Access to orphan medicines in Swedish healthcare

Usage and time to adoption according to established introduction processes in Sweden

The 21 regions in Sweden are responsible for providing healthcare nationwide, with the ultimate goal of promoting good health and well-being for patients and residents, today and in the future. Equal access to safe, effective, and affordable medicines – in sustainable ways for the healthcare system – is essential for achieving this goal. Scientific and technological advancements create new opportunities for pharmaceutical development. To stimulate the development of orphan medicines, various incentives have been introduced since the orphan medicines regulation was adopted in Europa, more than two decades ago. However, not all orphan medicines address real unmet medical needs of patients and treatment gaps in healthcare, and still today treatment remains unavailable for over 95% of rare diseases. Meanwhile, the orphan medicines market has grown into a lucrative market segment, often characterised by limited competition and relative high market dominance by companies.[1] In recent years, the pharmaceutical industry has criticised the Swedish healthcare system for poor and slow patient access, particularly for orphan medicines where Sweden is said to have below EU average coverage, according to the annual "WAIT report" commissioned by the European Federation of Pharmaceutical Industries and Associations (EFPIA). Swedish healthcare representatives do not share this image.[2] Other international comparisons identify Sweden as an "early adopter", in particular for essential and innovative medicines.[3]

This briefing paper presents an in-depth analysis of de facto access to orphan medicines in Sweden – from a healthcare perspective and with the Swedish context in mind. It also examines the time to patient access as well as the various routes for introduction and coverage through public funding. This is the third briefing paper of its kind and was developed by Region Västerbotten, Region Skåne, and Region Örebro County – with input from Region Stockholm, the Swedish Association of Local Authorities and Regions, and the Dental and Pharmaceutical Benefits Agency (TLV).

Key Messages

1. **Patient access and use of orphan medicines must be understood in relation to actual relevance**. This is influenced by factors such as patient population, demonstrated added clinical benefit, availability of other treatment options (not just medicines), pricing as well as costs. Time to adoption is also dependent on introduction processes. In Sweden, the time is affected by companies' strategies for marketing and supply, health economic assessments and reimbursement decisions made by the Dental and Pharmaceutical Benefits Agency (TLV), joint national introduction through negotiations between regions and companies, and recommendations for use, at the national and regional level.

2. **Expecting 100% or immediate patient access of authorised orphan medicines is neither realistic nor necessary from a patient perspective. Orphan medicines are not always the best option for rare and/or severe conditions when other relevant treatments exist**. Innovative medicines that address real unmet medical needs and contribute to scientific and technological advancements should be premiered over so called "regulatory innovation". Orphan designation and incentives should be used with greater precision.

3. **A shift toward reasonable, fair pricing of orphan medicines is necessary to lower barriers to patient access**. Escalating prices from companies and rising thresholds for accepted price levels by payers, risk distorting the market in favour of orphan medicines. Resources for well-established and effective treatments, including essential and lifesaving "basic" medicines and medicines for large patient populations, must not be displaced.

4. **A long-term sustainable healthcare system should be in the interest of all parties**. The Swedish healthcare system needs to prioritise medicines that provide added clinical benefits and represent safe, effective, and cost-effective treatment options – also considering the net health outcomes for the population. Sustainability will benefit pharmaceutical companies with relevant and reasonably priced medicines. Sustainability is the number one key factor for patient access and public health, today and in the future.

