Access to new medicines with EMA approval 2017-2019 in Sweden

26 March 2021

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Executive summary

Executive summary (1/2)

- This study investigated the level of access to 116 new medicines approved by EMA (European Medicines Agency) in 2017-2019 in Sweden in terms of:
  - The rate of availability (%), measured as the share of new medicines classified as available to Swedish patients
  - The average time to market (TTM), in days, for the medicines classified as available
  - To further analyse factors affecting non-availability and long TTM, a survey was sent to Lif members and the answers analysed

- In addition, a pragmatic assessment was conducted to characterise the consequences of non-availability of medicines by:
  - Identifying the share of non-available medicines for which there was at least one reasonably similar replacement option available in Sweden

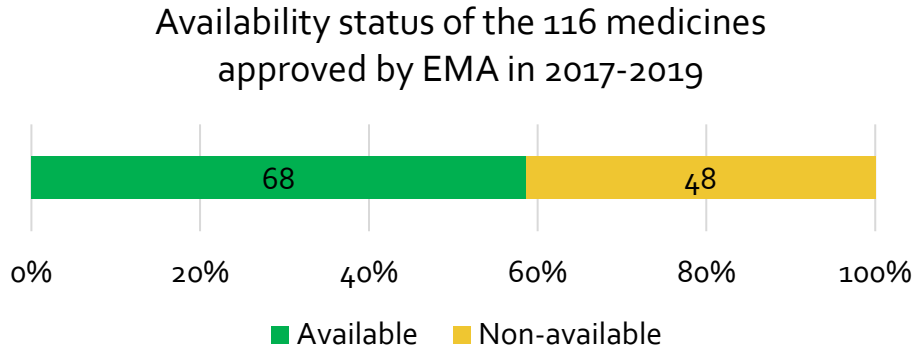
Executive summary (2/2)

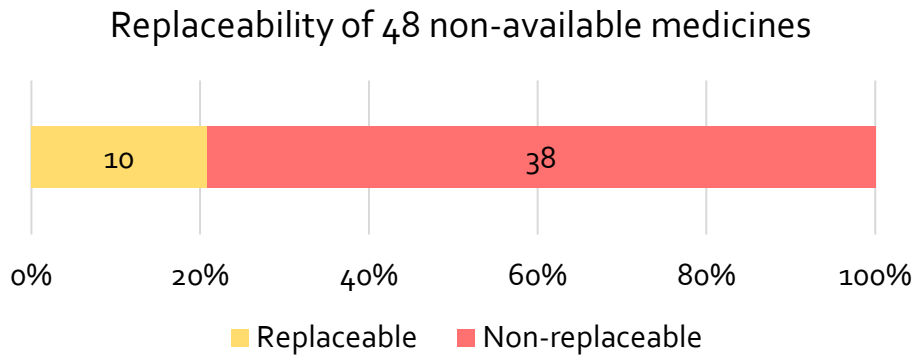
- Among the 116 new medicines at the 22 December 2020 analysis cut-off date:

- 68 were classified as available
  - Rate of availability: 59%
  - Average TTM: 7.9 months (239 days)
  - A vast majority of available medicines seem to reach patients (estimated as having any amount of sales in Sweden in 2020)

- 48 were classified as non-available
  - 10 (21%) were classified as replaceable (replacement option exists)
  - 38 (79%) were classified as non-replaceable (associated with added value for patients via one or more unique features)

- The rate of availability was somewhat lower and TTM slightly shorter (in absolute terms) compared to the previous studies of access to new medicines with EMA approval in 2014-2016, 2015-2017 and 2016-2018
  - Rate of availability: 59% vs. 61%, 70% and 65%
  - TTM (months): 7.9 vs. 8.5, 8.8 and 9.8





Background and objectives

Background and objectives

- Each year, the European Federation of Pharmaceutical Industries and Associations (EFPIA) presents its Patients Waiting to Access Innovative Therapies (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 available to patients in each country compared to the total number of new medicines approved by EMA during the period
  - The average TTM for available medicines from marketing authorisation (MA) date to the date of patient access

- The present study is a detailed review of access to new medicines with EMA approval in 2017-2019 in Sweden conducted by Quantify and commissioned by The research-based pharmaceutical industry (Lif).
  - Quantify has previously conducted similar analyses of new medicines approved in 2014-2016, 2015-2017 and 2016-2018

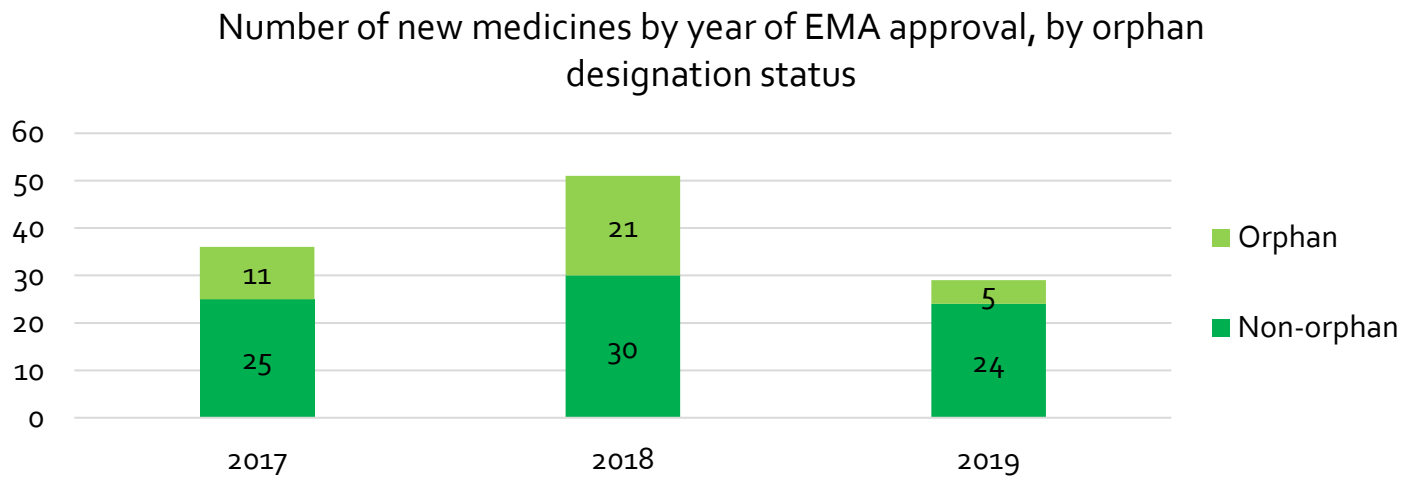
- This year's report makes use of a similar methodology and definitions compared to the previous studies (2014-2016, 2015-2017 and 2016-2018) to allow for comparability over time

- Methods and definitions are outlined in the Appendix

Study materials: an overview

- 117 new medicines with new substances, combinations or indications in orphan diseases were approved by EMA 2017-2019 and included in the analysis set
  - Following this, one medicine was excluded due to a withdrawn MA

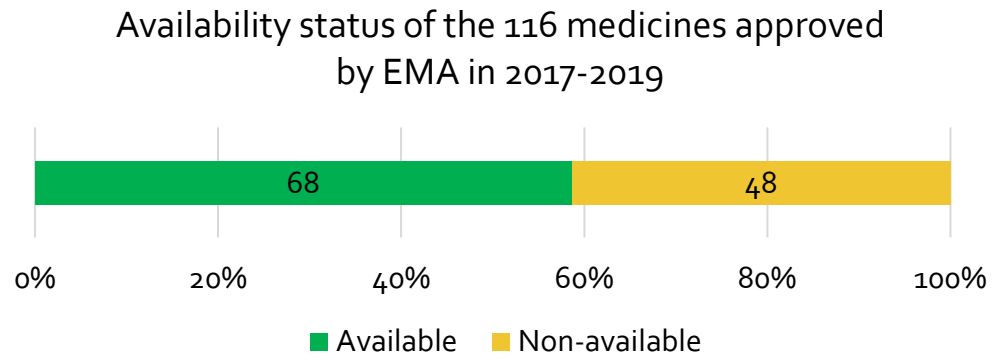
- A total of 116 medicines were included in the present study
  - 36, 51 and 29 were approved in 2017, 2018 and 2019, respectively
  - 37 (32%) had an orphan designation status, a majority of these (57%) were authorised in 2018

