Swedish national reimbursement of new medicines with EMA approval 2019-2021

QUANTIFY
A PARTNER YOU CAN TRUST

Final version
4 May 2023

Contents

Executive summary and reflections

Executive summary

The present report is a **detailed review of a cohort of 117 new medicines with European Medicines Agency (EMA) approval in 2019-2021** and their status in Sweden, both in terms of availability (being supplied) and reimbursement. The EFPIA report used a slightly different cohort, that covers new medicines with EMA approval 2018-2021.

Medicines were categorized according to three main routes to national reimbursement depending on the type of medicine (*communicable disease medicines, prescription medicines and hospital medicines*). The report is mainly based on publicly available data, complemented by date of supply and responses to a survey sent to pharmaceutical companies.

Out of the 117 medicines with EMA-approval in 2019-2021, 79 (68%) were supplied (by the company) in Sweden. **62 (53%) medicines were nationally reimbursed. All nationally reimbursed medicines were nationally supplied.** On average, new medicines were nationally reimbursed 301 days after being approved by EMA. The number of days is somewhat higher than what was presented in last years report (287 days for medicines approved by EMA in 2018-2020). Furthermore, TLV:s handling time (time to handle the application from the date an application is submitted and considered complete) has increased annually since 2018 (+28%, 101 days in 2018 compared to 129 days in 2021).

Out of the 117 medicines with EMA-approval in 2019-2021, **38 (32%) were not supplied in Sweden**. There is a lack of public information in Sweden with regards to submission status for 47% (18 out of 38) of these medicines. A company survey (non-public information) was conducted and contributed with further information on these medicines. In total, the company survey contributed with information on 29% (11 of 38) of the non-supplied medicines. With regards to the medicines for which there is a lack of public information in Sweden the company survey contributed with information on 39% (7 out of 18).

Reflections (1/2)

1 out of 3 new medicines in the evaluated cohort are not supplied in Sweden. **Potential explanations** discussed in this report **include rejections** (or anticipated rejections), **lack of experience** in the Swedish market (more than half MAHs with non-supplied medicines had no previous medicine in the Swedish reimbursement system), **perceived complexity of the Swedish reimbursement system** and that there is **no need to make medicines available** as other, for instance more efficient, alternatives might be already available. Such factors may result in companies not finding it worthwhile to apply/seek reimbursement and hence, make their medicines available in Sweden.

In some cases, the fact that some medicines are not supplied in Sweden may not cause any concern, as a potential patient group may be non-existing or when other (on all accounts at least) equally efficient medicines exist. Nonetheless, **as a large proportion of medicines are not made supplied, potentially large, patient value is lost.**

Availability (medicines being supplied) is closely linked with national reimbursement, as most medicines supplied in Sweden are also classified as nationally reimbursed. Reimbursement decisions are often associated with restrictions and/or price agreements. Hence, general subsidy (no restriction and/or price agreements) is not always sufficient for reimbursement, as such tools would otherwise not be needed. Such tools may complicate decisions but may also be a necessity for (early) launch of new medicines in Sweden. The use of such tools may also indicate that companies and authorities, at least in some cases, reach different conclusions with regards to the cost-effectiveness of new medicines.

Reflections (2/2)

The present report also shows that reimbursement decisions take time. After around three years from market authorization a more stable state is reached in terms of share of medicines being supplied in Sweden, although the share of medicines supplied never reaches 100%.

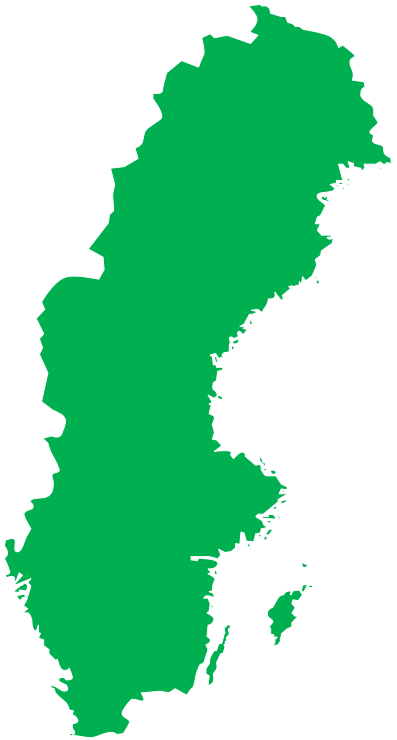
Making medicines available for Swedish patients is a complex process with close interactions between companies and public authorities. The routes of making medicines available for Swedish patients differs for medicines used in different settings (hospital drugs, prescription medicines and medicines used for communicable diseases). Companies often have to take both guidelines into consideration as well as practice from previous decisions. For instance, the mentioned common use of restrictions of decisions may in some cases be a result of anticipated decisions from authorities rather than company decisions despite restrictions being requested by companies. Such information is not always easy to access through publicly available information.

In conclusion, pharmaceutical companies not supplying medicines remain a challenge – as 1 out of every 3 new medicines were not supplied and hence, made available in Sweden. It is also apparent that reimbursement decision takes time. **From a societal perspective, as well as a company and authority perspective, there should be a continued effort to achieve faster access of medicines as prolonged access time, or no access, can result in lost patient value that could otherwise be avoided.**

Background and objectives

Background

- Each year, the European Federation of Pharmaceutical Industries and Associations (EFPIA) presents its Patients W.A.I.T.* Indicator for new medicines in European countries, assessing indicators of availability of medicines in rolling cohorts:
  - The rate of availability, measured as the number of medicines included in the national reimbursement list (EFPIA's definitions of availability are detailed in the Appendix) in each country compared to the total number of new medicines approved by EMA during the period
  - The average time to market (TTM) for available medicines measured from marketing authorisation (MA) date to the date of national access



- The present report is a detailed review of national reimbursement of new medicines with EMA approval in 2019-2021 in Sweden. It also includes some analyses on medicines approved in 2014-2018. This report was conducted by Quantify and commissioned by Lif. Similar analyses have previously been conducted for new medicines approved in 2014-2016, 2015-2017, 2016-2018, 2017-2019 and 2018-2020.

- The report from 2018-2020 was restructured and rephrased based on discussions between the Swedish regions, TLV and Lif on how to evaluate patient access to new medicines in Sweden considering the different routes to reimbursement. This year's report follows the same structure and is based on last year's revised definitions and methodology (see slide [12]) to more clearly highlight challenges in the processes for national reimbursement decisions and/or recommendations in Sweden from a company perspective.

- Further information about the revisions made can be seen in last year's report

* W.A.I.T.: Waiting to Access Innovative Therapies

Objectives

This report aims to present the advantages and challenges of the Swedish systems for national reimbursement of medicines from the perspective of pharmaceutical companies, to serve as a basis for constructive dialogue

Data collection and definitions

Data collection

- The report is based on the following public and non-public information:

EMA	Medicines approved in 2014-2021	List of ATMPs	Conditional marketing authorisation	Information on single-arm trials	
FASS	Marketing authorisation holder & presence in the Nordics	Supply status	Date of supply*		
Communicable Diseases Act (2004: 168)	Indications listed in the communicable disease program				
TLV	General, restricted and temporary reimbursement decisions	Rejected reimbursement decisions	Completed hospital drug assessments	Ongoing hospital drug assessments	Submitted and withdrawn reimbursement applications*
New Therapies (NT) council	Published recommendations	Information on inclusion in national managed introduction*			
Marketing authorisation holders (MAHs)	Company survey answers**	Company websites***			

- The complete dataset, excluding non-public information, can be provided upon request to Lif and/or Quantify Research

Several of these sources may have been used to extrapolate information; a medicine with ongoing hospital drug assessment may for instance also be subject to inclusion in the national managed introduction.
* Data not openly published on TLV's website but obtained upon request based on the principle of public access to information
** Non-public information received from source
*** Used to obtain information on share (and number) of companies with non-supplied medicines that are locally present in the Nordics

Definitions

Definition of national reimbursement

National reimbursement was defined as occasions when there are existing public documentation stating that the medicine should be partially or fully financed for patients.

For the purpose of this report, a medicine is classified as **nationally reimbursed** if it, on the **cut-off date 20 December 2022,** was:

Approved by the EMA

Listed as supplied in FASS

Ambulatory care (prescription medicines)		Medicines used in hospital setting (hospital medicines)		
	OR		OR	OR
Has received a positive reimbursement decision from TLV	Has an indication included in the communicable disease control program	Has a positive recommendation from the NT-council	Is not in national managed introduction	Has an indication included in the communicable disease control program

All other medicines are considered to lack national reimbursement. These may still be available at a regional level or for patient purchase

Routes to national reimbursement

Based on the definition, **three main routes to national reimbursement** are outlined, based on type of medicine:

1. Communicable disease medicines
2. Prescription medicines
3. Hospital medicines

Excluding communicable disease medicines

A medicine is classified as a **communicable disease medicine** if it has at least one indication included in the communicable diseases program.

A medicine is classified as a **hospital medicine** if:

- There is an NT-council recommendation of use at the cut-off date, and/or
- The medicine is administrated IV (without possibility to self-inject at home), and/or
- The summary of product characteristics (SmPC) states that clinical staff was required for administration.

All other medicines are considered **prescription medicines**.

Routes to national reimbursement

Communicable disease medicines

Automatic reimbursement

Prescription medicines

Company submits application to TLV → TLV assessment → TLV decides on pricing and reimbursement

180 days
(Possible to clock-stop for up to 90 days)

Three-party negotiations and price agreements with the regions can be added

Hospital medicines

NT-council initiates assessment by requesting HE assessment from TLV → TLV requests documentation from company → TLV assessment → TLV publishes HE assessment → NT-council recommendation

No legal timeframes

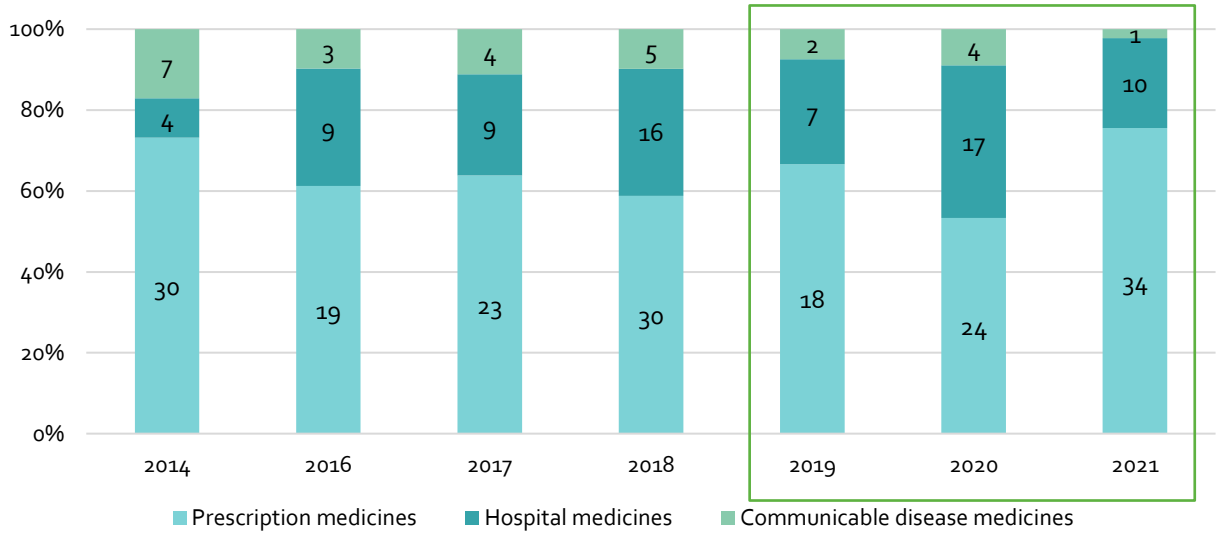
NT-council negotiations and price agreements with regions can be added

Medicines approved by EMA in 2014-2021

- **The focus of the report is on the 117 new medicines that were approved by EMA in 2019-2021**
  - 27 (23%), 45 (38.5%) and 45 (38.5%) medicines were approved in 2019, 2020 and 2021, respectively
  - 27 (23%) of the medicines approved between 2019-2021 were authorized under exceptional circumstances, having a conditional marketing authorisation or as undertaking a post-authorisation safety study (PASS) by the EMA

- In total, this report includes **321 new medicines** with new substances or combinations approved by EMA in 2014-2021 that were identified in EFPIA's W.A.I.T. report*
  - Medicines with withdrawn marketing authorization were excluded
  - Some analyses were also made using medicines approved in 2014-2018 in order to show longer trends
    - Data for medicines approved in 2014-2018 were updated, meaning that national reimbursement may have been achieved until the cut-off date (20 December 2022)

Number of new medicines approved in 2014-2021 by year of EMA approval and route to availability



*The complete dataset of publicly available information can be provided upon request to Lif and/or Quantify Research

Supply of new medicines in Sweden

QUANTIFY

Key takeaways

- **68 % of all new medicines were supplied in Sweden**
  - 1 out 3 new medicines were not supplied
- **There are no public information regarding almost half of the non-supplied medicines in Sweden**
  - A company survey was conducted to extract more information on this
- **Identified explanations for why 1 out of 3 new medicines were not supplied include:**
  - **Rejection** (or anticipated rejection) from authorities – *most nationally reimbursed new medicines are also nationally supplied*

Based on the company survey

- **Lack of experience** of the Swedish system – *more than 50% of all companies (MAHs) with non supplied medicines had no previous medicine in the Swedish reimbursement system*
- **Perceived complexity of the Swedish reimbursement system**

Note that even if medicines are not (defined) as nationally reimbursed they may still be used on a regional level through other routes of distributions – no such information were collected as a part of this report.

