have **increased headcount recently** and made progress in clearing the P&R backlogs in 2024, with strong time to access compared to other CEE countries
3. There are **variable objective criteria** for the **assessment of P&R applications** by the ZZZS; this can support the availability of new medicines by offering different negotiation possibilities (e.g., negotiating on a particular product or across a portfolio), but also h inder availability (as it creates an uncertain operating environment for MAHs and could lead to a proposed price decrease for other portfolio medicines)
4. There are limited **alternative access opportunities,** leading to difficulties in launching certain products (e.g., rare diseases)

Alternative access (4%)

- Previously, the **EHAP pathway** granted manufacturers a higher list price for innovative products, mitigating any internal concerns on IRP and launch sequencing. However, the JAZMP has reduced use of this pathway for innovative products and uses it mainly for securing the supply of older medicines
- There is an **unfunded CUP** to provide access **pre-regulatory approval** and a **named-patient program**, funded by ZZZS to **support patient access pre-reimbursement**
- Hospitals can also purchase medicines directly from their budget

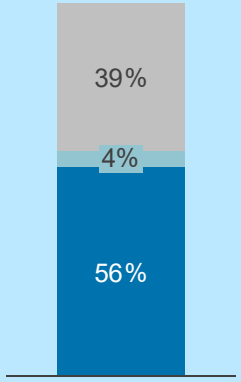
Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: ATMP = advanced therapy medicinal product; BI = budget impact; CE = cost-effectiveness; CUP = compassionate use programme; EHAP = Exceptional Higher Allowed Price; JAZMP = Agency for Medicinal Products and Medical Devices; MA = marketing authorization; MAP = maximum allowed price; OMP = orphan medicinal product; ZZZS = Health Insurance Institute of Slovenia;

All medicines must file for P&R to achieve reimbursement, but ambiguity in the process and a low population deters MAHs

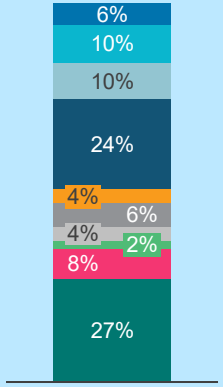
What does the Portal data tell us?

Status of P&R



- Reimbursed or filed for P&R
- Not yet filed for P&R (available through other public channel)
- Not yet filed for P&R (unavailable)

Reasons for non-filing



- Lack of healthcare infrastructure
- Lack of healthcare funding
- Size of the treatable population
- Lack of company presence in the local market
- The cost of launching is not recoverable
- Country filing requirements
- The impact of external reference pricing
- Evidence package unlikely to meet country reqs
- Low value attributed to class competitors
- Other

	Relative importance in Slovenia:	***Summary***
1 …because it is <u>unnecessary</u> to file to obtain access	○	The **named patient** and **compassionate use** schemes are unfunded and do not support widespread access, **so filing for P&R is necessary**
2 …because local requirements make it <u>difficult or impossible</u> for the MAH to file	◔	Although no **specific country filing restrictions,** challenges in **sourcing local data** to satisfy complicated P&R dossier requirements can **make filing difficult**
3 …because features of the local system make it <u>impractical</u> to file	◑	Broadly specified but partially unclear evaluation criteria creates **uncertainty** when filing for P&R, exacerbated by lengthy **delays** and negotiations involving a MAH's whole **portfolio**
4 …because it is <u>unsustainable</u> (the business case cannot be made) for the MAH to do so	◑	Relatively **low net prices** and **limited growth** of the pharmaceutical budget can make it difficult to **develop a viable business case** to launch in the face of a **small population** and **extensive P&R requirements**

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: P&R – Pricing & Reimbursement; MAH – Marketing Authorisation Holder; MAP – Maximal Allowed Price

Key: ◔ → ◑ → ◕ → ●

Relative importance (in the local context) of each potential argument for explaining the filing data

In Croatia, for products included in the Portal, there is a moderate filing rate overall (44%), but this is lower for rare and oncology drugs

P&R overview

- After MA, the manufacturer applies to HALMED to determine the **maximum permissible wholesale price** via **international reference pricing** where the price is usually the average of prices in Italy, Slovenia and Czechia*
- **HZZO** are then responsible for determining whether a product should be **placed on the reimbursement list**; the **MPC** make decisions based on specified reimbursement criteria, which are confirmed by the Governing Council
- Reimbursement negotiations involve the agreement on a **financial MEA** between the MAH and the HZZO (typically a value-cap agreement) **established at an indication level** (primarily for medicines on the list of especially expensive drugs)

New perspective on Root Causes

1. The price setting process is often timely (concluded within 30 days), but the subsequent reimbursement decision can take **between 6 months and 3 years**, with minimal communication to the MAH
2. More generally, there are political considerations in the appointment of the Drugs Committee and there is a **lack of transparency in how P&R regulations are interpreted by HZZO**, with many reasons for rejections either lacking specific objective feedback, or citing opaque factors
3. Once a medicine is included on the primary drugs list, all patients will have a **guaranteed access to the medicine**, but the full potential of treated patients would not be exceeded due to **hospital budget restrictions**. The **Special Fund** for expensive drugs was **established** as a source of funding outside hospital budgets to address this
4. Criteria on access on **Special Fund For Expensive Drugs (SFED)** are defined in 2023 Ordinance, but not always obeyed and are often **misinterpreted by the Payer**. There are no definitions on alternative funding processes beyond the basic drugs list and SFED

