TANDVÅRDS- OCH
LÄKEMEDELSFÖRMÅNSVERKET

Summary

TLV (the Dental and Pharmaceutical Benefits Agency) has been assigned by the government to analyse and propose how to strengthen access to medicines for patients with rare diseases.

A higher number of effective medicines are developed for rare and severe diseases that previously had no treatment. New medicines can mean great improvements to patients' quality of life and life span, and it is important that such treatments are made available. However, this is contingent upon reasonable costs to avoid crowding out other publicly funded interventions with equal or greater benefits.

TLV is assigned to analyse and propose ways to enhance patients' access to medicines for the treatment of rare diseases. The proposals made by TLV should not result in increased medicine costs for the government compared to the current system. TLV is also expected to consider the ethical platform for prioritisation in healthcare and equal access to care across the country.

TLV already takes specific considerations into account for medicines targeting rare diseases. The model for value-based pricing that TLV uses means that the greater benefit a treatment provides, the more it may cost. In line with the ethical principles of needs and solidarity, TLV considers the severity of the disease, meaning that more resources get allocated to those who need them most. For medicines targeting very rare diseases, TLV accepts an even higher cost than for medicines treating equally severe but more common conditions.

This report includes TLV's proposals to improve and ensure equitable access to medicines for patients with rare diseases while establishing sustainable pricing for medicines in Sweden. Many of these measures fall under TLV's jurisdiction. However, achieving the broader goal will require efforts from regions, companies, and the government, as outlined in the report.

The number of medicines for rare diseases has increased and is expected to continue rising, but the costs have risen even more.

EU regulations on orphan medicines have been in place for over 20 years and aims to promote the development of medicines for small patient populations. By the end of 2022, there were a total of 140 medicines with or formerly having an orphan designation with sales in Sweden, twice the number from a decade earlier. During the same period, the sales value of medicines with or formerly having an orphan designation increased more than fourfold. The trend is expected to continue, with approximately 150 orphan medical products potentially receiving market approval in the EU from 2024 to the first quarter of 2026. This development could offer many crucial treatment options for patients.

The orphan medicine market has become more commercially attractive since the legislation came into effect. At the same time, many EU member governments are facing increasing challenges in providing medicines at reasonable prices, and representatives of health technology assessment (HTA) agencies and payers in the EU express concerns about high prices hindering patient access to treatment and equitable healthcare.

TLV has conducted a survey covering all orphan medicines that TLV has handled from 2015 to 2022.

The survey aimed to provide insight into how the current system for health economic assessment, pricing and reimbursement decisions works for making orphan medicines available. About 60 percent of the medicines included in the survey were out-patient prescription medicines and had been subject to TLV's reimbursement process, while 40 percent were in-patient medicines. For the latter, the regionally coordinated expert group, the Council for New Therapies (NT Council), evaluated the value in relation to cost and provided recommendations for use.

One overarching conclusion from the review is that the current system has enabled many orphan medicines to be made available both through the reimbursement system via TLV and the process for in-patient medicines. However, there is a need for improvements to enhance patient access to treatment. There are significant variations among the medicines, for instance regarding benefit and cost. Many have high prices in relation to benefit.

For reimbursement applications, TLV's review shows that:

- TLV approved reimbursement for nearly two-thirds of the applications for orphan medicines.
- Medicines for very small patient groups appear to have been denied reimbursement to a greater extent.
- TLV has rejected reimbursement applications for some medicines for treatment of severe diseases, despite their potentially significant benefit to patients. Some medicines that TLV rejected for reimbursement have still been used after decisions by individual regions.
- TLV has, on several occasions, taken rarity into account by accepting a higher cost per quality-adjusted life-year (QALY) gained for orphan medicines than for equally severe but more common conditions.
- In its reimbursement decisions, TLV often accepts a high level of uncertainty in the health economic evaluation of the medicine.

Other significant observations include:

- Negotiations between regions (payers) and companies for lower medicine prices have often made it possible to assess medicines as cost-effective medicines and provide access to patients.
- More than two-thirds of the in-patient medicines covered by the review have received a positive recommendation from the NT Council.

- The conditions differ between out-patient and in-patient medicines, for example, in terms of negotiation opportunities and the time it takes for health economic evaluations to be conducted.

Given the identified needs, TLV proposes measures that can be implemented within the current system as well as in the longer term.