From EMA approval to supplied in FASS

EMA-approved medicines 2019-2021

117

(27 [23%] in **2019**, 45 [38.5%] in **2020**, 45 [38.5%] in **2021**)

Supplied in FASS	Not supplied in FASS
79 (68%)	**38 (32%)**

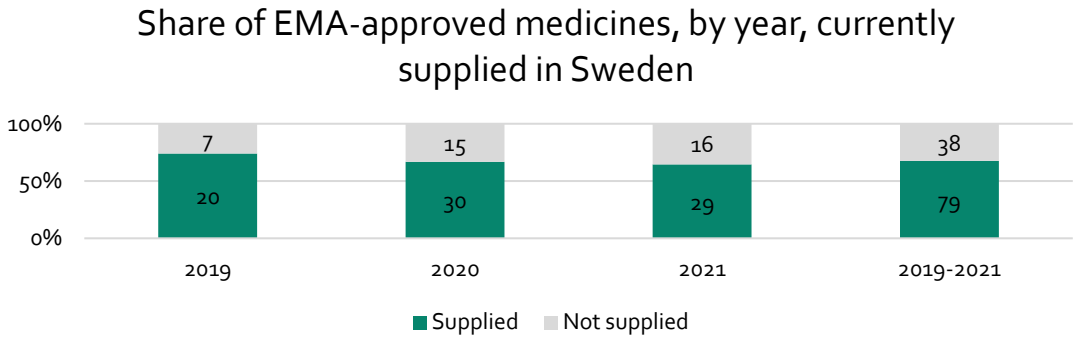
Communicable diseases	Prescription medicines	Hospital medicines	Communicable diseases	Prescription medicines	Hospital medicines
5 (6%)	**49 (62%)**	**25 (32%)**	**2 (5%)**	**26 (68%)**	**10 (26%)**

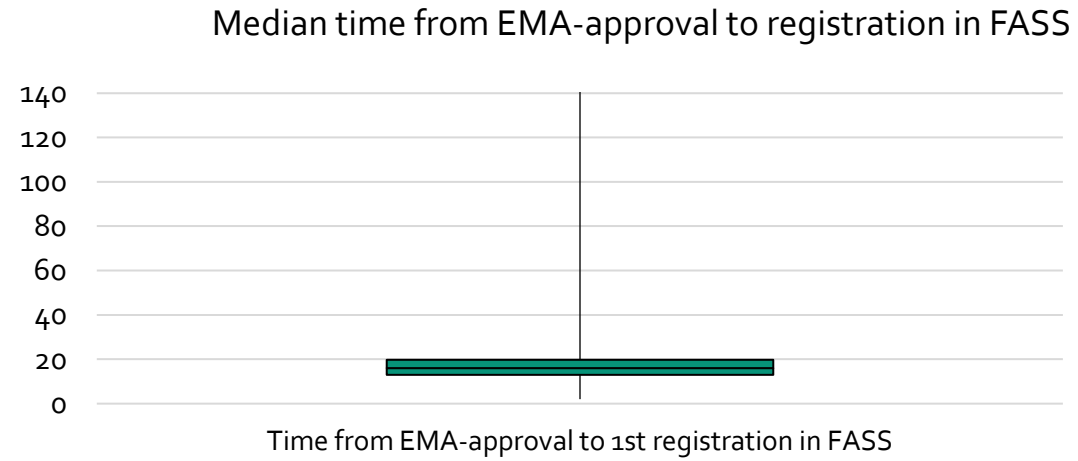
FASS is a database developed by Lif in close cooperation with pharmaceutical companies that provides extensive, quality assured and up-to-date information about all medicines supplied in Sweden. The basic information comes from Nationellt Produktregister för Läkemedel (NPL – the national product registry for medications), which is automatically downloaded to the FASS database. SmPCs, package leaflets and all other information are provided and uploaded by the pharmaceutical companies.

From EMA approval to supplied in FASS

- At the cut-off date, 79 (68%) of the 117 medicines with EMA-approval in 2019-2021 were supplied by the company in Sweden according to FASS
  - 38 medicines were not supplied in Sweden
    - Medicines may still have ongoing reimbursement processes
    - An attempt was made to identify whether TLV decisions or NT recommendations existed (see slide [18])
  - As expected, the proportion of medicines supplied increases with time from EMA approval; a bigger proportion of medicines approved in 2019 (74 %) was supplied than those approved in 2020 (67 %) or 2021 (64 %)

- Medicines was on average (median) registered as supplied **for the first time** in FASS 33 (16) days after EMA approval

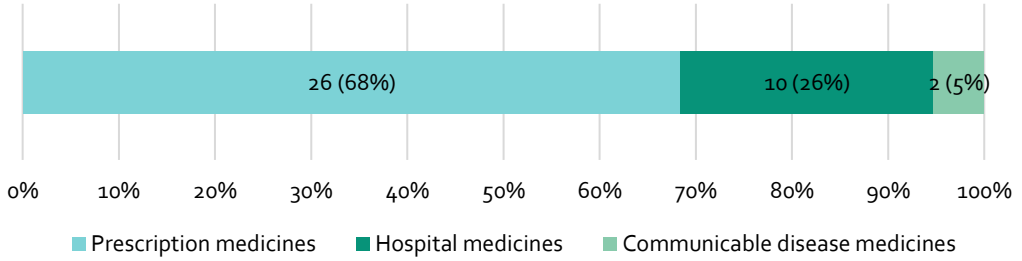




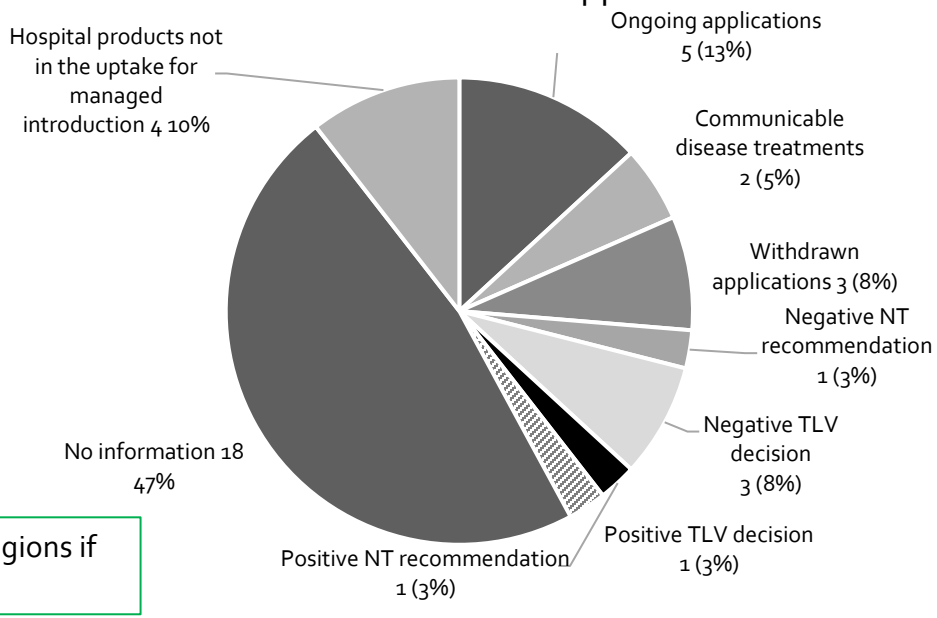
Non-supplied medicines – medicine characteristics

- At the cut-off date, 38 (32%) of the 117 medicines were not supplied by the company in Sweden according to FASS
  - The majority, 26, (68%) were prescription medicines
  - 25 (66%) were "ordinary" approvals – not subject to additional monitoring) and not approved through single-arm trials
  - 14 (37%) were subject to additional monitoring by EMA (i.e., authorised under exceptional circumstances, having a conditional marketing authorisation or PASS)
  - 7 (18%) were tested in single-arm trials
- Based on publicly available information:
  - 8 medicines would be classified as nationally reimbursed if supplied due to either being a communicable disease medicine, or a hospital product not being in the uptake for national managed introduction (introduced without need for health technology assessment [HTA]), or having a positive NT recommendation or TLV decision
  - 3 medicines had withdrawn TLV applications
  - 4 medicines had negative TLV decisions or NT recommendations
  - 5 medicines had ongoing assessments
  - Public information was missing for 18 (47%) medicines
    - A company survey was conducted in order to gain further insights into why some medicines were not supplied

Non-supplied medicines by route to national reimbursement



Reimbursement status of non-supplied medicines



MAHs are not required to supply their medicines before applying for national reimbursement in Sweden.

Non-supplied medicines can be imported by regions if needed.

Non-supplied medicines – will they launch?

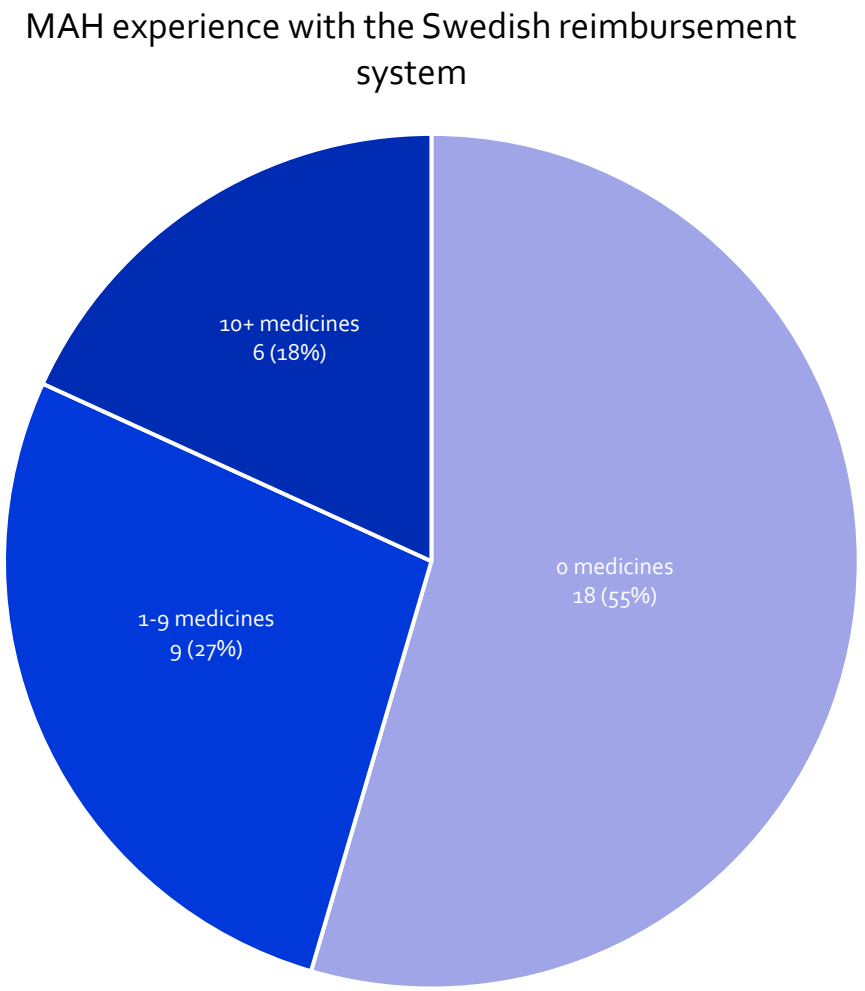
- 13 out of 38 (34%) non-supplied medicines had indicators suggesting they may become supplied, hence, could be introduced
  - 2 had received a positive decision/recommendation
  - 4 were being evaluated as hospital medicines
  - 4 were not in the uptake of national managed introduction (hence, introduced without need for HTA)
  - 1 had submitted an application to TLV
  - 2 were communicable disease medicines
- 4 medicines had received negative decisions/recommendations and additionally 3 had withdrawn their reimbursement application, which potentially discourages MAHs from supplying the medicines in Sweden.
- Of the 18 medicines left without public information, a company survey aimed to gain more information on why they were not supplied
  - 6 of these medicines (33 %) had orphan designation and 5 (28 %) were indicated for oncology.