Alternative access (6%)

- During the negotiation process, HZZO can decide to include new medicines on the **list of "especially expensive drugs"**, with the list favoring drugs for unmet need (rare diseases, early line oncology and haematology), and a separate national budget (SFED) allocated for reimbursement of these high-cost products
- An **unfunded EAP** allows access between EMA approval and Croatian reimbursement decisions

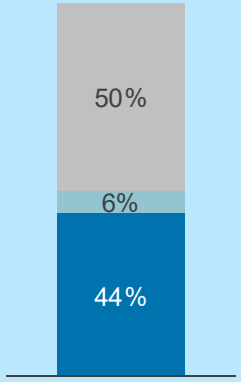
*where list prices are unavailable in reference countries, protocols are in place to ensure there is no delay resulting from the price setting stage

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)
Abbreviations: HALMED = Croatian Agency for Medicinal Products and Medical Devices; HZZO = Croatian Health Insurance Fund; MAH = marketing authorization holder; MPC = Medicinal Products Committee

A P&R system geared towards cost-containment and negative reimbursement outcomes presents significant challenge to filing

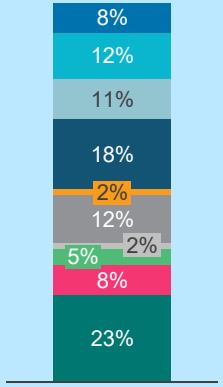
What does the Portal data tell us?

Status of P&R



- Reimbursed or filed for P&R
- Not yet filed for P&R (available through other public channel)
- Not yet filed for P&R (unavailable)

Reasons for non-filing



- Lack of healthcare infrastructure
- Lack of healthcare funding
- Size of the treatable population
- Lack of company presence in the local market
- The cost of launching is not recoverable
- Country filing requirements
- The impact of external reference pricing
- Evidence package unlikely to meet country reqs
- Low value attributed to class competitors
- Other

	Relative importance in Croatia:	***Summary***
1 …because it is <u>unnecessary</u> to file to obtain access	○	Aside from standard reimbursement, there is only an unfunded **EAP** which does not provide widespread access, meaning **filing for P&R is necessary**
2 …because local requirements make it <u>difficult or impossible</u> for the MAH to file	◑	12% 'country filing requirements' may be an underrepresentation, as HZZO can **cite a lack of reimbursement in other markets** as a reason to reject reimbursement
3 …because features of the local system make it <u>impractical</u> to file	◑	A significant lack of both **transparency in P&R decisions** and **consistency in the assessment criteria** discourages MAHs from filing for P&R
4 …because it is <u>unsustainable</u> (the business case cannot be made) for the MAH to do so	◑	The focus of HZZO on **obtaining the lowest possible price** and **limited opportunities to negotiate or implement MEAs** makes it a challenging business case to file

Sources: European Access Hurdles Portal data collection cycle 6 (N=94 products); CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: EAP – Early Access Program, HZZO - Croatian Health Insurance Fund, MEA – Managed Entry Agreement

Key: ◔ — ◑ — ◕ → ●

Relative importance (in the local context) of each potential argument for explaining the filing data

In North Macedonia, there is low availability (8%) of innovative medicines

P&R overview

- **MALMED** are responsible for regulatory approval of innovative products; although there is no automatic recognition of EMA decisions, manufacturers can submit largely the same dossier and there is fast approval if already centrally approved
- The National Pharmaceutical Pricing Authority, sitting within the MoH, set the maximum price using **IRP once per year,** taking the average of the **two lowest prices** within **Bulgaria, Croatia, Greece, Serbia** and **Slovenia**
- A committee within the MoH will then make a decision on reimbursement, including a clinical evaluation via a scoring system and KOL representation. If reimbursed, the budget must then be confirmed by the NHIF, who conduct a second round of IRP (at least once per year; taking the average of the two lowest from the same countries except Greece)
- Hospital products then need to be requested and procured by individual clinics **via tenders**

New perspective on Root Causes

1. The price setting system in North Macedonia is **restrictive,** with **two rounds of IRP** reducing the maximum price possible for innovative products. This reflects the wider environment of **insufficient funding for innovative products**
2. Following this, initially the **reimbursement list is not updated in a timely manner** and then the use of **tenders for innovative medicines** further constrains prices and delays patient access
3. Overall, the P&R process is **complex, bureaucratic** and **time-consuming,** making it difficult for manufacturers to achieve reimbursement and for clinics to gain access to new medicines; this is exacerbated by **many companies working through distributors**, rather than having a local presence
4. There is **insufficient infrastructure** outside of major cities to provide patient access to innovative medicines, affecting some therapy areas more than others
5. There is a **lack of synchronization** between the **reimbursement** and **pricing decisions**, for example, MEAs can be negotiated in theory, but they are disconnected with the reimbursement decision, so companies do not currently apply as it does not help to enable patient access