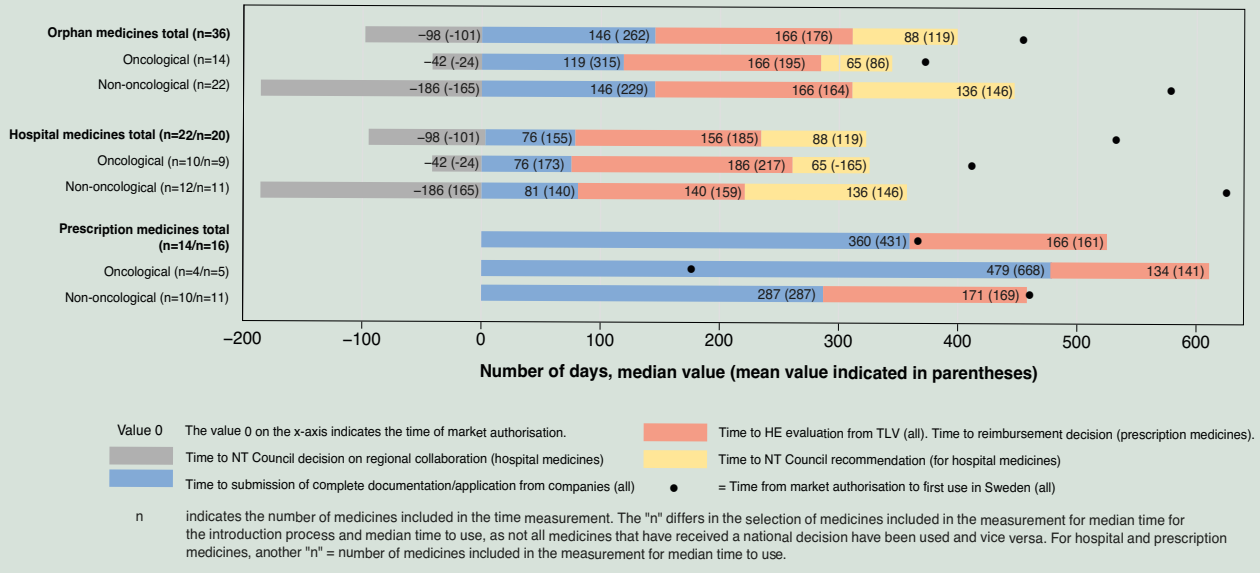
[1] SALAR (2021), Policy brief – Towards a pharmaceutical legislation that truly enhances public health and ensures sustainable health care systems in Europe https://www.regionvasterbotten.se/VLL/Filer/Policy%20brief_EU%20pharmaceutical%20legislation_tlg_20221031.pdf

[2] See e.g. IQVIA (2021), EFPIA Patients W.A.I.T. Indicator 2020 Survey; Quantify (2021), Access to new medicines with EMA approval 2017–2019 in Sweden (as well as the Swedish version of the same)

[3] See e.g. "IQVIA (2022), Defining Essential Innovative Medicines and Measuring their Use in Europe; Region Västerbotten och Region Örebro län (2022), Kunskapsunderlag, Tillgänglighet och användning av icke-onkologiska särläkemedel i svensk hälso- och sjukvård Region Västerbotten och Region Örebro län (2021), Kunskapsunderlag, Tillgänglighet till nya läkemedel för patienter i Sverige – utgångspunkter från svensk hälso- och sjukvård samt Dagens Medicin, "Lif ger en missvisande bild av tillgången till läkemedel", https://www.dagensmedicin.se/opinion/debatt/lif-ger-en-missvisande-bild-av-tillgangen-till-lakemedel/ (published 2021-07-06).