In cases where treatment alternatives exist, there is no patient population or if the MAH can offer the medicine to patients by a different way than national reimbursement, the lack of supply of medicines may not necessarily create problems for patients, but in other cases it may actually result in loosing patient value

The decision to supply the medicine is usually taken after the reimbursement decision/recommendation has been made

Non-supplied medicines – MAH characteristics

- 38 non-supplied medicines were marketed by 33 unique MAHs
- More than half (18; 55%) of MAHs had no prior medicines included in the Swedish reimbursement system based on information from TLV's price and decision database
- 42% of these MAHs did not have local presence in any of the Nordic countries



Nationally reimbursed medicines

QUANTIFY

Key takeaways

- **National reimbursement is important for availability (being supplied)**
  - 78% of all supplied medicines are also classified as nationally reimbursed
- **Restrictions and/or price agreements are commonly used tools for national reimbursement**
  - 48% are associated with restrictions
  - 42% are associated with price agreements
  - 23% are associated with price agreements and restrictions
- **Restrictions and/or price agreements = the "new normal"?**
  - The system in its "original" form does not function in many cases – otherwise these tools would not be needed
  - Both companies and authorities influence decisions on restriction
  - On one hand side these tools **may make decisions more complicated** on the other hand such tools might be a **necessity for** (early) **launch**
  - The need of such tools also indicate that **companies and authorities reach different conclusions regarding** the **cost-effectiveness** of new medicines in many cases

Note that even if medicines are not (defined) as nationally reimbursed they may still be used on a regional level through other routes of distributions – no such information were collected as a part of this report.

Overview of nationally reimbursed medicines in Sweden

- More than half of the medicines approved by EMA between 2019-2021 were considered nationally reimbursed as per the definition in the report
- 4 non-supplied medicines would have been considered as nationally reimbursed if they were supplied in Sweden
  - 1 had a positive TLV decision
  - 1 had a positive NT recommendation
  - 2 are communicable disease medicines

	Positive decision/ recommendation or no HTA required	Negative (or no) decision/ recommendation	Total
Supplied	62	17	79
Non-supplied	4*	34	38
Total	64	53	**117**

**According to the definition, these 4 medicines are categorized as not nationally reimbursed in Sweden*

Insights in nationally reimbursed medicines in Sweden

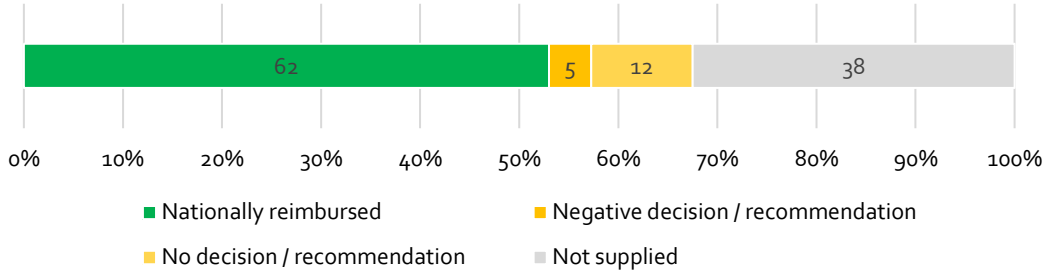
National reimbursement

- Overall, 62 medicines (out of the 79 supplied) were nationally reimbursed in Sweden

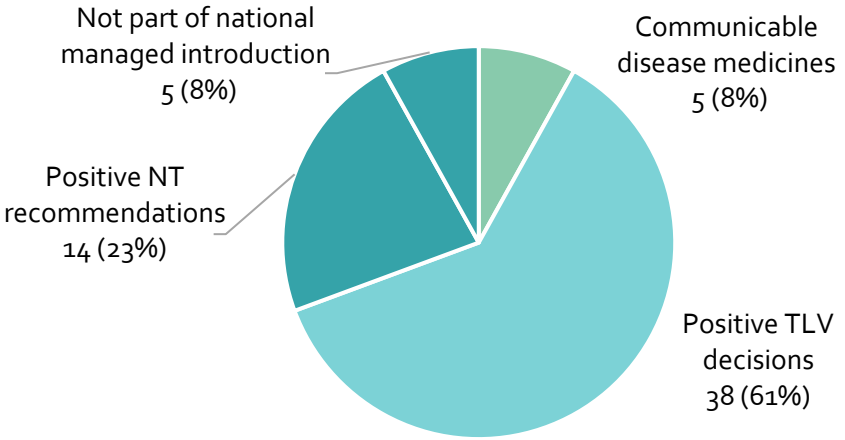
- Among the 62 medicines,
  - A majority (38; 61%) had positive decisions from TLV
  - 14 (23%) had positive NT recommendations
  - 5 (8%) were indicated in communicable diseases
  - 5 (8%) medicines were hospital medicines which were not in national managed introduction
- 10 (16%) medicines were tested in single-arm trials
- 17 medicines were not classified as nationally reimbursed because they had a negative TLV decision or NT recommendation, lacked a TLV decision (prescription medicines) or were in national managed introduction but did not yet have a published recommendation (hospital medicines)
  - Further information about these 17 medicines is presented in the section Company Survey

4 non-supplied medicines would have been classified as nationally reimbursed if supplied.

National reimbursement of all medicines approved by EMA in 2019-2021



Reason for national reimbursement among 62 reimbursed medicines approved by EMA in 2019-2021



EFPIA definition of limited availability

- In the EFPIA W.A.I.T indicator, countries report availability.
  - » In Sweden, this is defined as being supplied and either nationally reimbursed or, for some hospital medicines, not being in the uptake of managed introduction (hence, introduced without the need for HTA).
- According to EFPIA, medicines can either be reimbursed with or without limited availability

EFPIA definition on limited availability and information on whether this is applicable in this report (for Sweden)

EFPIA definition on limited availability	Is this definition applicable in this report?*
Limited reimbursement to specific subpopulation of approved indication	**Yes**.
Limited reimbursement on a national named patient basis (individual patient)	**Not applicable/used in this report.**
Limited reimbursement while decision is pending (where system permits)	**Yes**. For instance, medicines previously used with special permission (previously without market authorization) may be subject to temporary approval while decision is pending.
Availability through a special program (e.g. managed entry agreement)	**Yes.** However, managed entry agreements does not automatically indicate limited availability.

*Only brief explanations are given relating to definitions used in this report and should not be considered complete, especially with regards to regional routes of access.

Definitions on full vs restricted reimbursement in this report

- In Sweden, full reimbursement means that the reimbursement is valid for the full patient group within the indication, and without restriction to prescribers.
- Restricted reimbursement is classified as:
  - If reimbursed only to a subpopulation of the medicine's indication
  - If reimbursed only if prescribed by a specialist or in a specialist setting
  - If reimbursed while decision is pending (temporary reimbursement)
  - If restricted to a certain care setting

» In remainder of the report the following analysis of full and restricted reimbursement is presented on the following topics:
  - » The use of full vs restricted reimbursement
  - » The time from regulatory approval to national reimbursement
  - » National reimbursement for medicines in the following setting:
    - » Communicable diseases
    - » Prescription
    - » Hospital
  - » National reimbursement associated with single-arm trials
  - » Further analysis on national reimbursement decisions over time is also presented including an analysis of the use of price agreement.

Special conditions in national reimbursement

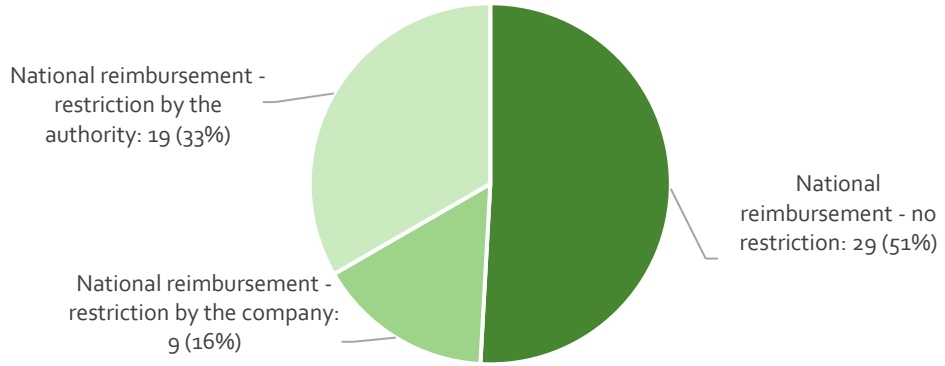
Restrictions in the subsidy

- 49% of all pharmaceuticals with national reimbursements were associated with restrictions (excluding new medicines for communicable diseases)
  - 57 new medicines were approved during the period 2019 to 2021 (62 including new medicines used for communicable diseases). 28 of these were associated with restrictions.
- Of the 28 new medicines associated with restrictions the company was applying, or seeking, restriction in 32% (9) of the cases.

National price agreements

- The national reimbursement depended on national price agreements in 25 (40%) of TLV decisions and NT recommendations
  - Moreover, 1 product for a communicable disease also had an agreement in place, but would have considered nationally reimbursed independent of the national price agreement

New medicines reimbursed during the period 2019-2021 with and without restrictions*



* Excluding new medicines indicated for communicable diseases

"Restriction by company" is defined as instances when the company applied for a restriction (or argued for a restriction). Based on public information from tlv.se (from the decision and/or the memorandum) or from NT-council's recommendation of use. The data presented for this variable should be analysed with cautiousness. For instance, if the company applies for a restriction, it may be due to previous communication (or decisions) from the authority. Furthermore, in some cases companies might have decided not to provide evidence (for example for a certain subpopulation) and in those cases "Restriction by the authority" is used (if it is not explicitly stated that the company applied/argued for a restriction).