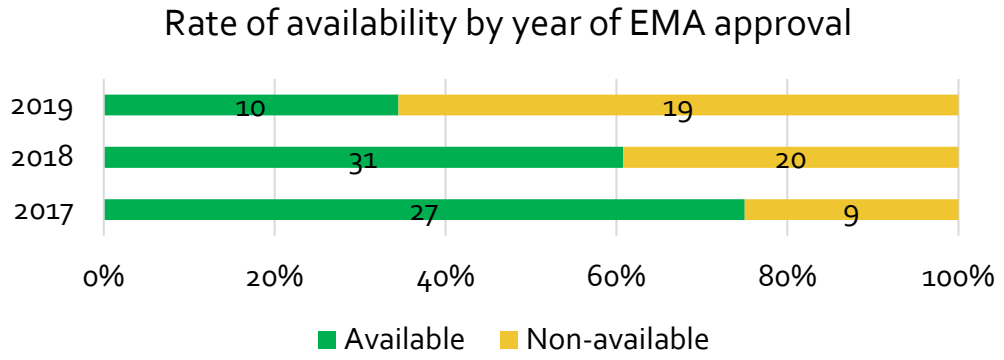


Rate of availability in Sweden

6 of 10 new medicines are available in Sweden

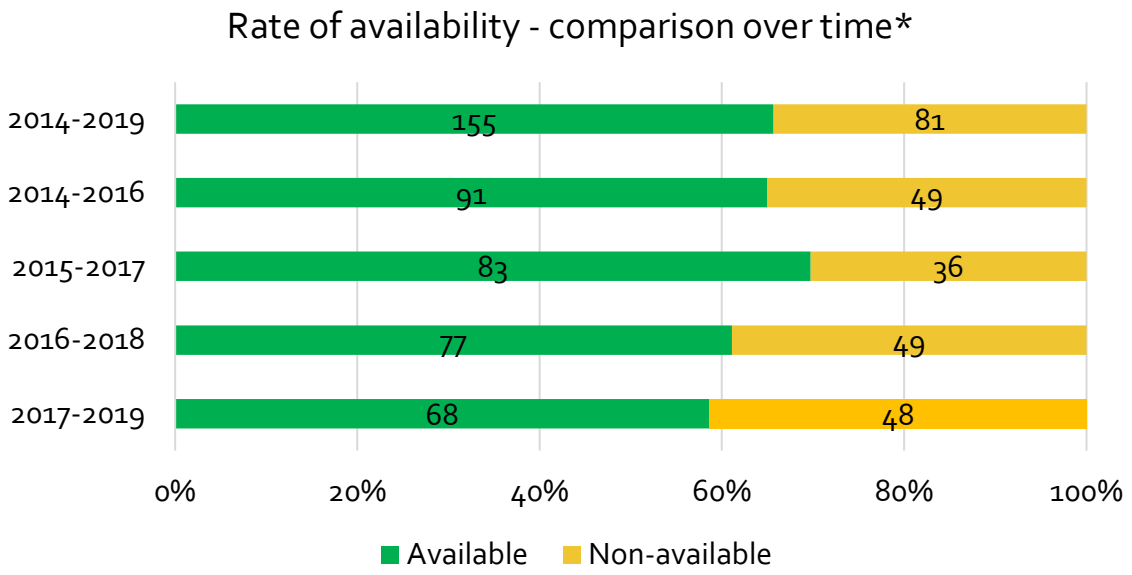
- At the 22 December 2020 cut-off date, 68 new medicines with EMA approval in 2017-2019 were classified as available in Sweden
- The corresponding rate of availability was 59%
- Stratified by year of EMA approval, the estimated rate of availability was:
  - 2019: 34%
  - 2018: 61%
  - 2017: 75%
- Note: longer follow-up time increases the likelihood of a medicine becoming available





Comparison of availability over time

- Over time, the rate of availability has fluctuated, yet remained relatively stable at approximately 60-70%
  - 66% of new medicines approved in 2014-2019 were available in Sweden

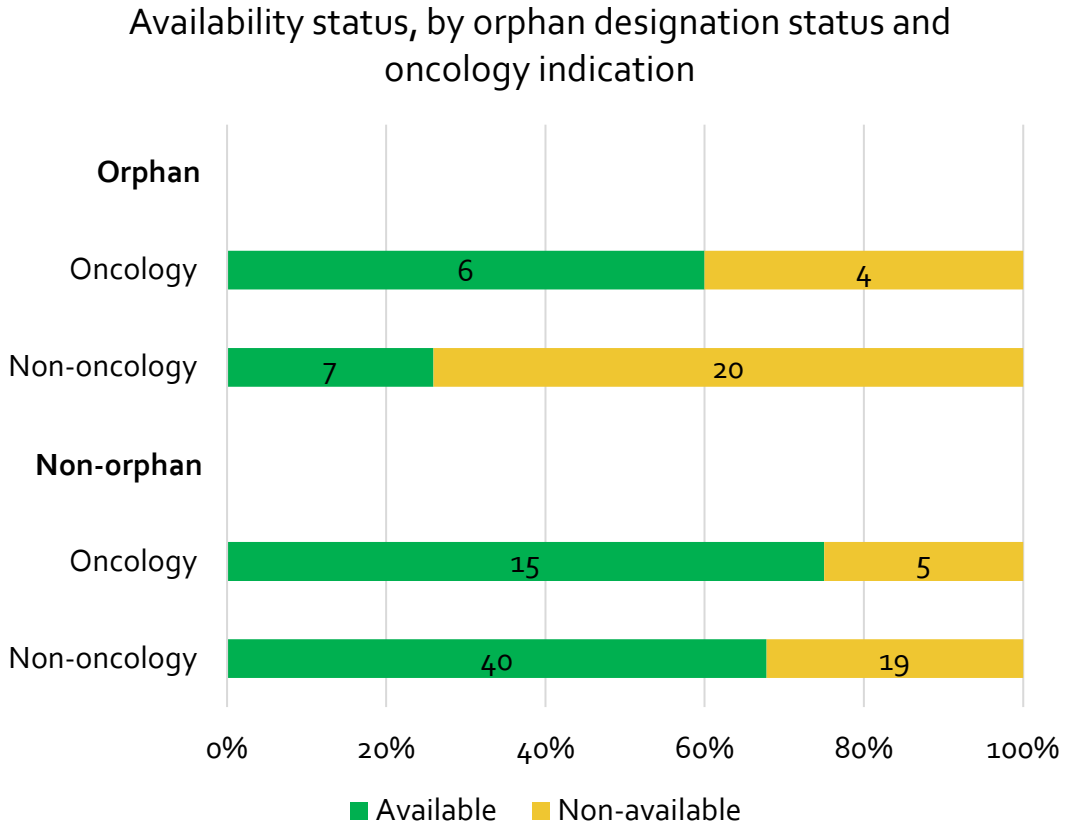


* Using the numbers from previous studies for 2014-2016, 2015-2017 and 2016-2018 but updated numbers for 2014-2019 and 2017-2019

Availability by orphan designation status and oncology indication

- Availability differed depending on **orphan designation status**
  - 35% orphan medicines were available
  - 70% non-orphan medicines were available

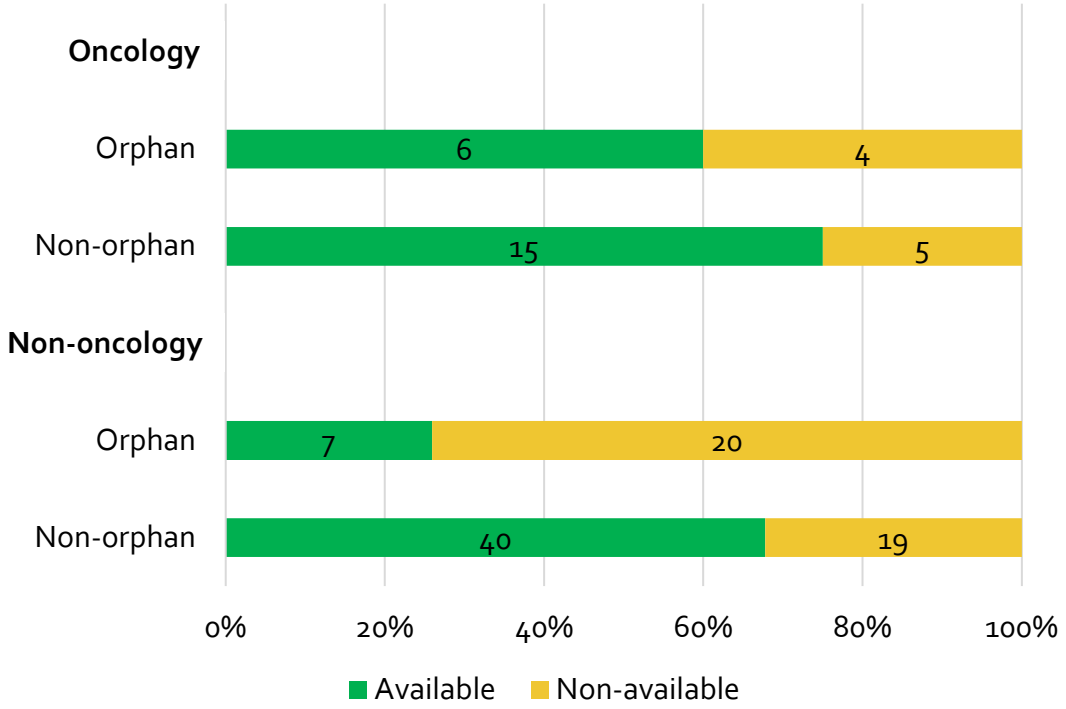
- Stratifying by **oncology indication**
  - Orphan
    - Oncology medicines were associated with a higher rate of availability than non-oncology medicines (60% vs. 26%)
  - Non-orphan
    - Oncology and non-oncology medicines had a similar rate of availability (75% vs. 68%)