Highlights from the report

- Based on the Swedish healthcare system and legislated "free prescription right", **100% of all orphan medicines that are authorised by European Medicines Agency (EMA) are available for use in Sweden**. Medicines that are not authorised for the European market can be prescribed with approval from the Swedish Medical Products Agency.
- **The introduction of new medicines in Sweden is based on different pathways.** National introduction and decisions on pricing and reimbursement within the national pharmaceutical benefit scheme is managed via the Dental and Pharmaceuticals Benefit Agency (TLV). Pharmaceutical companies submit applications for inclusion in the scheme and a health economic evaluation is conducted. This is the main pathway for prescription medicines. The introduction of hospital medicines can be nationally coordinated by the 21 regions in a joint process. This requires a decision for regional collaboration. TLV provide the regions with health economic evaluations based on documentation submitted by the companies. The NT Council is mandated to issue recommendations on use in the joint process. Medicines can also be introduced through decentralised procedures in the regions. This includes procurement. Negotiations between regions and companies are initiated on a needs basis. As such, **all parties – also the companies – have a responsibility to streamline the introduction processes and facilitate timely patient access of new medicines in Sweden.**
- Of the reviewed medicines, **30% (18/60) were oncology orphan medicines and 70% (42/60) were non-oncology orphan medicines.** 22% (13/60) were older and well-established medicines that had been approved for new areas of use (repurposed medicines). These were all prescription medicines. 13% (8/60) were advanced therapy medicinal products (ATMP), all of which were hospital medicines.[4] The review of the orphan medicines authorised by EMA between 2017 and 2022 shows that **a total of 60% had reached patients in Sweden** (36/60), all of which had been **granted reimbursement and cost-coverage** through national funding (prescription medicines included in the pharmaceutical benefits scheme) or by the regions (procured hospital medicines introduced through national or regional procedures). Cost-coverage can also be granted through individual reimbursement.
- **The median time from market authorisation to first use of the studied medicines was 456 days**. Differences can be discerned between prescription medicines introduced and reimbursed via the national pharmaceutical benefit scheme, and hospital medicines introduced via the joint national process of the regions.
- **75% of orphan medicines that had been used in Swedish healthcare had been introduced through national processes.** The national pathway for hospital medicines was faster, with a median time of 320 days, from marketing authorisation to national agreement and formal recommendation. Half of this time was derived from TLV's process for the health economic evaluation. For prescription medicines the median time to the final reimbursement decisions was 526 days. Two thirds of this median time (360 days) was traced back to the time from market authorisation to the companies' submission of an application and complete documentation needed for the evaluation. *See chart below.*



- **Understanding the different pathways and stages in the process can help identify bottlenecks for timely introduction. Large variation occur between different medicines.** The time from marketing authorisation to the first positive national decision and recommendation as well as de facto use for the reviewed orphan medicines is outlined in the charts on the next page (excluding medicines that lack national decisions/recommendations and that had not yet been used in Swedish healthcare). **Every day counts.**

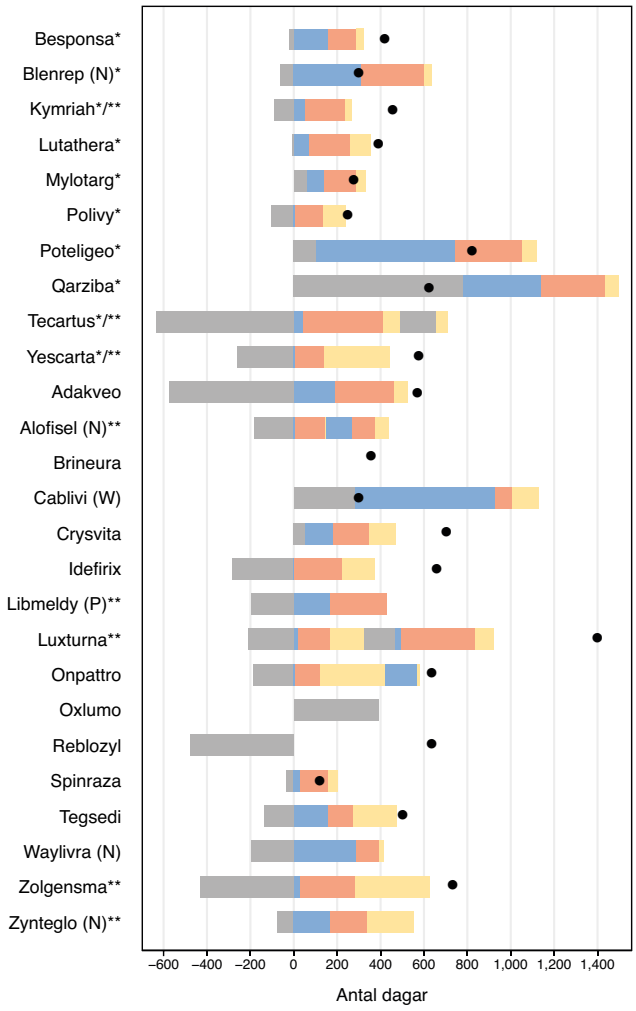
[4] Of all prescription medicines, 38% (13/34) were classified as repurposed. The ATMP share of the total number of hospital medicines was 31% (8/26).