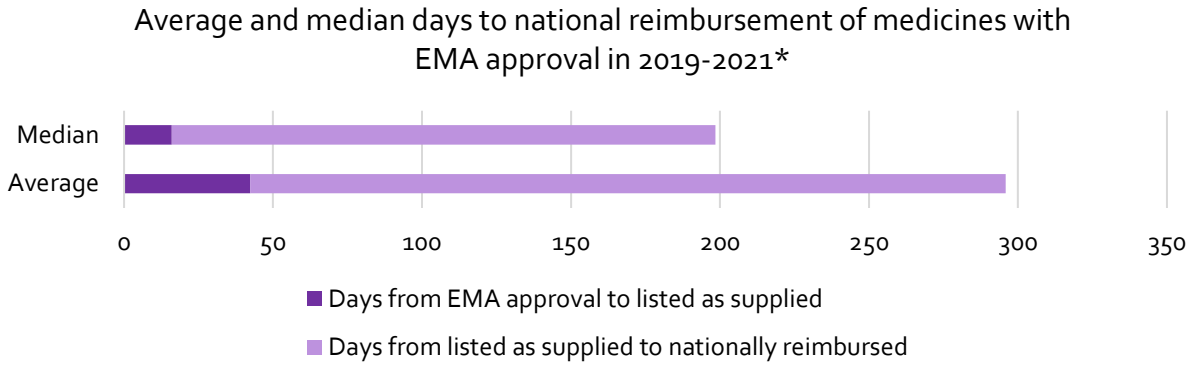
Time to national reimbursement

Time to national reimbursement

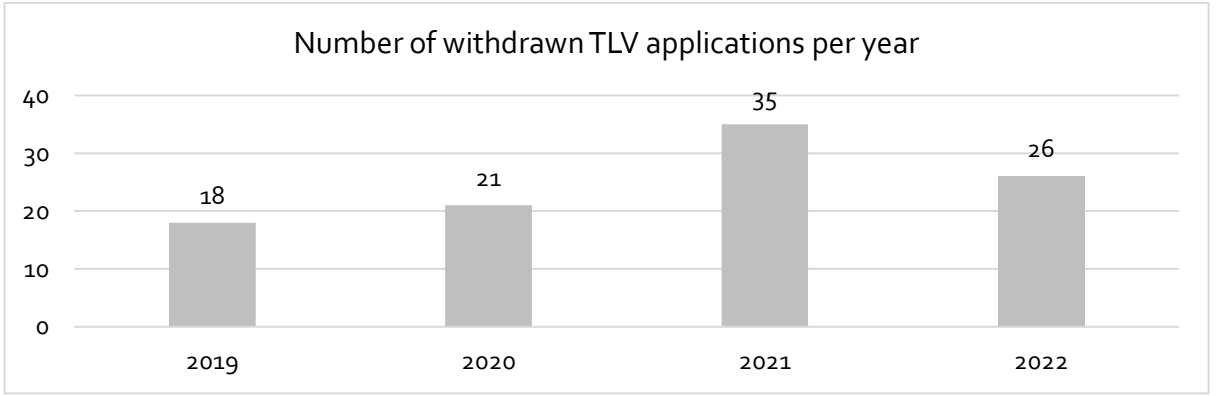
- Overall, nationally reimbursed medicines were on average (median) reimbursed 296 (199) days after EMA approval
  - These medicines were supplied 42 (16) days after EMA approval
  - Time to national reimbursement was 254 (183) days after being supplied

- MAHs marketing nationally reimbursed medicines were generally quick to supply these medicines in Sweden.
  - 77 (97 %) of medicines were supplied in Sweden within 6 months after the authorisation date

- Based on information from TLV, the number of withdrawn applications in 2019-2022 varied between 18 and 35 applications per year
  - Given that some of these medicines are included in the current report, these withdrawals will affect the time to national reimbursement
  - Some MAH may resubmit their reimbursement applications



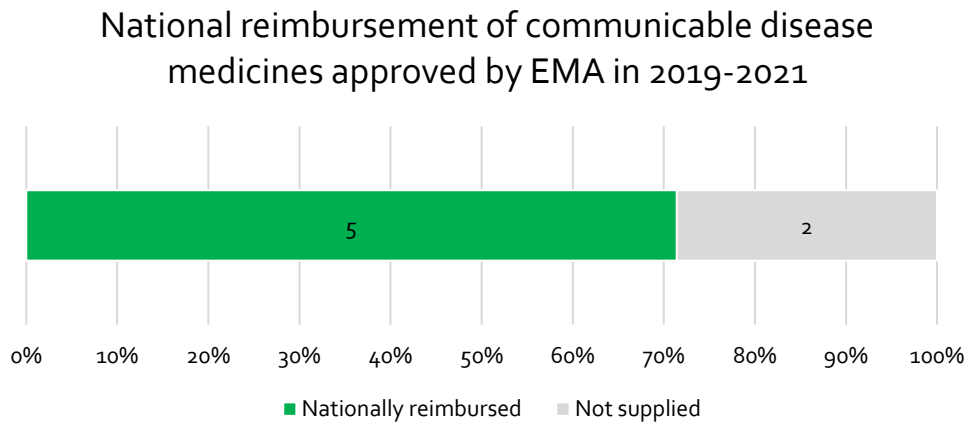
* Note: this includes communicable disease medicines and hospital medicines not in national managed introduction (i.e., medicines classified as nationally reimbursed when registered as supplied in FASS)



National reimbursement of communicable disease medicines

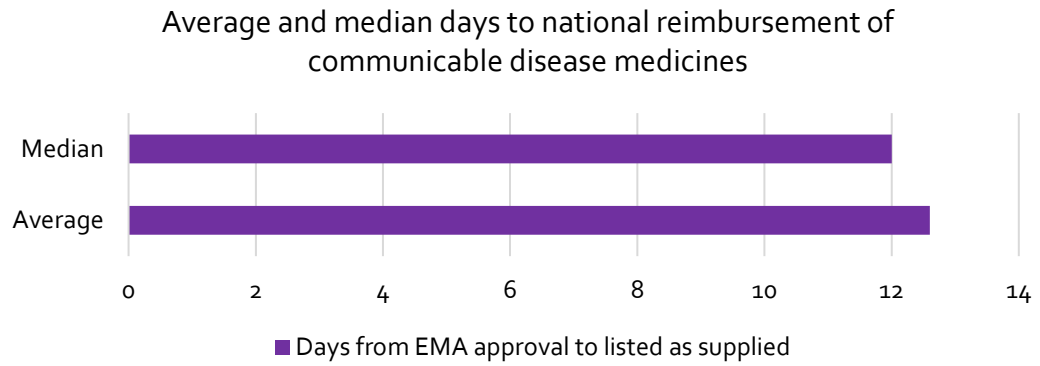
National reimbursement

- By definition, all medicines with indications included in the communicable disease program that were approved by the EMA and supplied in Sweden were considered nationally reimbursed
  - 5 out of 7 medicines were supplied in Sweden, and thereby classified as nationally reimbursed



Time to national reimbursement

- Average (median) time to national reimbursement of communicable disease medicines was 13 (12) days
  - Any delays in time to national reimbursement can only be explained by delays in supplying the medicine



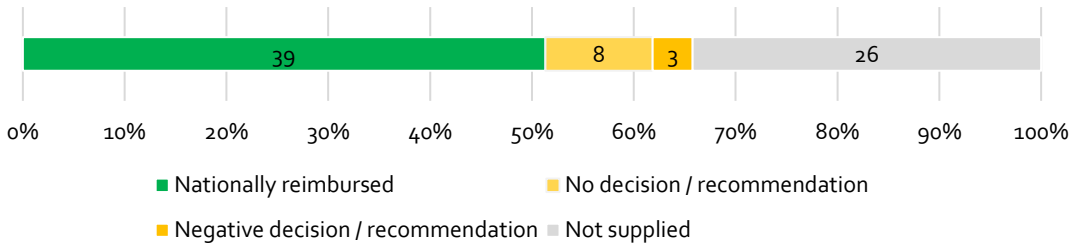
Communicable disease medicines were considered automatically nationally reimbursed from the first date of registration as supplied in FASS.

National reimbursement of prescription medicines

National reimbursement

- 39 prescription medicines approved by the EMA in 2019-2021 were nationally reimbursed
  - 38 had positive TLV decisions, 1 had a positive NT recommendation
  - This was 51% of all approved prescription medicines and 78% of the prescription medicines registered as supplied
- 14 (36%) of 39 medicines had national price agreements
- 11 supplied medicines were classified as not nationally reimbursed
  - 8 lacked TLV decisions
    - Reimbursement submissions had been withdrawn in 5 cases and was ongoing in one case, based on information supplied by TLV; no public information was available for the two remaining cases
  - 3 had received negative TLV decisions

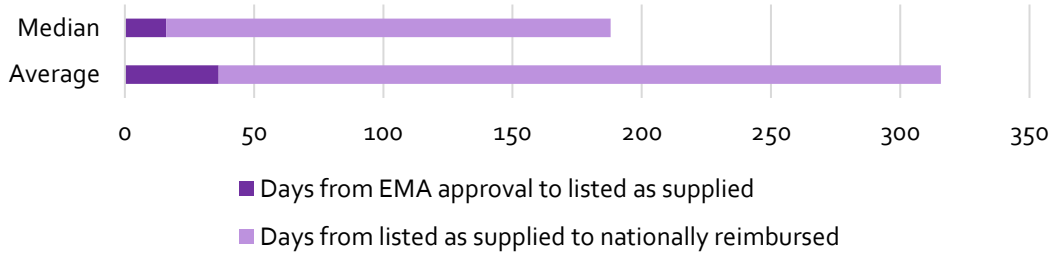
National reimbursement of prescription medicines approved by EMA in 2019-2021



Time to national reimbursement

- Prescription medicines were on average (median) supplied 36 (16) days and nationally reimbursed 315* (188) days after EMA approval
- The average handling time in 2022 was 129 days, including price negotiations, according to TLV's annual report
  - TLV has 180 days to handle a reimbursement application
  - Possibility to ask for an additional 90 days to submit new material (not included in the total handling time)
- Factors potentially causing delays in national reimbursement are:
  - MAHs waiting to apply for reimbursement
  - MAHs withdrawing reimbursement applications and applying multiple times

Average and median days to national reimbursement of prescription medicines



Prescription medicines were considered nationally reimbursed from date of reimbursement stated in the TLV decision.

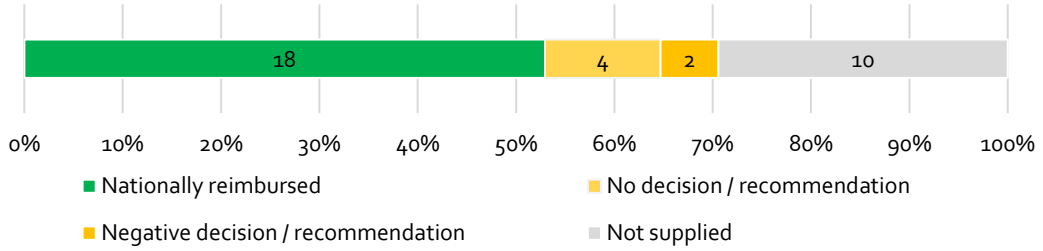
* The average time was heavily impacted by five cases where the time to national reimbursement was over 2 years

National reimbursement of hospital medicines

National reimbursement

- 18 hospital medicines approved by the EMA in 2019-2021 were nationally reimbursed in Sweden
  - This was 53% of all approved hospital medicines and 75% of the hospital medicines registered as supplied
  - 13 had positive NT recommendations
  - 5 were not in national managed introduction and therefore introduced without need for HTA
- 11 (61%) of 18 medicines had national price agreements
- 6 supplied medicines were classified as not nationally reimbursed
  - 2 because they had negative recommendations from the NT-council
  - 4 because they were in national managed introduction and had ongoing assessments, indicating that these medicines may become nationally reimbursed in the future

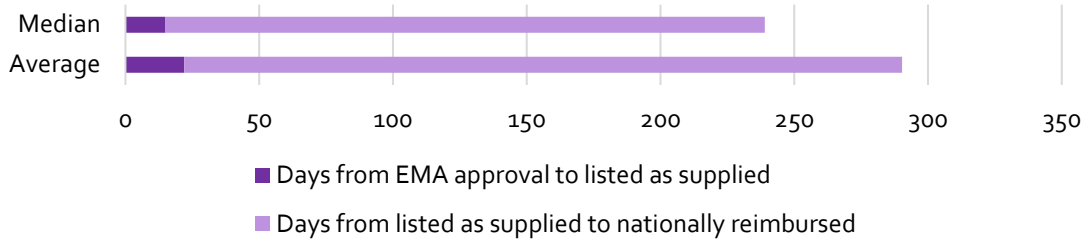
National reimbursement of hospital medicines approved by EMA in 2019-2021



Time to national reimbursement

- Hospital medicines were on average (median) supplied 22 (15) days after EMA approval and nationally reimbursed 268 (224) days after they were supplied
- Factors potentially causing delays in national reimbursement are:
  - Delays in inclusion of medicines in national managed introduction. This factor is out of companies' control as inclusion in national managed introduction cannot be applied for
  - MAH delays in sending material for assessment to TLV
  - Long-spun waiting times for health-economic assessments by TLV
  - Health-economic assessment by TLV is not limited to a certain time period
  - Long-spun price negotiations

Average and median days to national reimbursement of hospital medicines



Hospital medicines were considered nationally reimbursed from the date of NT recommendation. Medicines not in national managed introduction were considered nationally reimbursed from the date of registration as supplied in FASS.