Availability by oncology indication and orphan designation status

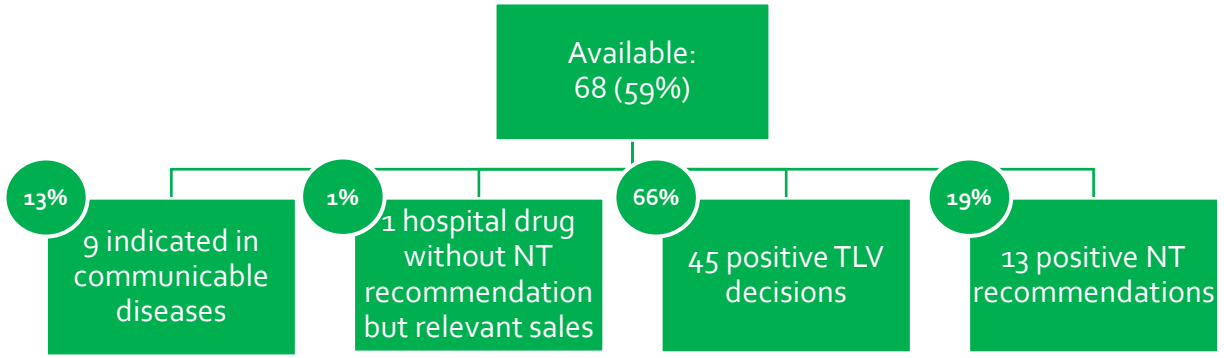
- Availability differed depending on **oncology indication**
  - 70% oncology medicines were available
  - 55% non-oncology medicines were available
- Stratifying by **orphan designation status**
  - Oncology
    - Non-orphan and orphan drugs had more similar rates of availability, but non-orphan drugs were still associated with a higher rate of availability than orphan drugs (75% vs. 60%)
  - Non-oncology
    - Non-orphan drugs were associated with a higher rate of availability than orphan drugs (68% vs. 26%)

Availability status, by oncology indication and orphan designation status



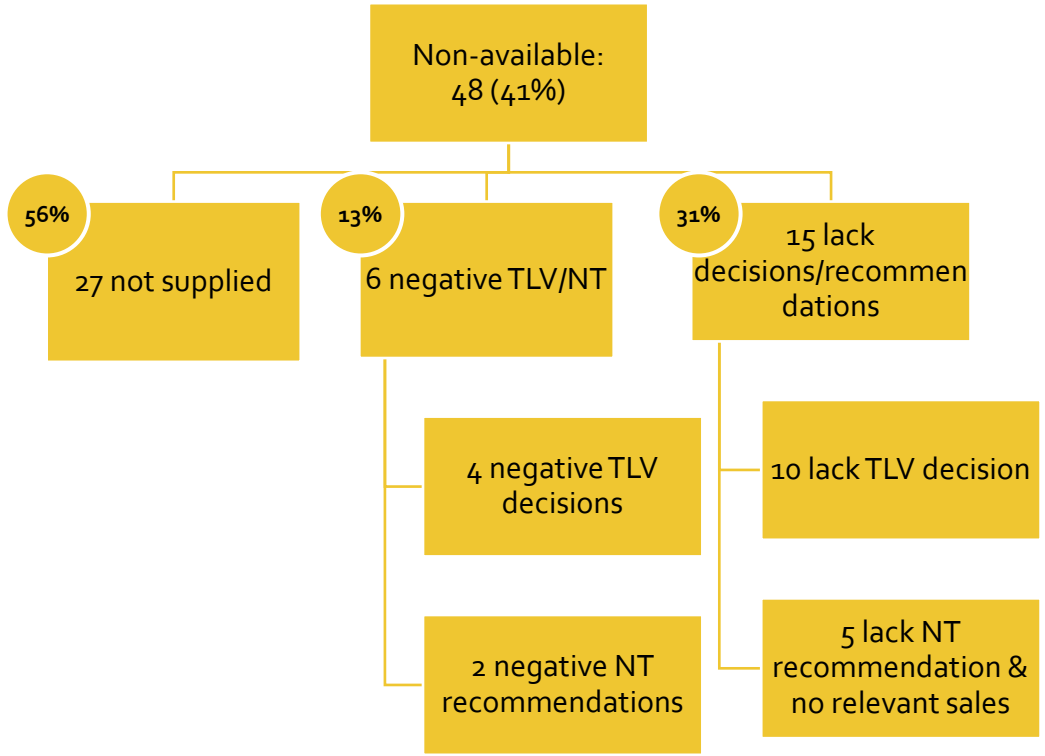
Reasons for availability in Sweden

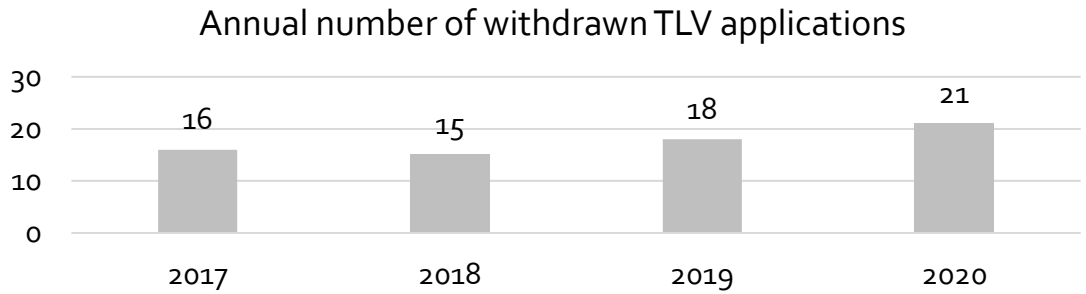
- 68 (6 of 10) new medicines were classified as available
- A majority (66%) had positive decisions from The Dental and Pharmaceutical Benefits Agency (TLV)
- 13 (19%) had positive New Therapies council (NT) recommendation
- 9 (13%) were indicated in communicable diseases, where a positive reimbursement decision is not required for market access
- A single medicine was a hospital drug which lacked recommendation, but was assessed to have relevant sales



Reasons for non-availability in Sweden

- 48 (4 of 10) new medicines were classified as non-available
- The majority (56%) were not registered as supplied in Sweden
- 15 (31%) lacked a TLV decision/NT recommendation
- 6 (13%) had received negative TLV decisions or NT recommendations
- To put this into perspective, the annual number of withdrawn TLV applications ranged from 15 to 21 in the years 2017-2020



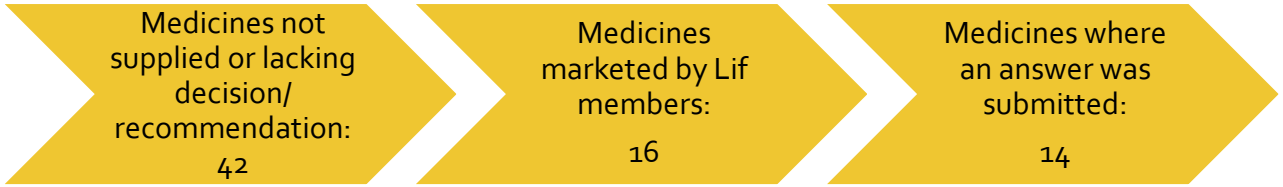


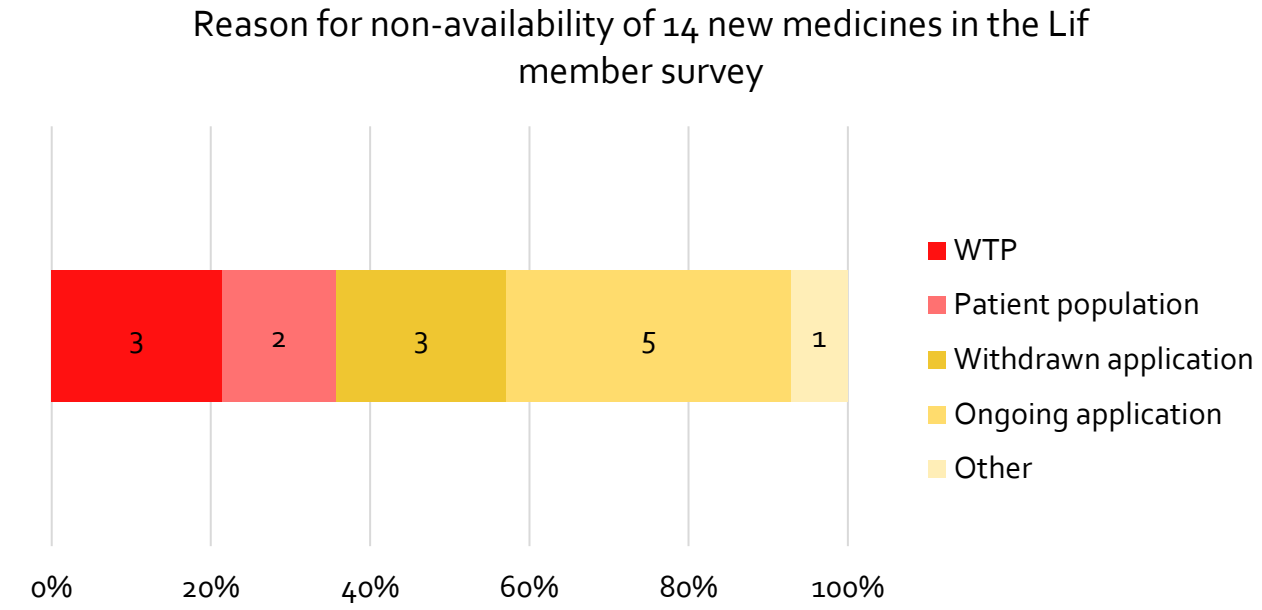
In-depth analysis of reasons of non-availability