Within the current system, without changes to the regulations and with the current roles of TLV, regions and companies, enhanced access to medicines for rare and severe diseases and sustainable medicine costs can be achieved by:

1. TLV accepting higher costs in relation to benefit for certain medicines for very rare diseases.
2. Requiring lower costs in relation to benefit when the medicine is used for a very common condition and/or has high sales value.
3. Developing the process for assessments and negotiations for out-patient medicines

TLV also sees a need for an assessment on broader and more substantial changes to the Swedish system for pricing and negotiation for pharmaceuticals, with a higher degree of national coordination. This could be done in parallel to carrying out the proposals described above.

Volume should be considered in pricing and reimbursement decisions to enhance access to medicines for rare diseases without increasing costs.

There are several socioeconomic reasons to consider volume in reimbursement decisions. Development and production of medicines are characterised by high fixed costs and low marginal costs; once the medicine is developed, approved, and the production facility is in place, the variable cost of producing additional doses is low. Therefore, for medicines sold in small volumes, higher margins (price above production cost) are needed than for medicines sold in large quantities, in order to cover the fixed costs.

Another socioeconomic reason for considering volume is that many other countries do so. If Sweden deviates significantly from pricing patterns in other countries, this could mean a risk of limiting access to certain medicines and overpaying for others.

Furthermore, there are ethical arguments for considering volume. Patients with very rare diseases should have the same opportunity for treatment as patients with equally severe but more common diseases. The principle of human dignity implies that the same opportunity for health outcomes for all should be pursued.

TLV believes that the proposed volume-based changes in reimbursement decisions can be implemented without the need for changes to regulations.

TLV can accept a higher cost in relation to benefit for certain medicines for very rare and severe diseases.

TLV believes that a higher cost in relation to benefit (incremental cost effectiveness ratio, ICER) than the current system allows, can be accepted in certain situations.

This would apply to medicines intended for treatment of conditions with very high severity, affecting fewer than 100 patients based on the prevalence in Sweden and the medicine's total scope of use. A long-term loss of quality of life and many life years lost should be highly weighted in the evaluation of the severity of the disease. The treatment's effect should be clinically relevant. TLV aims to develop a process where a preliminary assessment of whether a medicine meets the criteria for a higher accepted ICER is done as early as possible in the evaluation and reimbursement procedure.

We have developed a "staircase model" by which the level of ICER that TLV accepts should decrease gradually as the prevalence of the condition increases. This means that the ICER can be significantly higher if the medicine for instance is intended for 5 patients rather than 50 patients. The model is motivated by the calculations we have conducted, which show that the level of accepted ICER needed to cover the R&D costs for an average medicine decreases rapidly with an increasing number of patients.

A prerequisite for applying this "staircase model" is that there are ways to manage the risk of the number of patients turning out to be larger than expected when the decision was made. One approach is through an agreement between regions and companies on a payment model that ensures the right price is paid based on the actual, not the expected, number of patients using the medicine. Another way is for TLV, in its decision, to regulate that a certain price reduction should be made in case the number of patients or sales value exceeds a certain level.

In summary, this will result in a change in practice. The change consists of three main aspects: how the criteria are designed, TLV's ability to accept a higher ICER in multiple steps depending on rarity, and that the highest levels for accepted ICERs are higher than before.

The cost relative to the benefit should be lower if the medicine is used for a very common condition or has high sales value.

TLV also suggests that volume should be considered when assessing what is a reasonable cost for medicines for common conditions. This can be achieved in various ways, and most likely, different approaches need to be combined. One way is to require a lower ICER for medicines targeting more common conditions during the initial pricing and reimbursement decision. Another approach is to implement price reductions when the sales value exceeds certain thresholds. The methods for this have not been determined at this stage; in the report we give examples of what needs to be investigated further.

Developing the process for assessments and negotiations for prescription medicines

Agreements between regions (payers) and companies for confidential discounts, which result in the actual price paid being lower than the public price, are often crucial to provide access to a medicine. This is due to the fact that the international pharmaceutical market has moved towards high public prices, while companies are often willing to provide confidential discounts. Thus, there is a need to enhance the

conditions for negotiations to strengthen access to medicines that meet an important need.

The developed process we propose builds upon the existing process for three-party negotiations and collaboration between TLV and the Swedish regions regarding new medicines. One significant change compared to the current process is that TLV, as early as possible, informs the regions that the medicine may be eligible for a higher accepted ICER and shares information that justifies this. TLV can support the parties during negotiations by evaluating the impact of payment models.