National reimbursement of medicines with single-arm trial as main study for EMA approval

Usual challenges associates with single-arm trials:

- Medicines with single-arm trial as the main study for EMA approval have specific challenges in HTA
- The effect is not shown in relation to another medicine and/or placebo
- The comparison with current treatment options has to rely on indirect treatment comparisons
- Thus, the uncertainty in the health economic evaluation is often greater, which makes it difficult to assess the incremental cost-effectiveness ratio

- In an overview of the number of trials with single-arm reported under 'main study' in the European Public Assessment Report (EPAR):
  - Almost 20 %, 23 out of 117, medicines had a single-arm trial as main study
  - Of these, a slightly lower share of the medicines where reimbursed (44%), compared to medicines with a control arm (55%)

	Supplied		Non-supplied*	Total
	Reimbursed	Not reimbursed	Not reimbursed	
Single arm	10 (44%)	6 (26%)	7 (30%)	23
Not single arm	52 (55%)	11 (12%)	31 (33%)	94
Total	62 (53%)	17 (15%)	38 (32%)	**117**

** non-supplied medicines cannot be nationally reimbursed according to the definition in W.A.I.T*

National reimbursement over time

QUANTIFY

Key takeaways

- **Reimbursement decisions take time**
  - 23% of medicines approved in 2014-2018 were not reimbursed as of December 2022, whereas about 47% of medicines approved in 2019-2021 were not reimbursed
- **Even after four years some medicines are still not supplied, some possible explanations:**
  - **No need to make medicines supply** as newer, more effective, alternatives may have already been introduced or it may be the case that some medicines lack a patient population in Sweden
  - **Negative decisions/recommendations** from authorities

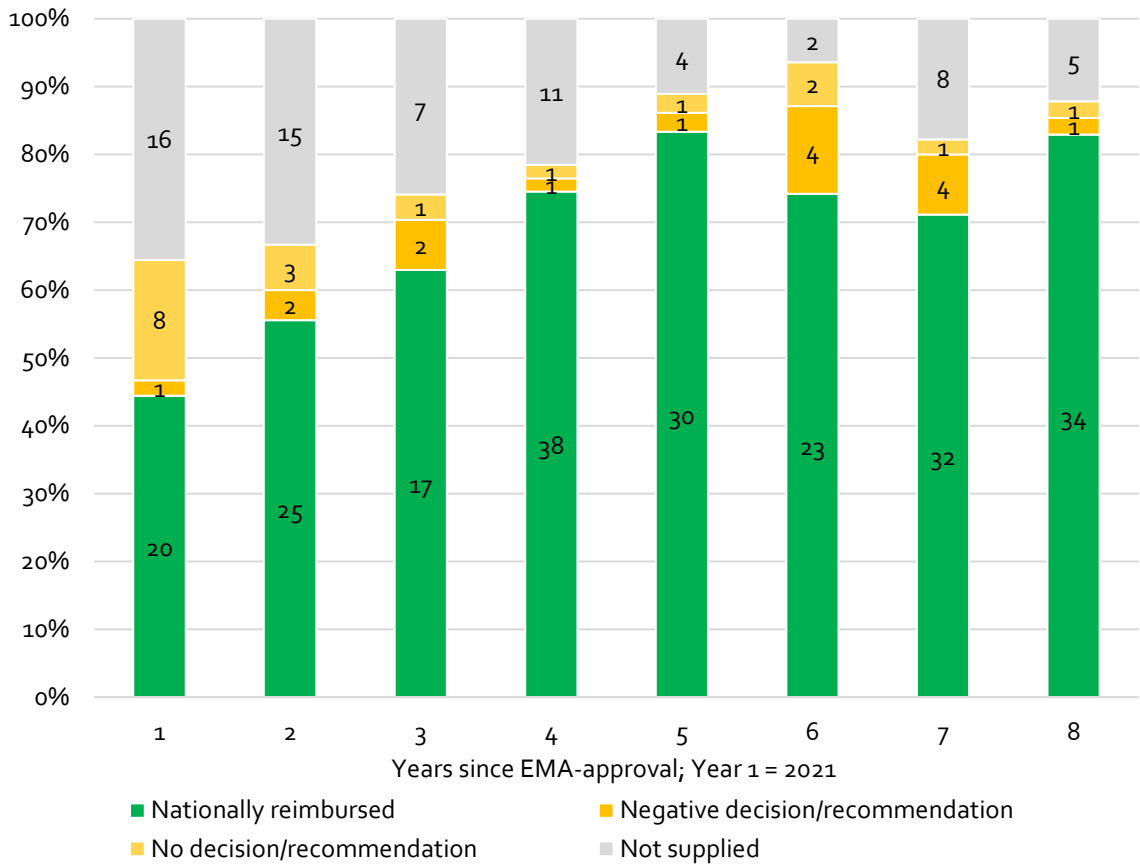
  … in other cases, **companies may anticipate a negative decision/recommendation, or they** may lack knowledge of the Swedish market and therefore **do not find it worthwhile to apply**
- **Fewer three-party negotiations within the pharmaceutical reimbursement scheme in 2020, 2021 and 2022 compared to 2019**
  - The continued use of such tools indicate that they are still needed
- **Application handling time at TLV has increased** – 28% higher in 2022 compared to 2018 (129 days in 2022 compared to 101 days in 2018)
- **Orphan medicines are nationally reimbursed in less extent than medicines overall**
  - Could be due: companies not planning to launch/supply (for instance because of negative anticipations of the prospect for a positive recommendation), companies and payers value medicines differently and/or complex evaluation (lack of data and small patient populations)

Note that even if medicines are not (defined) as nationally reimbursed they may still be used on a regional level through other routes of distributions – no such information were collected as a part of this report.

National reimbursement over time

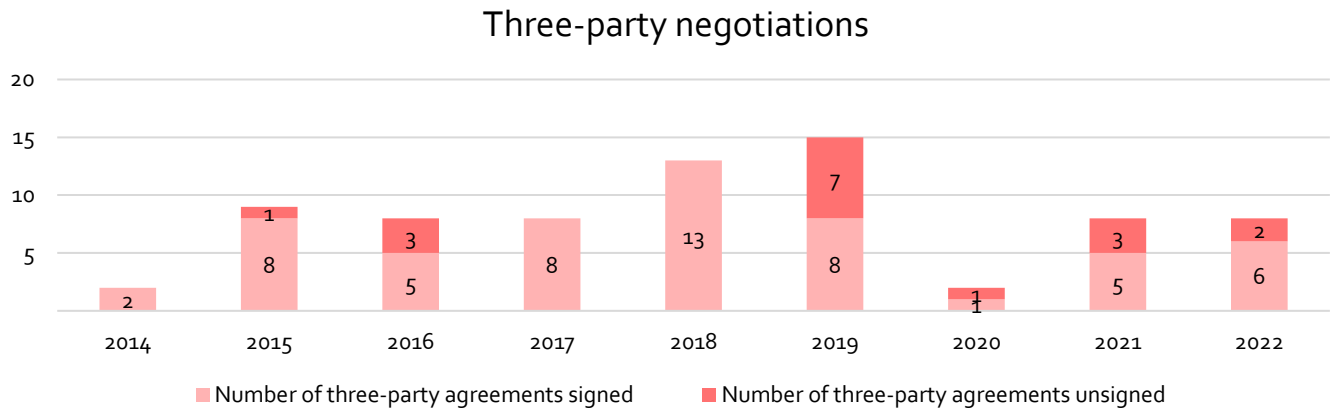
- To evaluate whether medicines can be assumed to become supplied and/or nationally reimbursed over time, we analysed data for all medicines approved by the EMA in 2014-2021, excluding medicines with withdrawn marketing authorisations
  - The definitions presented in slide [12] were used and the data were updated at the cut-off date (20 December 2022)
- The proportion of medicines supplied was higher among medicines approved in 2014-2017 than in 2018-2021
  - It seems to take approximately 3 years until a steady state is reached
- Between 78% and 88% of medicines approved in 2014-2018 were supplied, compared to 64%-74% of the medicines approved in 2019-2021
- The proportion of medicines supplied did not reach 100% for any of the annual cohorts

National reimbursement status of medicines with EMA approval in 2014-2021, by year since EMA approval



Three-party negotiations and price agreements of prescription medicines

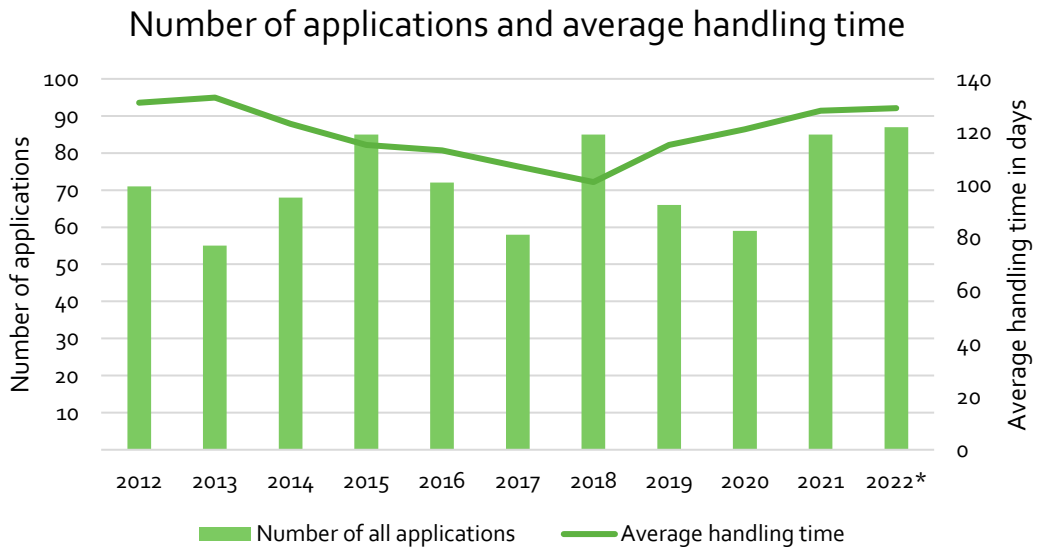
- Three-party negotiations can take place as part of a reimbursement application
  - This include price negotiations between the pharmaceutical company and the regions. TLV acts as a coordinator of the price negotiations
  - May lead to an agreement between the pharmaceutical company and the regions
  - Can help manage uncertainties regarding use and effect – and lead to reimbursement of new innovative medicines
- 20 agreements were reached between 2019-2022

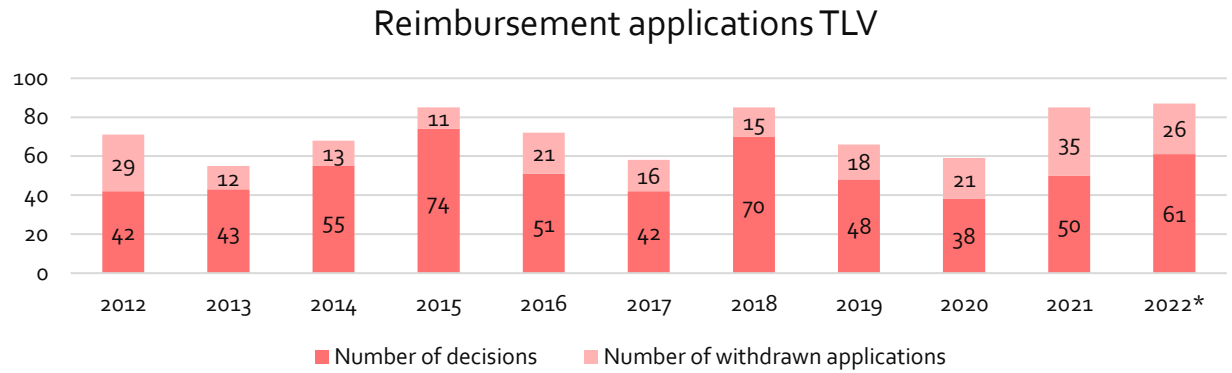


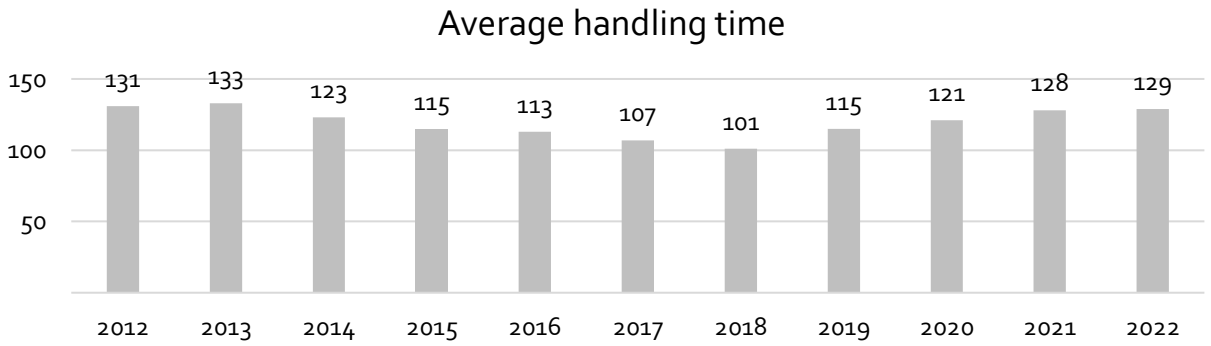
Data for the number of three-party agreements were retrieved from TLV's annual reports and do not include price negotiations for hospital medicines.