- An in-depth survey analysis aiming to explain the reasons for non-availability of new medicines was conducted

- The analysis included 14 new medicines marketed by Lif members which were not supplied in Sweden, had not received a reimbursement decision from TLV or had not received a recommendation from NT
  - 6 were not supplied in Sweden
  - 5 did not have a TLV decision
  - 3 did not have a NT recommendation and lacked relevant sales

- The survey showed that:
  - No member company lacked resources or local presence to launch the product
  - Willingness to pay (WTP) was considered too low in 3 (21%) cases
  - 2 (14%) medicines had too small patient populations in Sweden for NT to request an evaluation
  - 3 (21%) medicines had withdrawn applications
  - 5 (36%) medicines had ongoing applications
  - 1 (7%) medicine was not available due to other reasons





Almost all available new medicines seem to reach patients

- A sales analysis was conducted to evaluate the actual perceived access to patients of available new medicines.
  - The sales data analysed stretched from January to November 2020
- A vast majority (91%) of the **available** medicines had at least low levels of sales in 2020, and 85% had sales of at least 105 packages per month (5 packages per month in each of Sweden's 21 regions)
- Furthermore, 18 **non-available** medicines were considered **privately available**† in Sweden. Among these, 44% (N=8) had non-zero sales
  - Consequently, 60% (N=70) of all 116 new medicines had non-zero sales in Sweden during the period

New available medicines		
Sales criteria*	**N=68**	**%**
Non-zero sales 2020	62	91%
Sales 2020 ≥ 5 packages/month	62	91%
Sales 2020 ≥21 packages/month	61	90%
Sales 2020 ≥105 packages/month**	58	85%

* 2020 sales data included the first eleven months: January – November
** 5 packages per month in each of Sweden's 21 regions

† A medicine was privately available if it was supplied in Sweden (listed as supplied in FASS), and per 22 December 2020 was available for purchase at www.apoteket.se. This does not necessarily mean that the patient paid for the medicine privately.

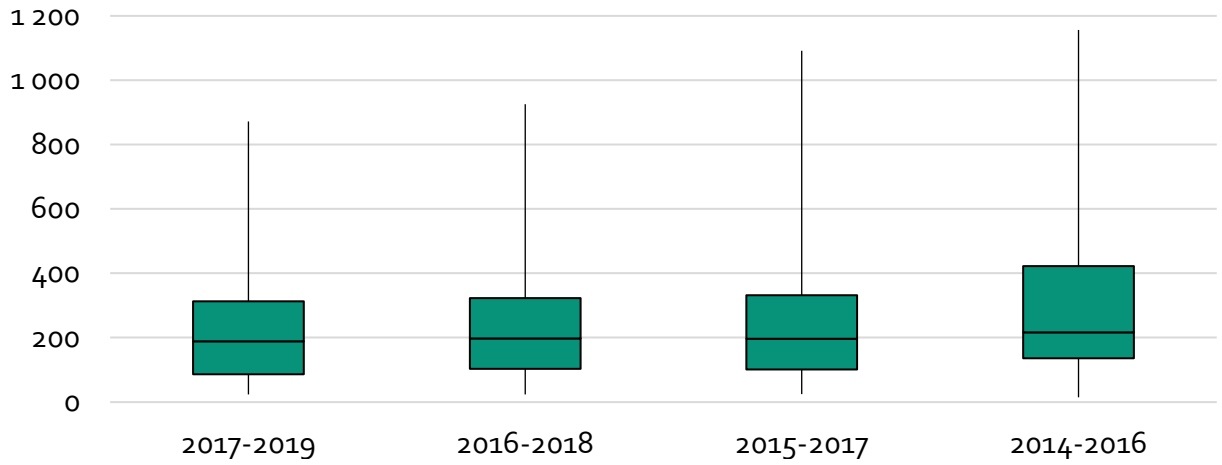
Time to market (TTM) in Sweden

Positive trend towards shorter TTM over time overall

- The average TTM for the 68 available new medicines was 239 days (~7.9 months)
  - The shortest TTM was 23 days and the longest 872 days
  - In line with the previous reports, more than 20% of the medicines had a TTM exceeding one year
  - 47 (69%) of the medicines had a TTM shorter than 270 days†
- A positive trend towards shorter access times over time was observed

TTM in days	2017-2019 N=68	2016-2018 N=77	2015-2017 N=83	2014-2016 N=91
Average	239	258	269	297
25th percentile	87	103	101	136
Median	189	197	196	216
75th percentile	313	323	332	422
Percentage with TTM >365 days	21%	21%	22%	27%

TTM in days – comparison over time*



† TLV's statutory processing time + 90 days of additional time for complements within the application

* The graph presents the minimum, 25th percentile, median, 75th percentile and maximum number of days.

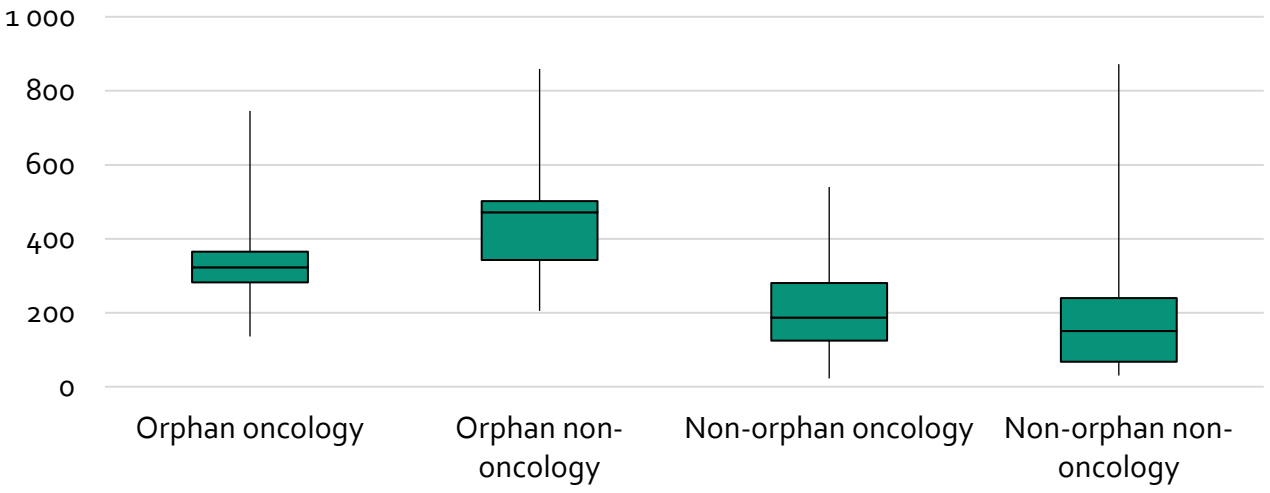
TTM by orphan designation status and oncology indication

- Estimated average TTM:
  - Orphan drugs: 416 days (min 136 – max 859)
    - Oncology: 363 days (min 136 – max 746)
    - Non-oncology: 461 days (min 205 – max 859)
  - Non-orphan drugs: 197 days (min 23 – max 872)
    - Oncology: 216 days (min 23 – max 540)
    - Non-oncology: 190 days (min 31 – max 872)

- The longest average TTM was observed among orphan non-oncology drugs

TTM in days	Orphan N=13*	Non-orphan N=55
Average	416	197
25th percentile	269	77
Median	380	158
75th percentile	481	251
Percentage with TTM >365 days	54%	13%

TTM in days by orphan designation status and oncology indication



* Note: relatively small sample

** The graph presents the minimum, 25th percentile, median, 75th percentile and maximum number of days.

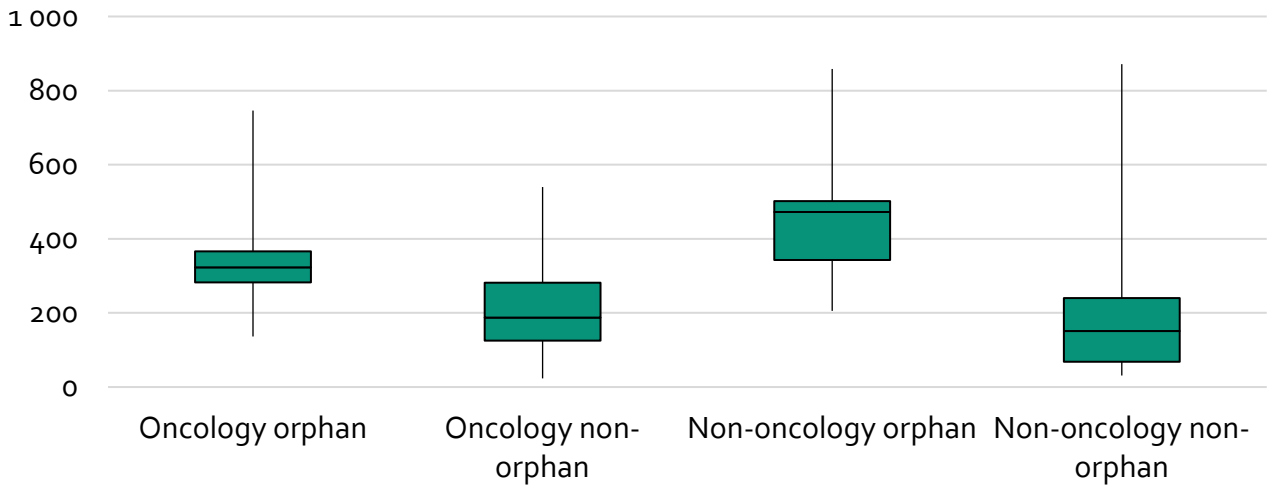
TTM by oncology indication and orphan designation status