Alternative access

- Rare diseases go through an **alternative access scheme** via the **National Committee for Rare diseases**, with specific funding coming form an **alcohol and tobacco tax.** Although this works well, access is endangered by **yearly tenders**
- A **conditional funding mechanism** allows reimbursement as separate from the standard process if this is requested by major clinics, with ~60 innovative medicines currently on this list due to faster access and greater flexibility shown by HIF

Sources: EFPIA Patients W.A.I.T. Indicator 2024 Survey; CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: IRP = international reference pricing; KOL = key opinion leader; MALMED = Agency for Medicines and Medical Devices of the Republic of North Macedonia; MEA = managed entry agreement; NHIF – National Health Insurance Fund

Clinician-led conditional funding requests play an important role in enabling patient access in addition to the standard P&R process

	Relative importance in North Macedonia:	***Summary***
1 …because it is unnecessary to file to obtain access		Access via a **conditional funding mechanism** following clinic-initiated requests represents a **significant route of access for innovative medicines**
2 …because local requirements make it difficult or impossible for the MAH to file		**The two rounds of IRP** as the initial steps of the P&R process means reimbursement in other markets is supportive to the process in North Macedonia, but not mandatory
3 …because features of the local system make it impractical to file		A lack of **synchronization** between **reimbursement decisions** and **negotiations**, coupled with a **complex and bureaucratic P&R process** diminishes MAH opportunities
4 …because it is unsustainable (the business case cannot be made) for the MAH to do so		**Insufficient infrastructure to implement a reimbursement decision** and **restrictive pricing practices** in an already small market diminishes the incentive to launch here

Sources: CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: IRP = international reference pricing; MAH = marketing authorization holder; P&R = pricing and reimbursement

Key: 

Relative importance (in the local context) of each potential argument for explaining the filing data

In Montenegro, there have been recent efforts to strengthen the P&R process, but some access barriers remain

P&R overview

- Manufacturers can only submit applications for national marketing authorization after EC decision; **CInMED** are responsible for regulatory approval decisions, and they review applications **in line with the EMA's methodology** for assessments with a timeline of 150 days
- **CInMED** are then responsible for determining the **maximum wholesale price** using **IRP,** taking the **average price of Czechia, Romania and Serbia** (if no prices are available, the reference price is the lowest of the EU Member States)
- A reimbursement commission (comprised of clinicians, health economists, **HIF** and **MOH** representatives) is then responsible for determining which medicines are included on the **positive reimbursement list**; then these are procured via tenders

New perspective on Root Causes

1. The process for registering a new medicine in Montenegro typically only begins **after EMA approval** (to leverage efficiencies from the dossier and published decision from the centralized European process); marketing authorization therefore typically happens later (~1 year) in Montenegro than in the EU
2. The **frequency of updates to the positive list** were previously unpredictable and varied across years; new regulations have improved consistency of this process (three updates per year), but this may affect historical patterns on unavailability and delays
3. The **decision-making process** for updates to the positive list remain **opaque and constrained by insufficient budget**; lack of budget availability has led to a backlog of medicines awaiting inclusion in the list (with no ability to track where medicines are in the process) and unclear reasons for rejection of applications
4. It is **not possible to negotiate MEAs** to support introduction of new medicines as there is not sufficient data infrastructure to implement these, instead, all new innovative products are subject to a financial discount decided during a **Special Agreement** during the negotiation process

Alternative access

- Clinicians can request **named patient reimbursement for rare disease therapies** by applying to the Ministry of Health. This can accelerate patient access, but access is less predictable and sustainable than the standard P&R process (as approvals are typically given for a three-month period before being re-reviewed)
- This pathway is **relatively new** (established ~4 years ago)

Sources: CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: CALIMS = Agency for Medicines and Medical Devices; CInMED = Institute for Medicines and Medical Devices; HIF = Health Insurance Fund of Montenegro

Reimbursement backlogs and lack of ability to implement innovative access solutions can impede access to some medicines

	Relative importance in Montenegro:	***Summary***
1 …because it is unnecessary to file to obtain access		For **rare disease therapies** it is not necessary to file to obtain patient access; clinicians make requests for **named patient reimbursement**
2 …because local requirements make it difficult or impossible for the MAH to file		Although local data is **difficult to source** in a country of only 600,000 people, but local data are **not usually requested in the P&R process**
3 …because features of the local system make it impractical to file		Budget constraints have driven a **backlog** of medicines awaiting reimbursement. If a new medicine is likely to require an MEA beyond a special agreement with a financial discount, then it may not be possible to launch in Montenegro
4 …because it is unsustainable (the business case cannot be made) for the MAH to do so		**Budget constraints** combined with **the small treatable population** can make launching a new medicine in Montenegro unsustainable

Sources: CRA literature review and interviews with pharmaceutical companies and trade associations (conducted Dec 2024-Feb 2025)

Abbreviations: IRP = international reference pricing; MAH = marketing authorization holder; P&R = pricing and reimbursement

Key: 

Relative importance (in the local context) of each potential argument for explaining the filing data