The reimbursement system for prescription medicines over time

- The number of reimbursement applications to TLV varied between 55 and 85 submitted applications in 2012-2022
  - Between 11 and 35 applications were withdrawn each year
- The average application handling time varied between 101 days and 133 days in 2012-2022







There is no obvious correlation between the number of applications and the average handling time

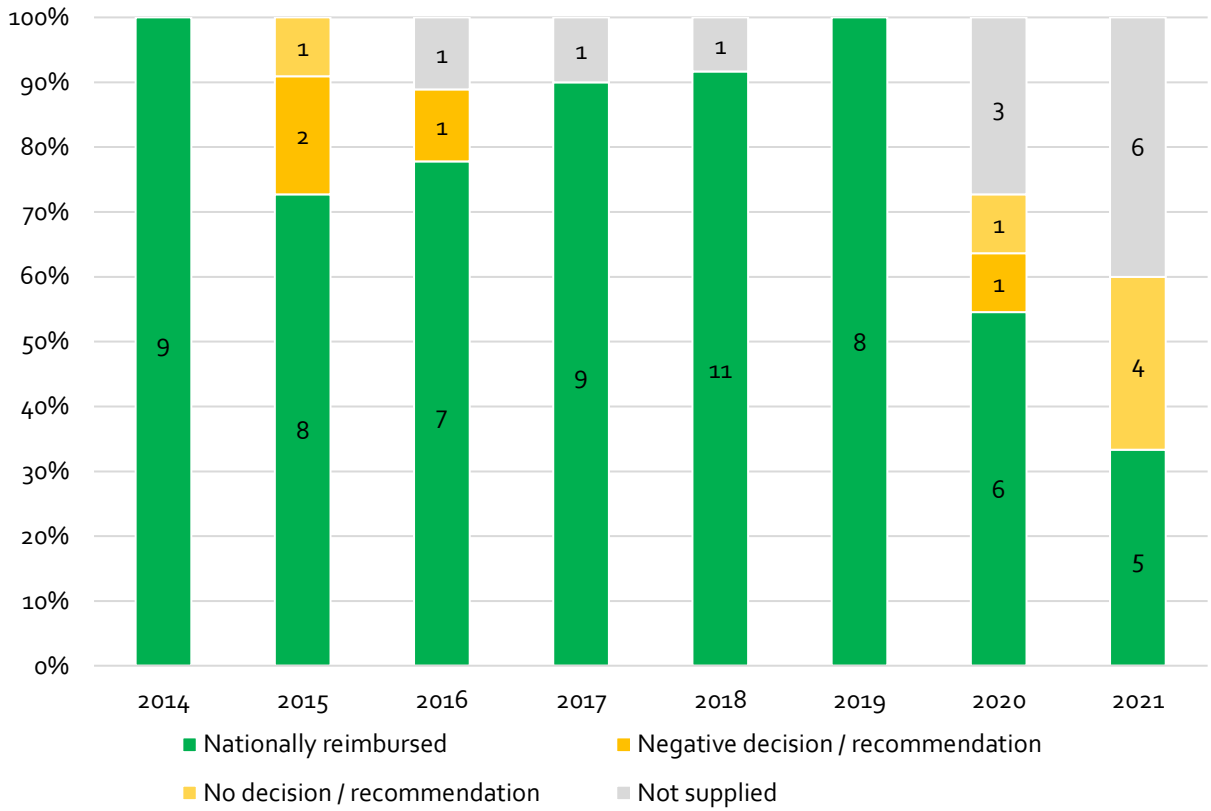
Source: TLV's annual reports

National reimbursement of oncology medicines over time

- 86% of the oncology medicines that received EMA approval between 2014-2018 are nationally reimbursed

- 56% of the oncology medicines that got EMA approval between 2019-2021 are nationally reimbursed*
  - That is slightly higher than the overall reimbursement rate (53%)

National reimbursement status of **oncology medicines** with EMA approval in 2014-2021, by year of EMA approval



* This report focuses on the 2019-2021 cohort while the W.A.I.T. study report shows results for the 2018-2021 cohort.

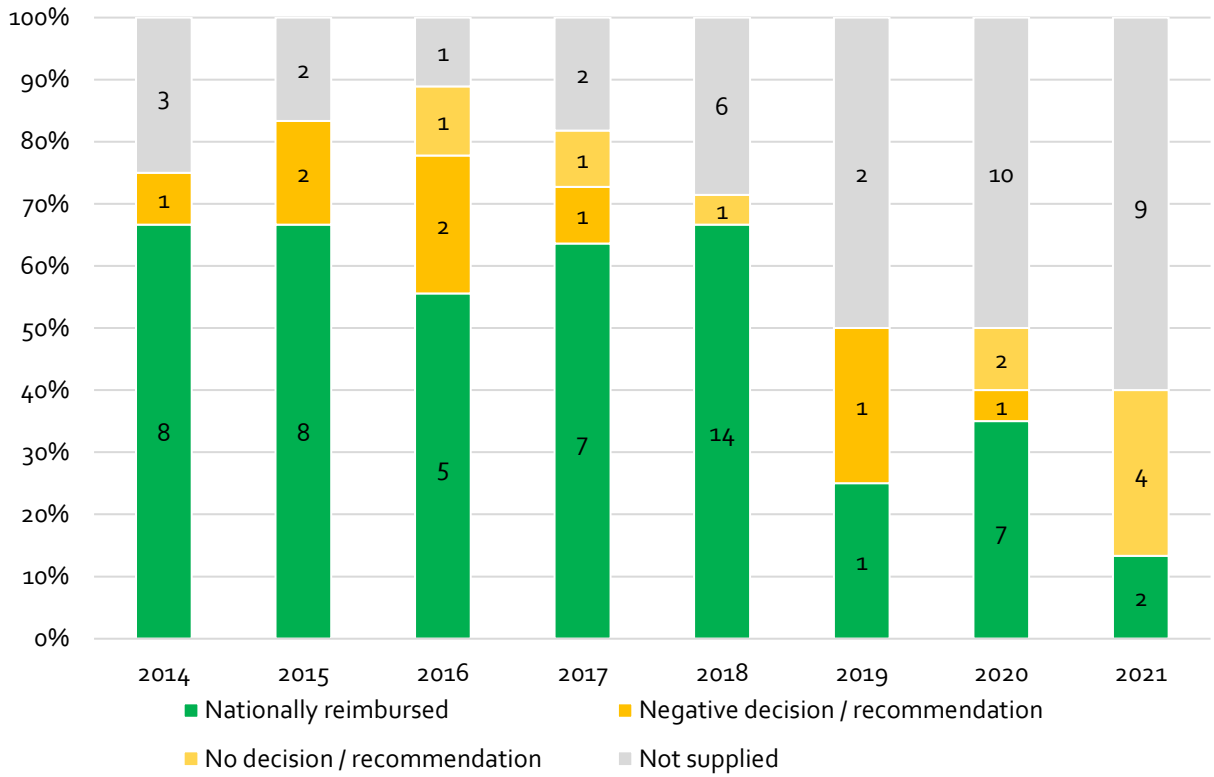
National reimbursement of orphan medicines over time

- 39 orphan medicines received EMA-approval between 2019-2021
  - 18 (46%) of the orphan medicines were supplied
  - 10 were nationally reimbursed, this was:
    - 26% of all orphan medicines approved
    - 56% of all orphan medicines supplied
  - 8 (21%) of the orphan medicines that were not nationally reimbursed were tested in single-arm clinical trials, and 14 (36%) was under additional monitoring by EMA

- 65% of the orphan medicines that got EMA approval between 2014-2018 are nationally reimbursed
  - 22% of the orphan medicines that got EMA approval between 2014-2018 are not supplied

- 26% of the orphan medicines that got EMA approval between 2019-2021 are nationally reimbursed*
  - 54% of the EMA-approved orphan medicines between 2019-2021 are not supplied

National reimbursement status of **orphan medicines** with EMA approval in 2014-2021, by year of EMA approval

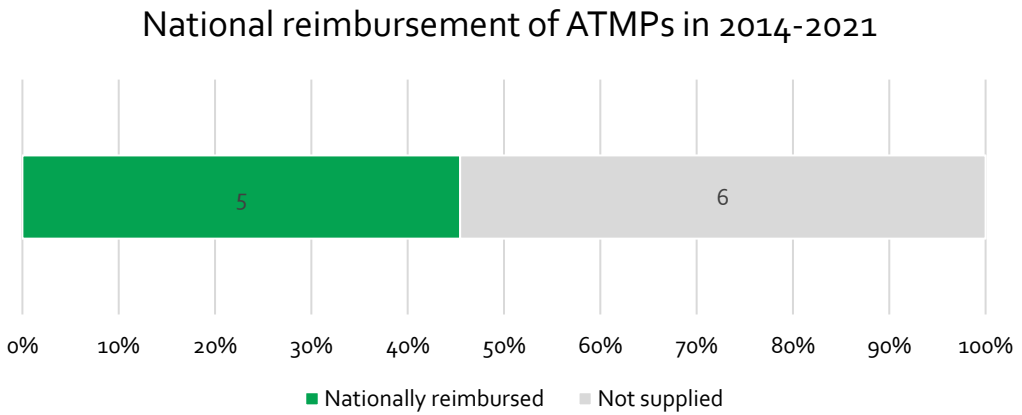


An orphan drug is a drug used to treat, prevent or diagnose life-threatening or chronically debilitating condition that is rare or where the medicine is unlikely to generate sufficient profit to justify research and development costs.

* This report focuses on the 2019-2021 cohort while the W.A.I.T. study report shows results for the 2018-2021 cohort.

National reimbursement of ATMPs over time

- 11 ATMPs received EMA-approval between 2014-2021
  - 7 were tested in single-arm clinical trials
  - 5 (45%) of the ATMPs were supplied and nationally reimbursed
  - 9 (82%) are orphan medicines
  - 4 received EMA-approval between 2019-2021
    - All were tested in single-arm trials
    - 1 (25%) of the 4 was supplied and reimbursed, the other three had either a positive recommendation or was under evaluation indicating that they may become nationally reimbursed in the future
    - 3 (75%) of the 4 were under additional monitoring by EMA



ATMP stands for Advanced therapy medicinal products.

The sub-classes of ATMPs are: Gene Therapy Medicinal Products (GTMP), Tissue Engineered Products (TEP), Somatic Cell Therapy Medicinal Products (sCTMP) and combined ATMPs.