- Estimated average TTM:
  - Oncology drugs: 258 days (min 23 – max 746)
    - Orphan: 363 days (min 136 – max 746)
    - Non-orphan: 216 days (min 23 – max 540)
  - Non-oncology drugs: 230 days (min 31 – max 872)
    - Orphan: 461 days (min 205 – max 859)
    - Non-orphan: 190 days (min 31 – max 872)

- The longest average TTM was observed among non-oncology orphan drugs

TTM in days	Oncology N=21	Non-oncology N=47
Average	258	230
25th percentile	144	77
Median	195	160
75th percentile	323	279
Percentage with TTM >365 days	24%	19%

TTM in days by oncology indication and and orphan designation status



* The graph presents the minimum, 25th percentile, median, 75th percentile and maximum number of days.

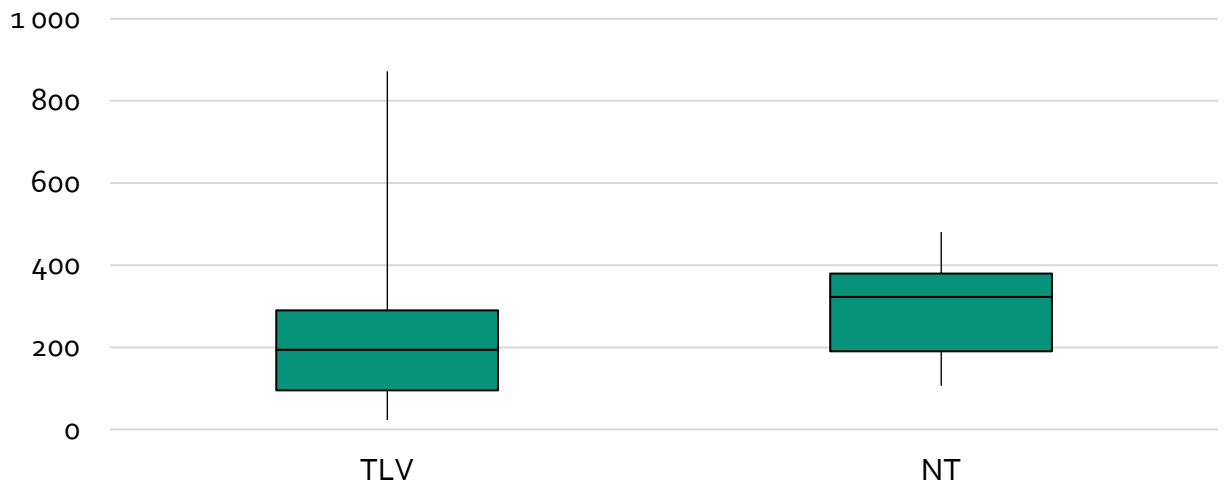
TTM by TLV decision or NT recommendation

- Of 68 available new medicines
  - 45 (66%) had a positive TLV decision
    - Of which 5 (11%) were orphan
  - 13 (19%) had a positive NT recommendation
    - Of which 8 (62%) were orphan

- Estimated average TTM:
  - Medicines with positive TLV decision: 255 days (min 23 – max 872)
  - Medicines with positive NT recommendation: 296 days (min 106 – max 481)

TTM in days	TLV decision N=45	NT recommendation N=13*
Average	255	296
25th percentile	95	190
Median	194	323
75th percentile	290	380
Percentage with TTM >365 days	22%	31%

TTM in days by decisionmaker**



* Note: relatively small sample

** The graph presents the minimum, 25th percentile, median, 75th percentile and maximum number of days.

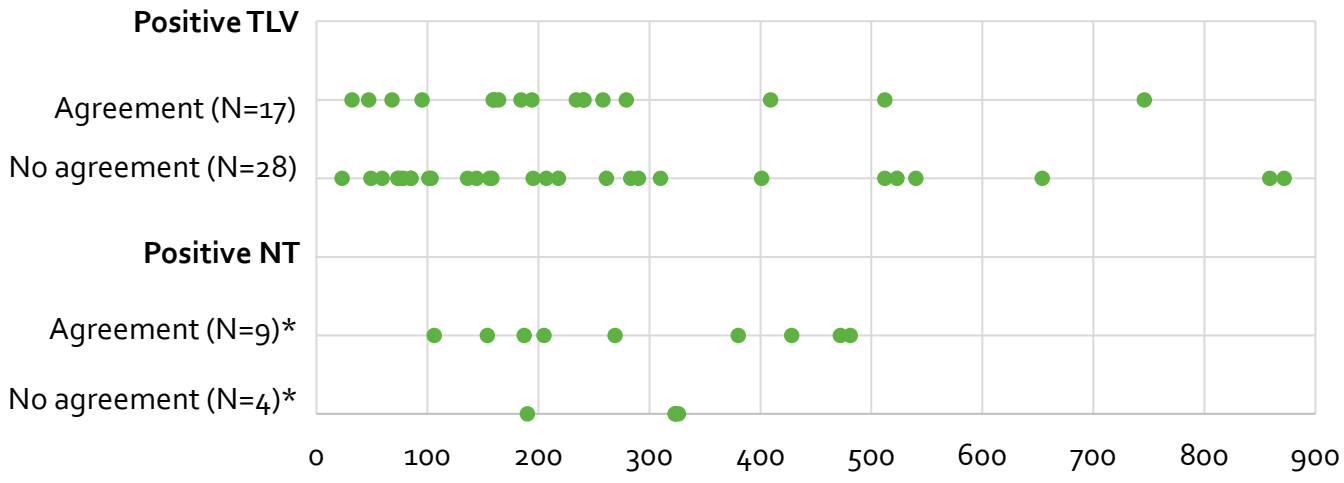
TTM by TLV decision or NT recommendation and national price agreement status

- Estimated average TTM:
  - Medicines with positive TLV decision: 255 days
    - Agreement: 237 days (min 32 – max 746)
    - No agreement: 266 days (min 23 – max 872)
  - Medicines with positive NT recommendation: 296 days
    - Agreement: 298 days (min 106 – max 481)
    - No agreement: 291 days (min 190 – max 326)

- New medicines decided upon by TLV that had national price agreements on average had a somewhat shorter TTM than those without an agreement

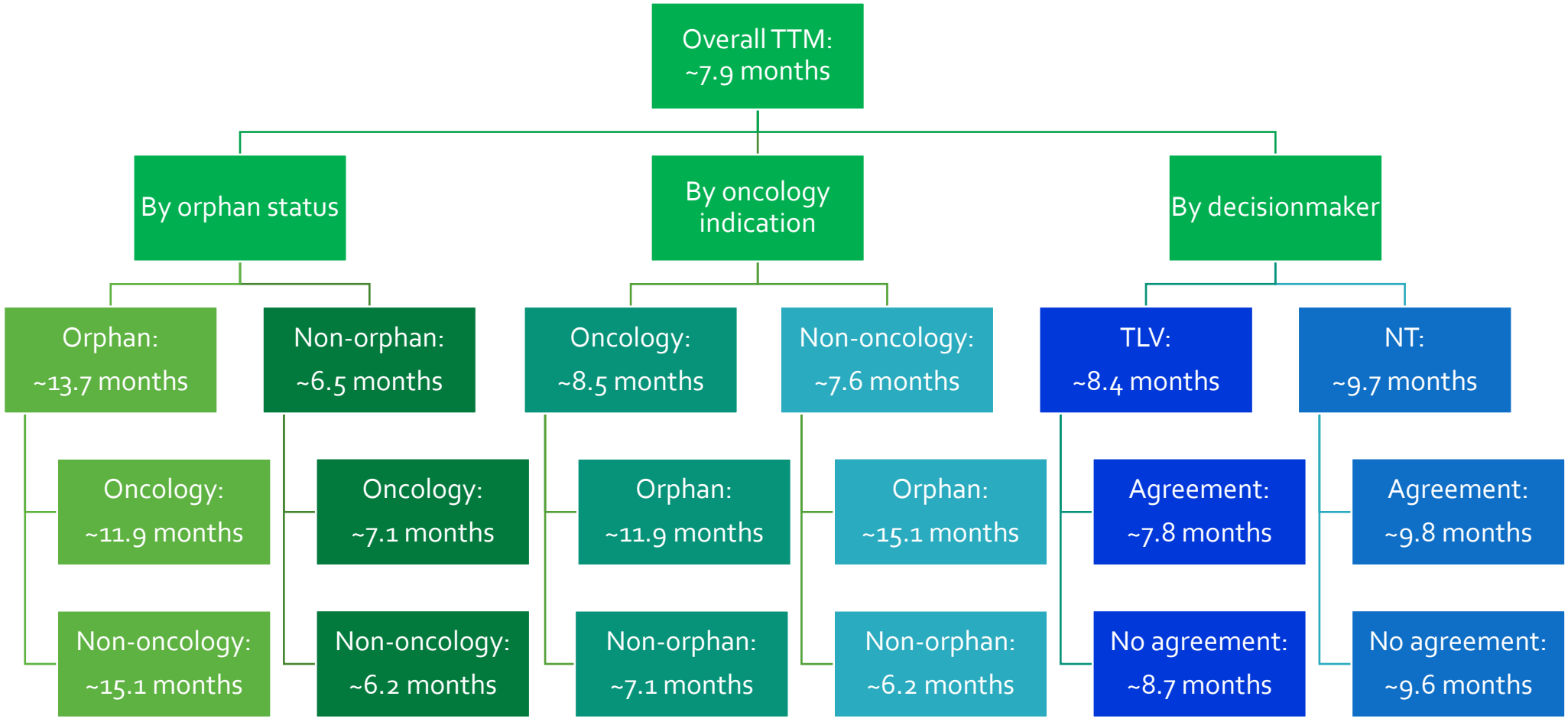
TTM in days	Positive TLV		Positive NT	
	Agreement N=17	No agreement N=28	Agreement N=9*	No agreement N=4*
Average	237	266	298	291
25th percentile	159	85	187	290
Median	194	177	269	323
75th percentile	258	333	428	324
Percentage with TTM >365 days	18%	25%	44%	0%