Every day counts: Time measurement to understand different stages of the process for introduction of new medicines in Swedish healthcare

TIME FROM MARKET AUTHORISATION TO FIRST POSITIVE DECISION AND USAGE

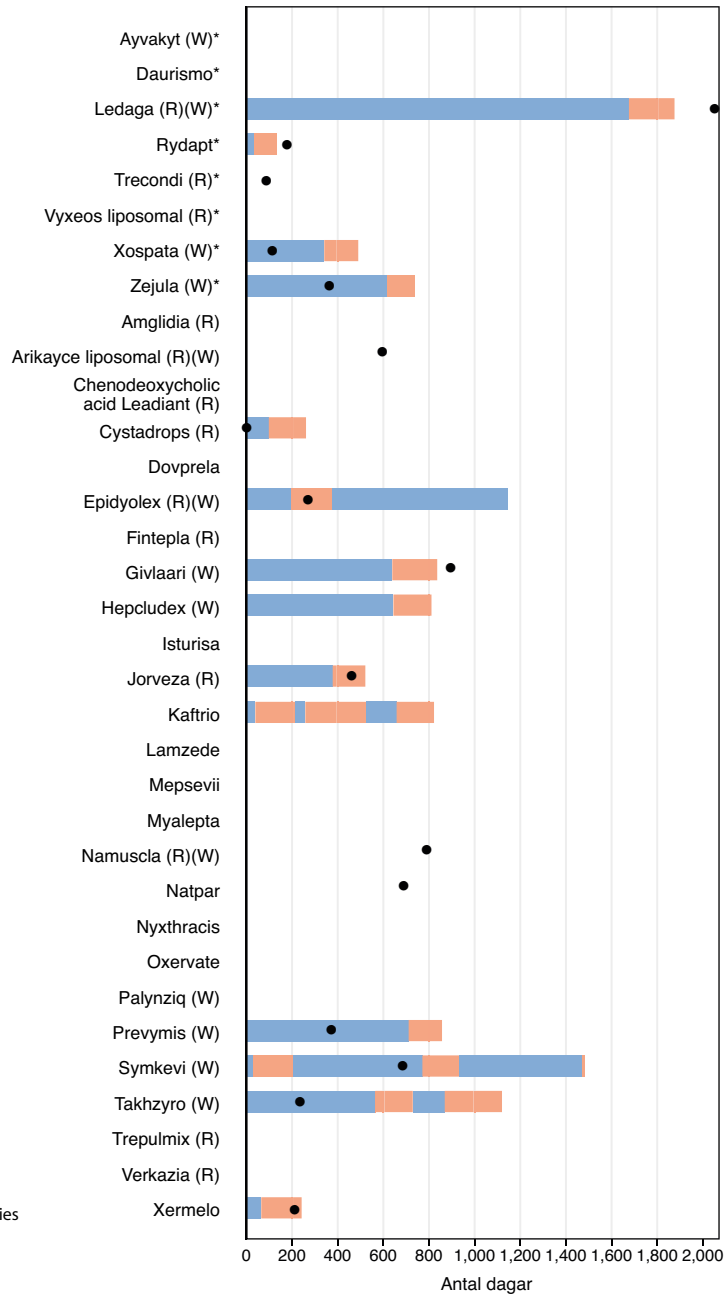
HOSPITAL MEDICINES

reported based on different parts of the introduction process



PRESCRIPTION MEDICINES

reported based on different parts of the introduction process



Value 0 The value 0 on the x-axis indicates the time for market authorisation

Time to NT Council decision on regional collaboration and nationally coordinated introduction (hospital medicines)
Time to new NT Council decision on regional collaboration and nationally coordinated introduction, round 2