Company survey

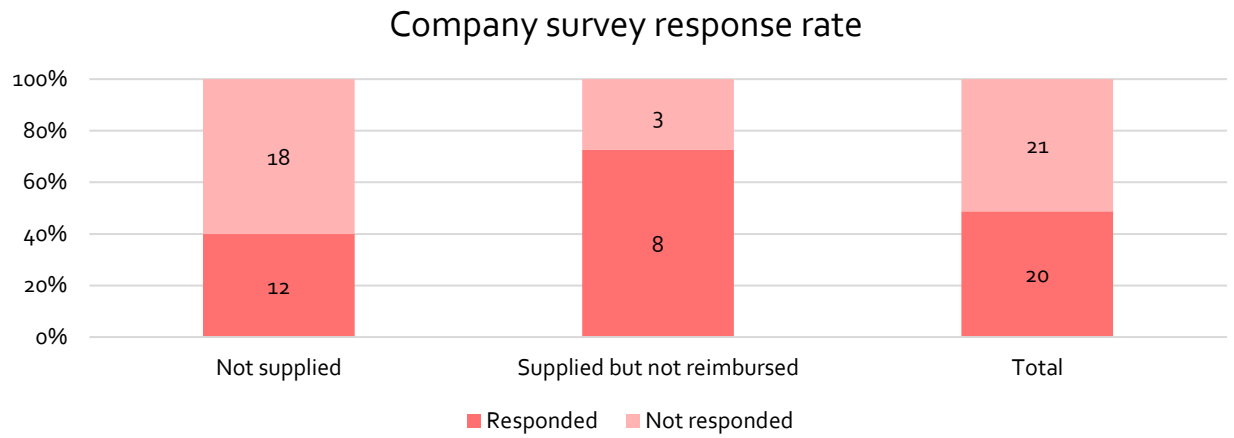
Key takeaways

- **A company survey was conducted to understand why:**
  - some medicines are not supplied, or
  - are supplied but lack national reimbursement
- **64% (7 out of 11) of the companies with non-supplied medicines, that responded to the company survey, are not planning to launch their medicines**
  - **Possible explanations include; lack of resources/local presence** in the Nordics or **negative anticipation on the prospect for** a **positive** reimbursement **decision**.
  - 44% (12 out of 27) companies with non-supplied medicines are not locally present in the Nordics
- **Half of the medicines supplied but not nationally reimbursed have received negative reimbursement decisions (or negative recommendations) or have withdrawn their application**
  - Possible explanations on why these companies choose to still supply their medicines: companies are waiting on data for resubmission and/or companies are examining other reimbursement routes

Background and participation

- To understand the MAH's perspective on why some medicines approved 2019-2021 were not supplied or supplied but not nationally reimbursed, an e-mail survey was sent to all 33 unique MAHs of the:
  - 30 medicines that were not supplied
  - 11 medicines that were supplied but not nationally reimbursed

- Replies were received for 20 (49%) of all medicines from 15 (45%) MAHs
  - Answers were received for 12 (40%) medicines that were not supplied
  - Answers were received for 8 (73%) medicines that were supplied but not reimbursed
  - Among responders, 80% were locally present in the Nordics and 67% had at least one other medicine in the Swedish reimbursement scheme
  - Among non-responders, 44% were locally present in the Nordics and 28% had at least one other medicine in the Swedish reimbursement scheme



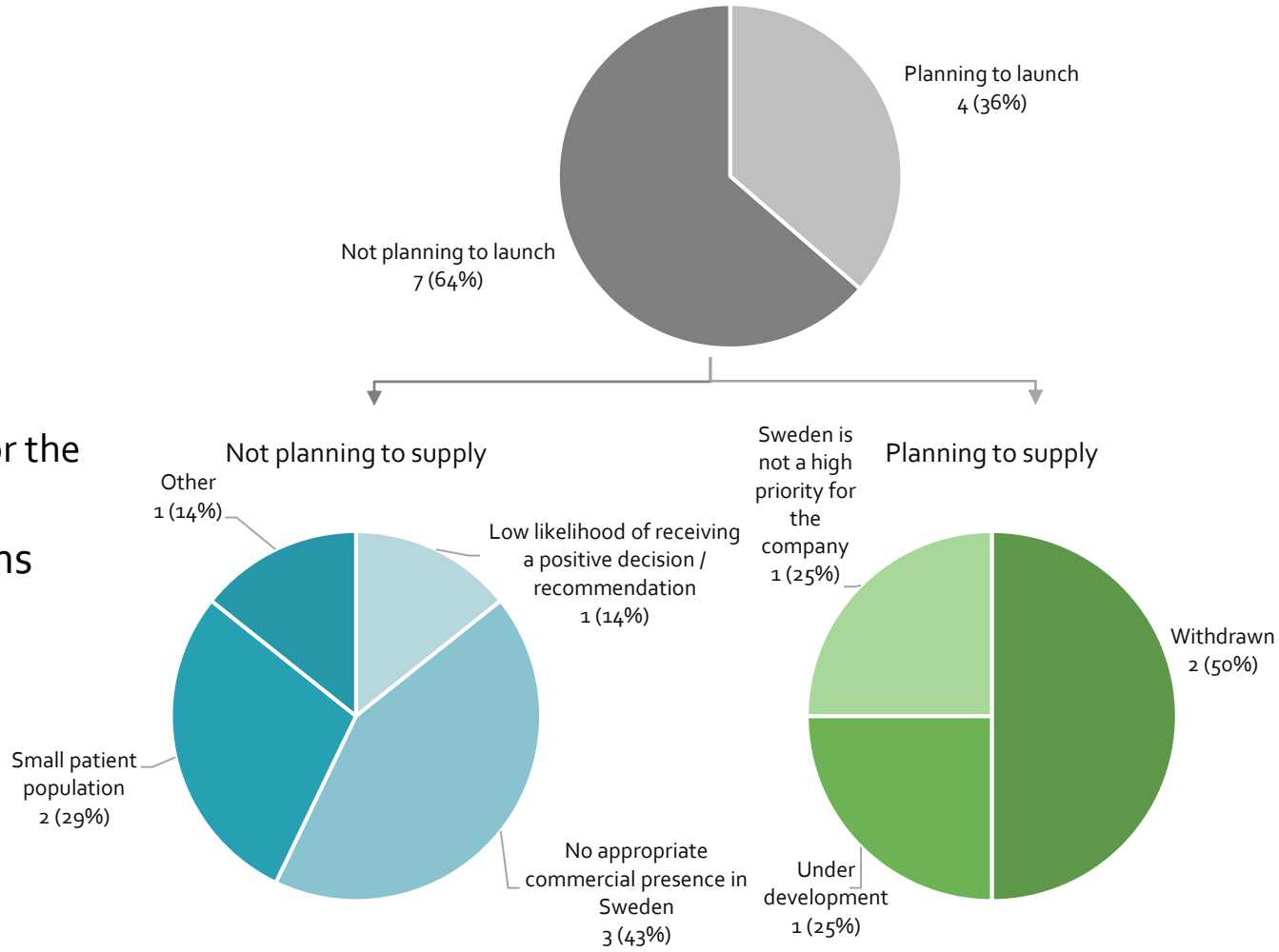
MAHs for medicines which became supplied, and/or reimbursed after the study cut-off date, as well as those with a negative reimbursement decision/recommendation during the study period were excluded from the survey (n=14)

Why were 38 medicines not supplied?

- Answers were received from 11 individual MAHs marketing 12 medicines
  - One company did not want to comment on future plans
- Among MAHs planning to supply, companies were in different stages of the process
  - 1 out of 4 MAHs were still developing the submission
  - In 2 of the 4 cases, the reimbursement application was withdrawn
  - 1 out of the 4 MAH did not consider Sweden a priority for the company
- Among MAHs not planning to supply, the main reasons were:
  - Lacking the necessary resources or presence (3; 43%)
  - Having a too small patient population (2; 29%)

33 companies are MAH for the 38 non-supplied medicines:
» 61% are locally present in the Nordics
» 45% have at least one other medicine in the Swedish reimbursement scheme

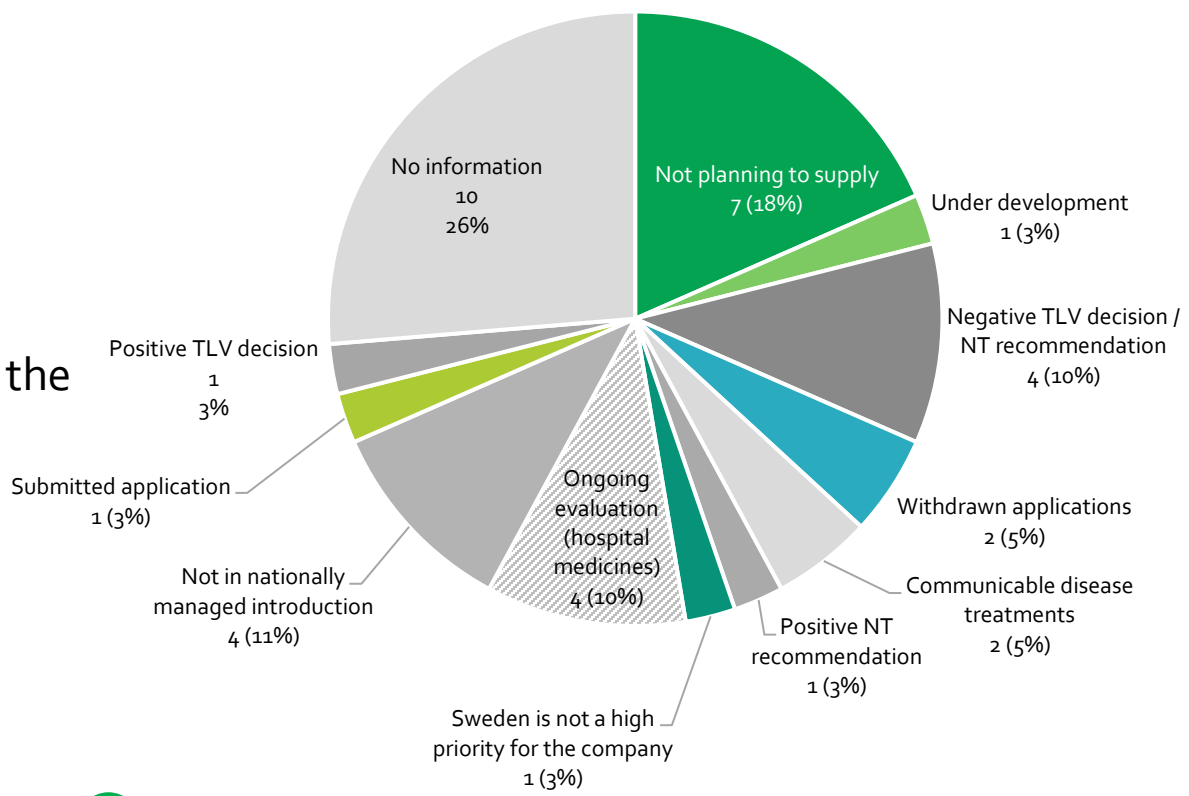
Is the MAH planning to launch the medicine in Sweden? (n = 11)



Are the 38 non-supplied medicines going to be supplied?

- The company survey contributed with information on 7 of the 18 non-supplied medicines for which there was no publicly available information (see slide [20])
  - In 2 cases, the MAHs have withdrawn the applications
  - 5 medicines were not planned to be supplied in Sweden
    - All these medicines were prescription medicines
- 1 medicine received a positive NT recommendation after the cut-off date
- Despite the survey, it was still not possible to obtain information on 10 medicines

Information available about 38 non-supplied medicines



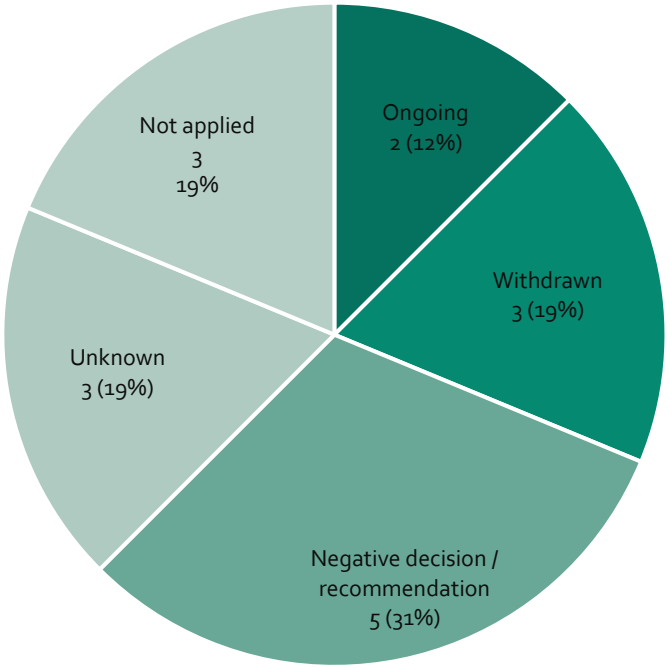
The information marked in colours is obtained from the company survey. The remaining information in grey scale is from publicly available information.