TTM in days for individual medicines, by decisionmaker and agreement status



* Note: relatively small sample

Time to market of new medicines approved in 2017-2019



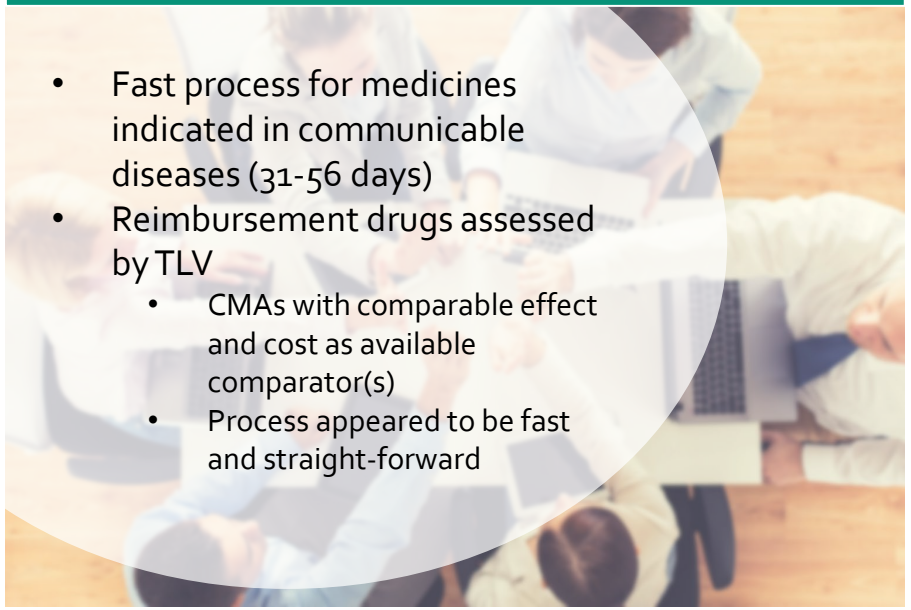
Deep-dive into the 10 new medicines with the shortest TTM

- The ten new medicines with the shortest TTM were assessed
  - TTM: 23-59 days

- 5 medicines were indicated in communicable diseases
  - TTM: 31-56 days
  - A reimbursement decision was not needed to be classified as available
    - 3 still had positive reimbursement decisions
  - In line with expectations; new medicines not requiring a national health technology assessment (HTA) assessments were introduced relatively quickly

- The 5 other medicines were all reimbursed by TLV:
  - TTM: 23-59 days
  - All were non-orphan drugs
  - 1 oncology drug, 4 non-oncology drugs
  - All had a similar effect at same or lower price in relation to comparators (according to cost minimisation analyses [CMA])
    - 2 had tripartite agreements

Top 10 shortest time:
23-59 days

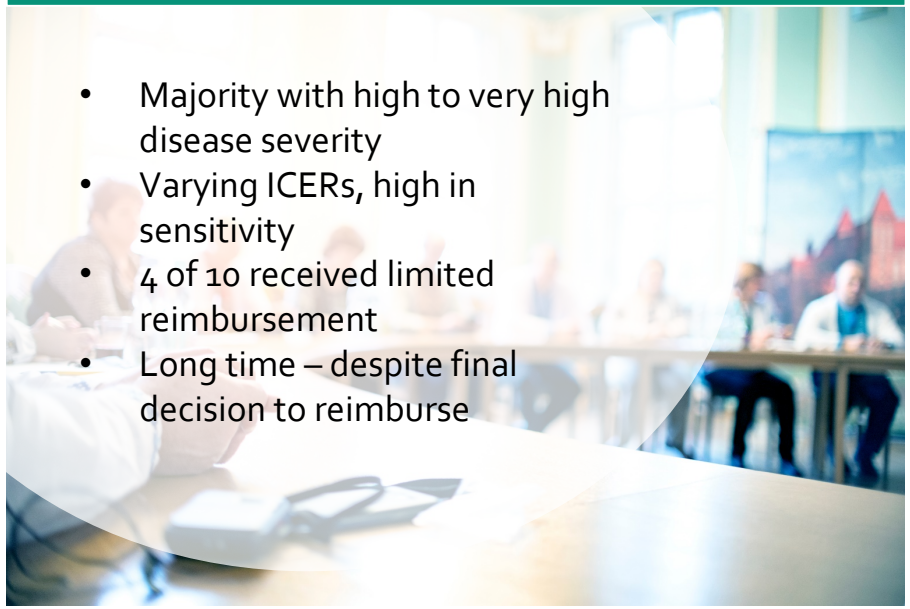


- Fast process for medicines indicated in communicable diseases (31-56 days)
- Reimbursement drugs assessed by TLV
  - CMAs with comparable effect and cost as available comparator(s)
  - Process appeared to be fast and straight-forward

Deep-dive into the 10 new medicines with the longest TTM

- The ten new medicines with the longest TTM, 472-872 days, were assessed
  - 1 had a conditional approval from EMA
  - 2 were orphan drugs and 8 were non-orphan drugs
  - 2 received positive NT recommendations and 8 were reimbursed by TLV
  - Disease severity was classified as high for 7 of the medicines and medium, low or varying for 3
  - Cost utility analyses (CUAs) were used in 7 applications, indicating differences in effect and price existed in relation to comparators
    - Incremental cost-effectiveness ratios (ICERs) were reported by TLV in all applications, and ranged between:
      - Base case: 142 000 - 4 900 000 SEK
      - Sensitivity analysis: 196 000 - 12 000 000 SEK
  - CMAs were used in 3 applications, showing similar effect offered at the same or lower price in relation to comparators
  - 4 received limited reimbursement in Sweden
  - 2 had national price agreements

Top 10 longest time:
472 – 872 days

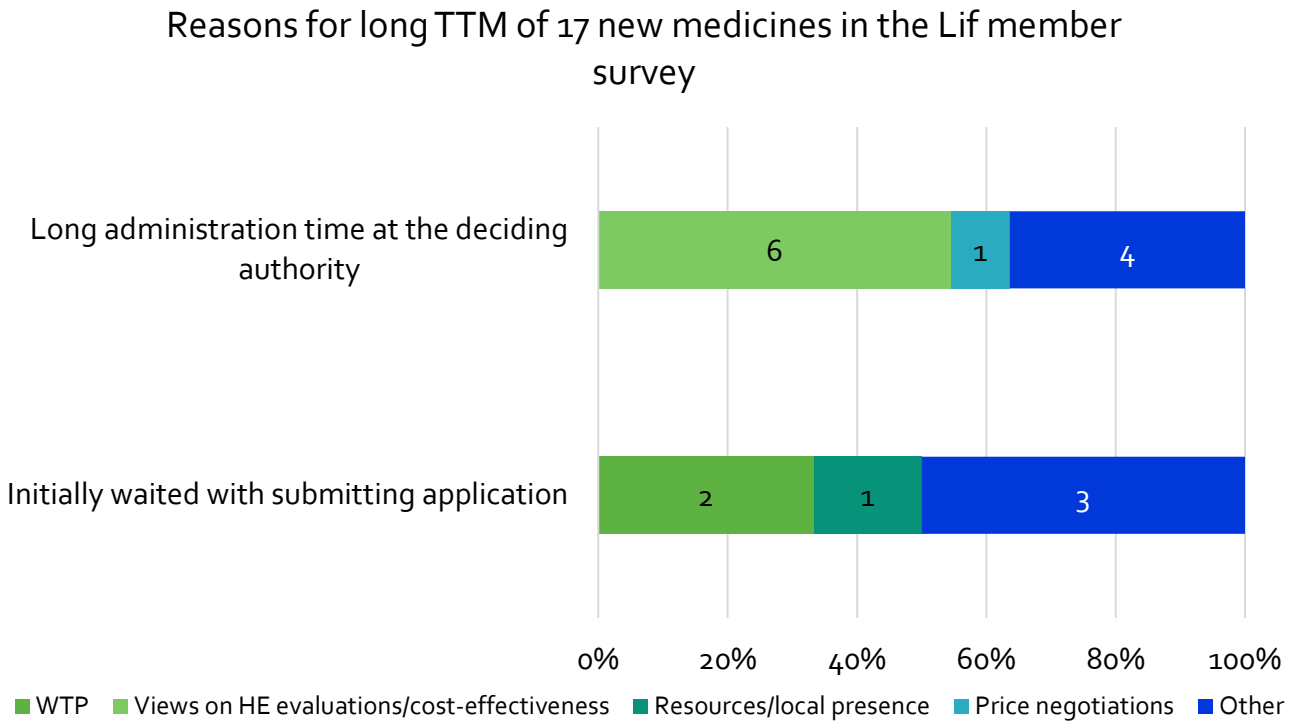


Factors affecting delayed availability

- Similar to non-availability, an in-depth analysis was conducted to understand the underlying reasons for delayed availability, defined as TTM exceeding 270 days (TLV's statutory processing time + 90 days of additional time for complements within the application)
  - MAHs that were members of Lif were asked to provide insights into the factors affecting delayed TTM
  - Answers were submitted for 17 medicines (3 orphan)