Both regions and companies need to contribute to the developed process. The regions can use their existing joint processes to assess whether a forthcoming medicine is expected to bring significant patient benefits and whether cooperation through negotiations and possibly other regional joint efforts is necessary. Both regions and companies need to be open to discussing the most appropriate payment model for the specific case. Companies are responsible for offering reasonable prices and applying for reimbursement with complete documentation for TLV's evaluation.

Consequences of TLV's proposals

The application of a higher accepted ICER for medicines for very rare and severe diseases would lead to an increase in the Government's costs for reimbursed medicines. The cost increase is partially due to including more medicines for rare diseases in the reimbursement system and partly due to the fact that the public would pay more for medicines that would already be included in the reimbursement system with today’s approach. Costs are expected to increase every year as new medicines enter the market.

We have estimated the cost savings from potential price reductions for high-selling medicines. The calculations show that a relatively small reduction could lead to significant cost savings for medicines with high sales volume.

The government can accelerate and strengthen the proposals, and regions and companies need to contribute within their areas of responsibility

Many of the measures studied under this government assignment are within TLV's jurisdiction. However, TLV cannot by itself effect all the changes necessary to enhance access to valuable medicines. Companies have a significant responsibility through their pricing and their documentation, that are the basis for TLV's evaluations. Regional collaboration is of central importance for equal access to medicines, both through the handling of in-patient medicines via the NT Council and through conducting negotiations for agreements with companies when needed.

According to our assessment, the government already has tools that could facilitate the implementation of the proposed changes. As described, the conditions for negotiations are of great importance, both to strengthen access to new essential medicines and to create price competition for patented medicines, thereby ensuring sustainable medicine costs. One way for the government to achieve better conditions for negotiations could be to strengthen the incentives and possibilities

for the regions to participate in negotiations with pharmaceutical companies, by using the agreement between the government and the regions on the subsidy for pharmaceuticals.

Another measure for the government to strengthen the negotiation conditions is to review the regulations in terms of considering the possibility of extended time for TLV's assessments. The purpose of doing this is to provide better conditions for complex health economic assessments as well as negotiations, which would lead to a more efficient evaluation and negotiation process for new medicines.

Another way for the government to support access to medicines for rare diseases is to ensure that TLV has long-term resources to carry out its task of health economic evaluations of in-patient medicines, since these represent a significant proportion of medicines for rare diseases.

Continued work and resources are required to implement the proposals.

Continued work is needed to establish a sustainable system where patients with rare as well as common diseases have access to medicines as needed. Before the changes can be implemented, TLV needs to investigate further how the proposals on how patient size and sales volume affect the accepted cost, should be carried out in practice.

Both ongoing investigative work and additional tasks within the framework of the agency's responsibilities require the government to allocate additional resources.

TLV proposes an investigation of the need for a more substantial change to the system for medicine pricing and negotiations.

The proposals outlined above are feasible within the current Swedish system and existing legal conditions. However, we believe that there are limitations in the current structures for medicine pricing and negotiations that cause difficulties in achieving satisfactory and equal access to medicines for both rare and common conditions, at costs that are sustainable in the long term. Therefore, TLV proposes an assessment on a more substantial change in the system for pricing and negotiations of pharmaceuticals.

Denmark and Norway are examples of countries that have developed strong national negotiation functions, which have had positive effects on access and costs.

Challenging prioritisation decisions will remain.

Despite the measures we propose in this report, decisions to make certain medicines available for rare diseases will entail prioritisation decisions. This may mean that not all medicines become available, due to companies' pricing strategies and uncertain evidence of the medicines' benefits.

There are several conflicts of interest in the decision-making process for the availability of new high-cost medicines. These include conflicts between patient access on one hand and not paying unreasonably high prices on the other. There is also a tension between fast introduction and the risk that the medicine at a later

stage may not remain within the reimbursement system because it does not meet the necessary conditions. In our meetings with representatives from other countries' authorities, the expressed experience is that despite the establishment of special procedures for medicines for rare diseases, no country has a system that they consider fully satisfactory.

Our proposals are expected to lead to better access to effective medicines for patients with severe rare diseases. However, continued work, collaboration, and responsibility from all stakeholders will be necessary to maximise patient benefits using our shared resources.