Why were 17 supplied medicines not nationally reimbursed?

- Answers were received from 6 individual MAHs marketing 8 medicines
  - The MAHs had applied or planned to apply for national reimbursement for 5 medicines
    - 3 had a withdrawn submission
    - 2 applications were under development or ongoing
  - The MAHs had not applied for national reimbursement for 3 medicines
  - 3 individual MAHs marketing 3 medicines did not reply to the survey

- Outside of the company survey, the following information is relevant for why these medicines were not reimbursed
  - 5 had received a negative decision/recommendation
  - 1 was nationally reimbursed after the cut-off date

Reason for not being nationally reimbursed (n = 16)



Appendix

QUANTIFY

EFPIA's definitions

- **Rate of availability**: measured by the number of medicines available to patients in European countries. For most countries this is the point at which the product gains access to the reimbursement list (this does not necessarily indicate uptake / usage)

- **Time to availability**: measured by the average time between marketing authorisation and availability, using days from the date of marketing authorisation to the day of completion of post-marketing authorisation administrative processes (whether it is attributable to companies or competent authorities)

- Since the present report explores the different routes to accessibility depending on the type of medicine, there is not a direct correspondence between EFPIA's categories of availability and the definitions used in this report

Availability definition

Description	Status
Full reimbursement through a national reimbursement system	Available
Full automatic reimbursement by a hospital budget (e.g. Nordic system)	
Limited reimbursement to specific subpopulations of approved indication	Available (marked LA*)
Limited reimbursement on a named patient basis (individual patient basis)	
Limited reimbursement while decision is pending (where system permits)	
Availability through a special program (e.g. managed entry agreements)	
Available only within the private market at the patients expense	Only privately available
Not reimbursed, or not reimbursed while awaiting decision	Not available

Colour codes

- EMA approved medicines
- Supplied in Sweden (FASS)
- Not supplied in Sweden (FASS)
- Communicable disease medicines
- Prescription medicines
- Hospital medicines
- Time from EMA approval to listed as supplied in FASS
- Time from listed as supplied in FASS to national reimbursement
- Nationally reimbursed
- Not nationally reimbursed
- Not supplied

Medicines with EMA approval 2019-2021 included in the report (1/3)

Medicines included in the report: 38 non-supplied medicines		
Abecma	Imcivree	Quofenix
Adtralza	Isturisa	Rhokiinsa
Artesunate Amivas	Klisyri	Rizmoic
Aspaveli	Koselugo	Roclanda
Ayvakyt	Libmeldy	Sogroya
Brukinsa	Mulpleo (previously Lusutrombopag Shionogi)	Sunosi
Bylvay	Nexpovio	Tecartus
Copiktra	Nilemdo	Trepulmix
Daurismo	Nustendi	Trogarzo
Dovprela (previously Pretomanid FGK)	Obiltoxaximab SFL	Waylivra
Elzonris	Oxlumo	Xenleta
Evkeeza	Palynziq	Zynrelef
Fintepla	Qinlock	

As of the cut-off date (20 December 2022)

Medicines with EMA approval 2019-2021 included in the report (2/3)

Medicines included in the report: 62 supplied and nationally reimbursed medicines			
Adakveo	Fetcroja	Ontozry	Talzenna
Ajovy	Gavreto	Orladeyo	Trecondi
Atectura Breezhaler / Bemrist Breezhaler	Giapreza	Phesgo	Trixeo Aerosphere
Beovu	Givlaari	Piqray	Trodelvy
Bimzelx	Hepcludex	Polivy	Tukysa
Byfavo	Idefirix	Ponvory	Ultomiris
Calquence	Inrebic	Recarbrio	Vazkepa
Cibinqo	Jemperli	Rekambys	Vitrakvi
Doptelet	Jyseleca	Rinvoq	Vizimpro
Dovato	Kaftrio	Rozlytrek	Vocabria
Enerzair Breezhaler / Zimbus Breezhaler	Kesimpta	Rukobia	Vumerity
Enhertu	Leqvio	Rybelsus	Xospata
Erleada	Libtayo	Ryeqo	Zeposia
Evenity	Lorviqua	Sibnayal	Zolgensma
Evrenzo	Mayzent	Skyrizi	
Evrysdi	Nubeqa	Spravato	

As of the cut-off date (20 December 2022)

Medicines with EMA approval 2019-2021 included in the report (3/3)

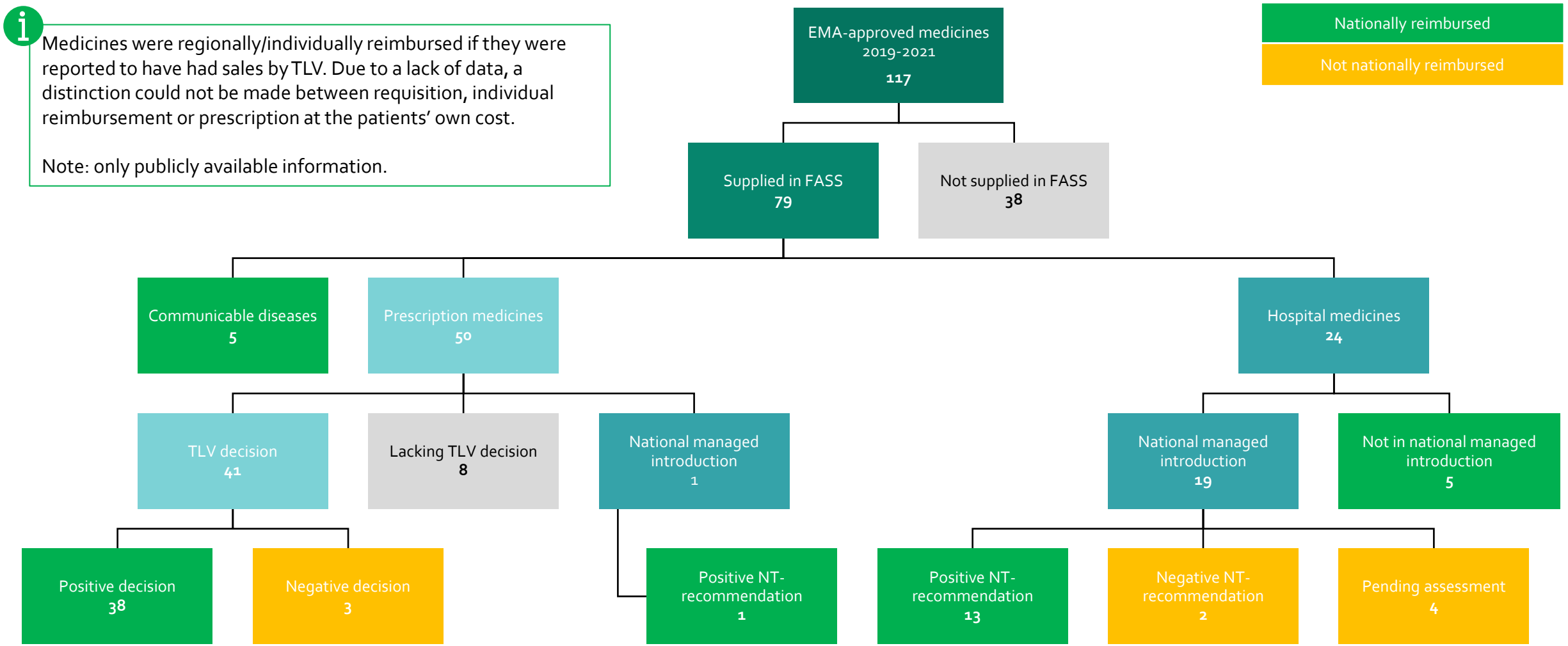
Medicines included in the report: 17 supplied non-nationally reimbursed medicines
Arikayce liposomal
Baqsimi
Besremi
Blenrep
Drovelis/Lydisilka
Enspryng
Epidyolex
Minjuvi
Pemazyre
Reblozyl
Retsevmo
Rybrevant
Sarclisa
Tavlesse
Verquvo
Voxzogo
Xofluza

As of the cut-off date (20 December 2022)

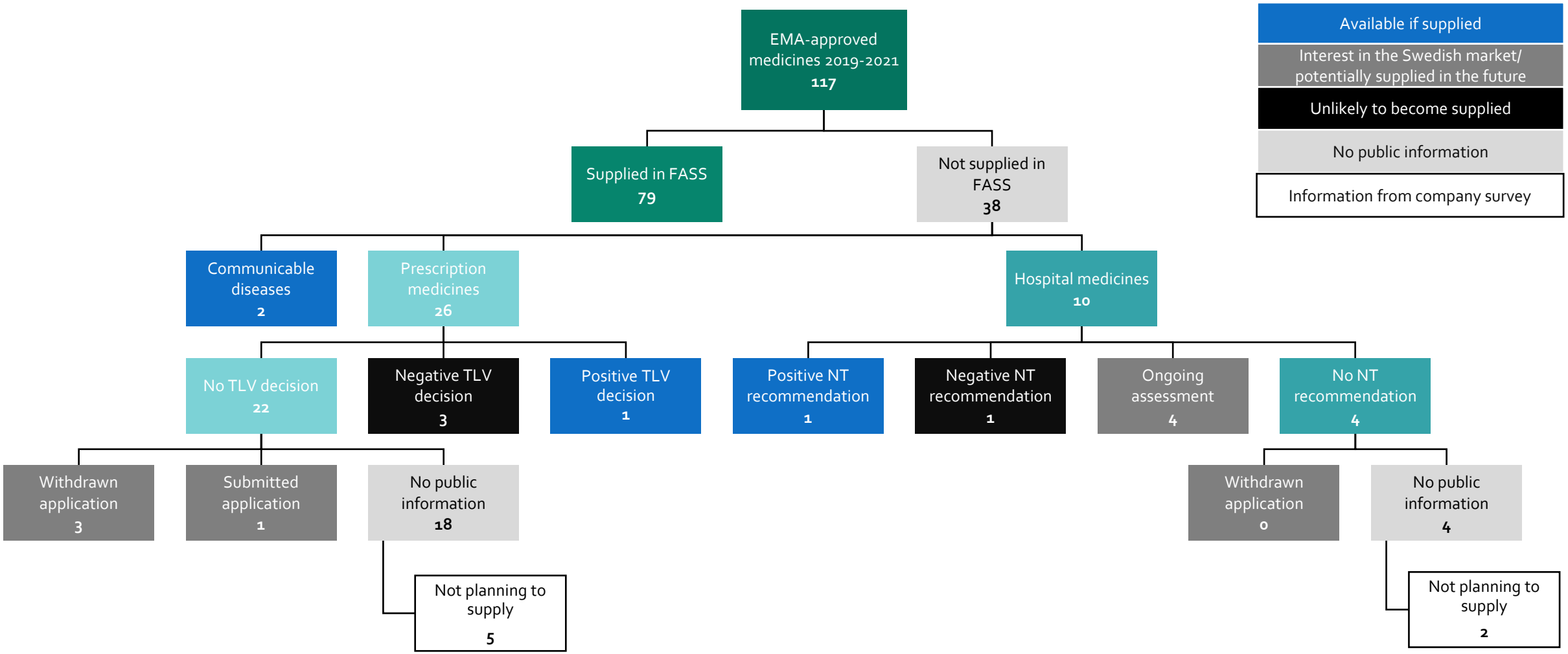
Overview: Medicines supplied in Sweden

Medicines were regionally/individually reimbursed if they were reported to have had sales by TLV. Due to a lack of data, a distinction could not be made between requisition, individual reimbursement or prescription at the patients' own cost.

Note: only publicly available information.



Overview: Medicines not supplied in Sweden



Authors and contact

Contact

Lena Jacobs | Senior Research Analyst

Quantify Research

+46 70 796 90 32

lena.jacobs@quantifyresearch.com

Linnea Oldsberg | Payer Strategy Expert/Senior Project Leader

Quantify Research

+46 736 54 95 58

linnea.oldsberg@quantifyresearch.com

Konstantin Macheridis | Senior Project Leader

Quantify Research

+46 70 038 47 97

konstantin.macheridis@quantifyresearch.com

This report was commissioned and funded by Lif, The research-based pharmaceutical industry.

The complete dataset of publicly available information can be provided upon request to Lif and/or Quantify Research.