- MAHs of 11 (65%) medicines experienced long administration times
  - 6 due to differing views on health economic (HE) data, evaluations or cost-effectiveness
  - 1 due to long-spun price negotiations
  - 4 due to other reasons

- MAHs of 6 (35%) medicines initially waited with submitting the application
  - 2 due to a too low WTP
  - 1 due to a lack of resources or local presence
  - 3 due to other reasons
  - No members reported the patient population being too small



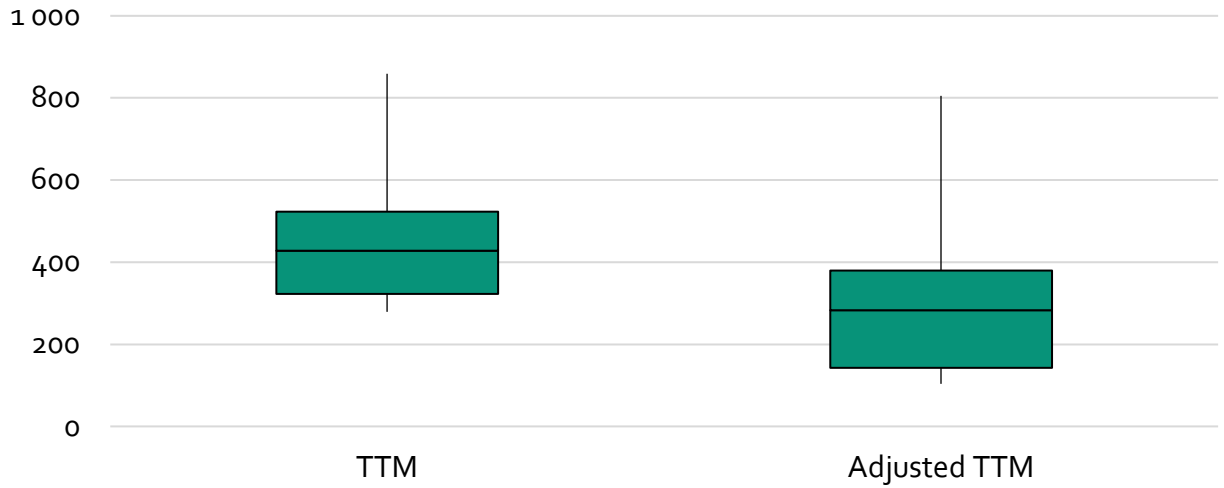
Adjusted TTM based on Lif survey

- The answers in the Lif member survey were used to calculate a normal TTM, based on date of EMA approval and an adjusted TTM, based on reimbursement submission date, for the 17 new medicines

- Accounting for delays in submission by MAHs
  - The average TTM was 308 days (min 104 – max 805) instead of 462 days (min 279 – max 859)
  - 53% and 29% of new medicines had a TTM of >270 and >365 days instead of 100% and 65%, respectively

TTM in days	Normal N=17	Adjusted N=17
Average	462	308
25th percentile	323	143
Median	428	283
75th percentile	532	380
Percentage with TTM >270 (>365) days	100% (65%)	53% (29%)

Time to market and adjusted time to market of medicines in the Lif member survey

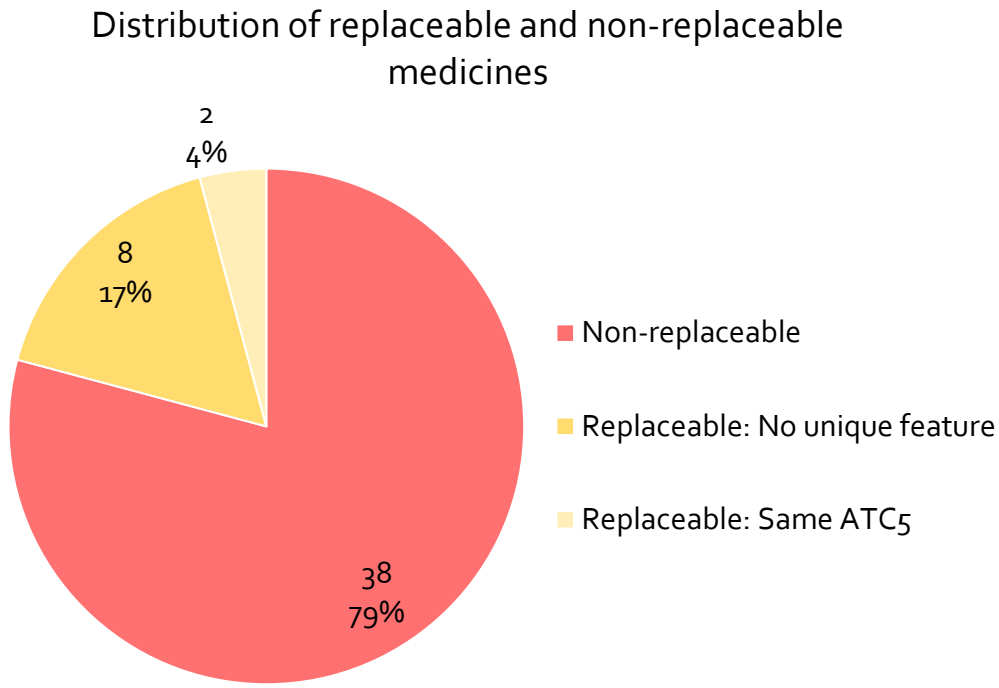


* The graph presents the minimum, 25th percentile, median, 75th percentile and maximum number of days.

Assessment of replaceability of non-available medicines

Assessment of replaceability of non-available new medicines

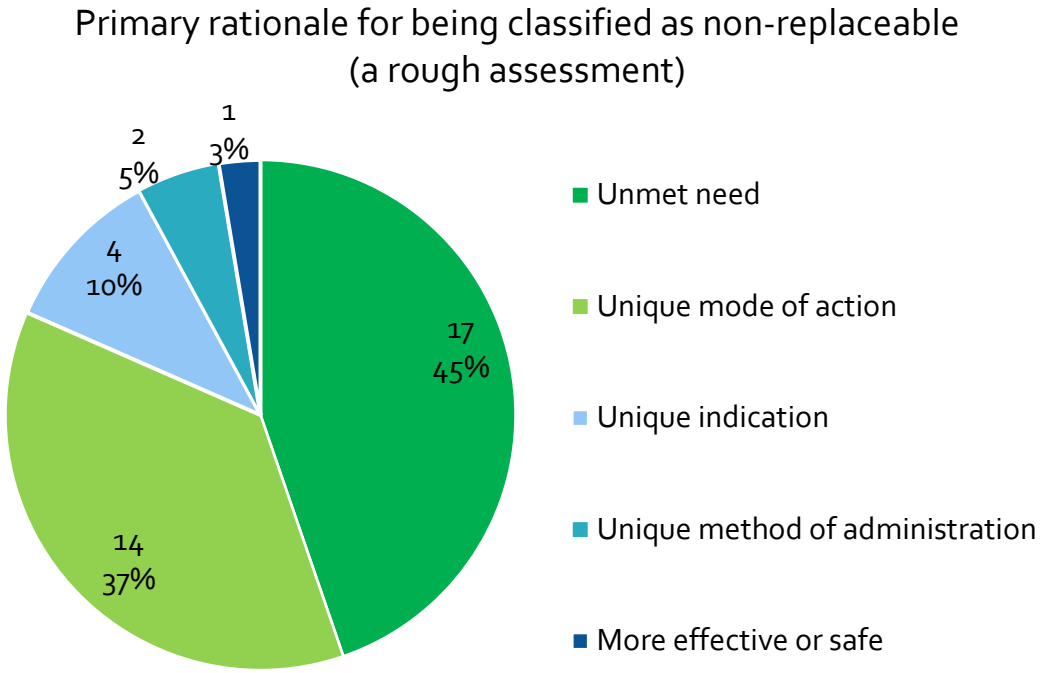
- Non-availability may not have a negative impact on patients if similar replacement options are available
  - A pragmatic effort was made to identify new medicines with no evident unique feature associated with added value for patients, based on the five parameters of uniqueness assessed
- Of the 48 non-available medicines
  - 38 (79%) were classified as non-replaceable
  - 10 (21%) were classified as replaceable
- The primary rationale for classifying medicines as replaceable was:
  - Another medicine with the same anatomical therapeutic chemical (ATC-5) code was available for a similar indication in 2 cases
  - No evident unique feature believed to provide relevant added value to patients relative to comparators was identified in 8 cases