Time to submission of complete documentation/applications from companies (all medicines)
Time to new submission of complete documentation/applications from companies, rounds 2 and 3

Time to new HE assessment from TLV (all medicines). Time to reimbursement decision (prescription medicines).
Time to HE assessment and/or reimbursement decision, rounds 2 and 3

Time to NT Council recommendation for use (hospital medicines)
Time to new NT Council recommendation for use, round 2

● Time from market authorisation to first use in Sweden

(N) = Medicine holds only negative national reimbursement decision/ recommendation
(P) = The medicine is in an ongoing national process, pending decision/ re commendation (time to decision missing)
(R) = Repurpose, dvs. äldre och beprövade läkemedel som godkänts för nya användningsområden eller i ny beredningsform
(W) = Application cancelled or withdrawn by the company in at least one process

* = Oncological medicine
** = Advanced therapy medicinal products, ATMP

The charts report the times for various stages in the processes for introduction of new medicines in Swedish healthcare - up to the time of the first positive national decision or recommendation (or the last negative decision/recommendation). Medicines that have undergone and completed the national processes are marked with bars. The various stages are colour-coded.

Medicines that have not initiated or completed national processes or have discontinued national processes as a result of a cancelled or withdrawn applications are excluded from time measurements and marked with empty fields.

Medicines that have a registered use are measured from the time of marketing authorisation to the date of first sale (regardless of sales volume). The time of use is marked with a black circle in the chart. This also applies to medicines that lack positive national decisions and recommendations as well as medicines that have never undergone a completed national process for introduction.

This English translation is an abbreviated version of the original briefing paper, published in Swedish 2023. The review illustrates that there are several reasons for why patients' access to orphan medicines can be delayed or hindered. The time measurement of the different stages of the introduction process confirms that counting days to introduction, reimbursement or de facto access require deeper understanding of the pharmaceutical systems. Furthermore, to draw conclusions about the use of orphan medicines based on European marketing authorisations, require an understanding of what types of medicines that have been approved, how they have been introduced, and how long this has taken. It is not possible – based on statistics only – to determine whether it is "right" or "wrong" to use or not use an orphan medicine or to decide what constitutes a reasonable time for decision making in the introduction process. Ultimately, clinical choices and decisions on use are founded in patient needs and the effectiveness of treatment options as well as the relevance to the healthcare system. Documentation on added clinical benefit provides key insights that can facilitate decision making. Every day counts from a patient perspective. The findings presented in this briefing paper confirms that patient access is a joint responsibility – including the key role that pharmaceutical companies play in terms of streamlining introduction processes at the national level.

Effective, safe, and reasonably priced, cost-effective medicines should be prioritised and premiered for better healthcare and highest possible health outcomes for residents and patients, with minimal displacements within the healthcare system. The sustainability of healthcare systems in Europe is a prerequisite for public health, today and in the future. This will benefit pharmaceutical companies with relevant treatments and contribute to the competitiveness of Europe in the global arena.

KEY CONCEPTS[5]

Availability: The medicine is available for use. This mainly requires a marketing authorisation and can be governed by prescription rights for healthcare professionals. Company strategies for marketing and supply as well as production and delivery can also matter.

Affordability: The medicine is available at a reasonable price and a cost that the "payer" can absorb. Depending on how the healthcare system is financed, affordability can be measured at the individual level or at the societal level. In some countries, patients cover various degrees of the pharmaceutical cost out-of-pocket or through privately financed insurance systems. In other countries, cost-coverage mainly occurs via taxes and through various public funding mechanisms and patients pay a smaller portion of actual costs. All healthcare systems are characterised by resource constraints and, as a result, will require some level of prioritisation.

Accessibility: The medicine reaches all the way to patients with real unmet medical needs. The optimal level of accessibility is difficult to measure. Patient access is dependent on both availability and affordability. Other factors that can affect patient access is associated with introduction and implementation processes and includes but are not limited to cost-effectiveness criteria, risks and uncertainties on safety and efficacy, competencies of healthcare professionals and acceptability of new medicines, treatment guidelines, as well as relative benefits in relation to other available treatment options. The OECD stresses that it is not reasonable to expect automatic, full and immediate patient access. It is neither always necessary from a patient perspective.

[5] OECD (2020), Addressing Challenges in Access to Oncology Medicines, Analytical Report

*** How was the review conducted?** The analysis focused on orphan medicines with European marketing authorisation from 2017 to 2020, based on data from EMA's EPAR database. 30 November 2022 was used as the cut-off date for introduction, reimbursement decisions/recommendations and medicine use, based on publicly available information as well as complementary information collected from TLV and the regions/regional collaboration model on the basis of the Public Access to Information and Secrecy Act. Sales statistics gathered primarily from the eHealth Agency's Concise database. A qualitative assessment of medicines was conducted by medical and pharmacological experts from within the Swedish healthcare system, in addition to a review of supplementary referenced literature. Note that available sales data is not linked to specific indications, which means that it is not possible to definitively determine that the occurrence of use corresponds to a specific orphan indication. For medicines with recorded sales before the date of marketing authorisation, the date of first use has been standardised to the date of marketing authorisation (e.g. for already well-established and now repurposed medicines or as an indication of off-label use).

The analysis included the following orphan medicines, authorised for the European market between 2017 and 2022: Adakveo, Arikayce liposomal, Brineura, Besponsa, Blenrep, Cablivi, Crysvita, Cystadrops, Epidyolex, Givlaari, Hepcludex, Idefrix, Jorveza, Kaftrio, Kymriah, Ledaga, Luxturna, Mylotarg, Namuscla, Natpar, Onpattro, Prevymis, Polivy, Poteligeo, Qarziba, Reblozyl, Rydapt, Spinraza, Symkevi, Takzhyro, Tegsedi, Trecondi, Vyxeos liposomal, Waylivra, Xermelo, Xospata, Yescarta, Zejula, Zolgensma, Alofsel, Amglidia, Ayvakyt, Chenodeoxycholic acid Lediant, Daurismo, Dovprela, Fintepla, Isturisa, Lamzede, Libmeldy, Lutathera, Verkazia, Myalepta, Mepsevii, Obiltoxiximab SFL, Oxervate, Oxlumo, Palynziq, Tecartus, Trepulmix, Zynteglo.

DO YOU WANT MORE INFORMATION?

Jörn Schneede
Head of Pharmaceutical Center
Region Västerbotten
jorn.schneede@regionvasterbotten.se

Maria Landgren
Head of Pharmaceuticals
Region Skåne
maria.landgren@skane.se

Maria Palmetun-Ekbäck
Head of Pharmaceutical Center
Region Örebro län
maria.palmetun-ekback@regionorebrolan.se

Örjan Norberg
Head of Innovation Center
Region Västerbotten
orjan.norberg@regionvasterbotten.se

Gustaf Befrits
Health economist, Pharmaceutical Unit,
Region Stockholm
Health economic advisor, NT Council
gustaf.befrits@regionstockholm.se

Mikael Svensson
Pharmaceutical strategist and negotiation coordinator
Swedish Association of Local Authorities and Regions
mikael.svensson@skr.se

BRIEFING PAPER ON PATIENTS' ACCESS TO MEDICINES IN SWEDEN
Access to orphan medicines in Swedish healthcare - Usage and time to adoption according to established introduction processes in Sweden

Content: Elham Pourazar, Jörn Schneede och Örjan Norberg, Region Västerbotten; Carl-Johan Glans, Region Skåne; Maria Palmetun Ekbäck, Region Örebro County.
Statistics and data: Hanna Lindström, Umeå university.
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