Reasons for non-replaceability

- 38 (79%) of non-available new medicines were assessed to be non-replaceable
  - A majority (N=22, 58%) of these were not supplied in Sweden

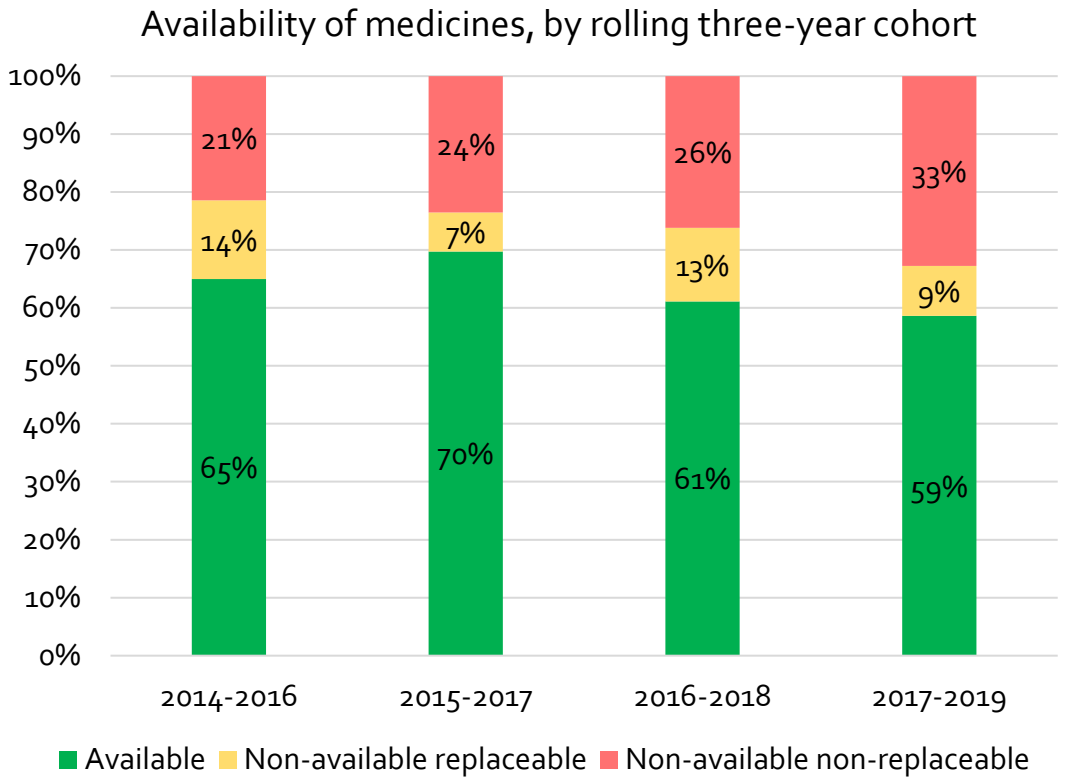
- The primary reason for non-replaceability was (medicines may have multiple ones):
  - 17 (45%) based primarily on information supporting an unmet medical need and limited other treatment options
  - 14 (37%) were considered to have a unique mode of action, indicating value for example for certain subgroups of patients refractory to other options and/or with tolerability problems
  - Additional features included unique indication, mode of administration and improved efficacy or safety



An alternative estimation of availability

- Adding the number of available- and non-available replaceable medicines may be viewed as an alternative estimation of the rate of availability:
  - 59% + 9% = 68% rate of availability in 2017-2019
  - 79%, 77% and 74% rate of availability in 2014-2016, 2015-2017 and 2016-2018, respectively

- Over time, similar to the rate of availability, this alternative rate of availability showed rather constant estimates at ~70-80%



* The figure depicts the new medicines by three-year rolling cohort and availability status, where non-available medicines have been separated based on replaceability. Numbers from previous reports have been used for 2014-2016, 2015-2017 and 2016-2018 (N=140, N=119, N=126 and N=116 for 2014-2016, 2015-2017, 2016-2018 and 2017-2019, respectively)

Characteristics of the 38 non-available non-replaceable new medicines and MAHs

- A majority were indicated in
  - Oncology (N=30, 79%)
  - Orphan diseases (N=22, 58%) and/or
  - Diseases with a high severity (N=19, 50%)
- A significant proportion were indicated in a disease area where existing treatment was symptomatic (N=16, 42%)
- A majority (56%) of the companies were assessed to have limited experience from the Swedish HTA and reimbursement system
  - The remaining MAHs had received reimbursement for at least one other medicine previously

Non-available non-replaceable new medicines*	N=38	%
Drug characteristics		
Oncology medication	30	79%
Hospital drug	16	42%
Orphan drug	22	58%
Non-oncology and orphan	19	50%
Disease severity and treatment options		
High disease severity	19	50%
Existing treatment is symptomatic	16	42%
MAH characteristics	**N=32**	**%**
MAHs with local presence	13	41%
MAH's experience with the Swedish reimbursement system		
0 reimbursed medicines	18**	56%
1-9 medicines	8	25%
10-19 medicines	1	3%
20+ medicines	5	16%

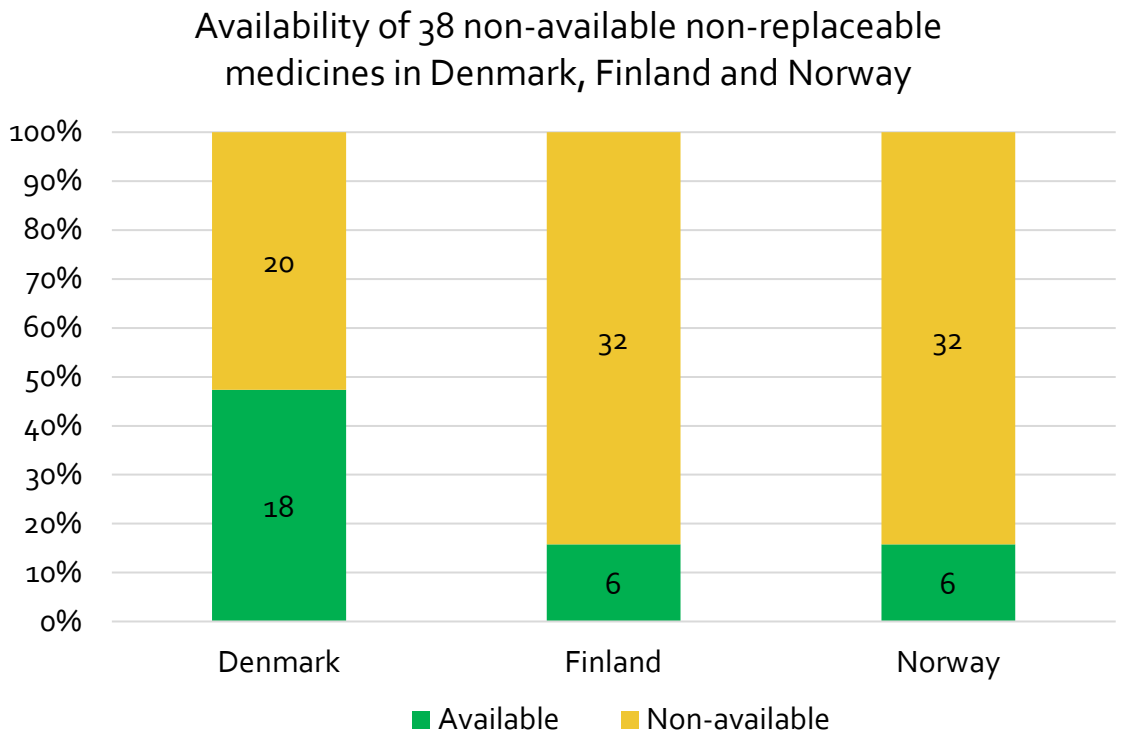
* A medicine may have several of these characteristics, meaning that the numbers will not sum to 100%
** Includes 18 of 19 MAHs with no local presence in Sweden

Comparison with three Nordic countries

Non-available non-replaceable medicines in three Nordic countries

- The 38 medicines that were non-available non-replaceable in Sweden, were available in Denmark, Finland and Norway to the following extent:
  - Denmark: 18 (47%)
  - Finland: 6 (16%)
  - Norway: 6 (16%)

- 17 (45%) were non-available and 2 (5%) were available in all three countries



Characteristics of the non-available non-replaceable medicines that were available in Denmark

- Reason for not being available in Sweden
  - 7 (39%) were not registered as supplied in FASS
  - 4 (22%) received a negative NT recommendation / TLV decision
  - 7 (39%) lacked decisions
- 10 MAHs had at least some experience with the Swedish reimbursement system and had one or more reimbursed medicine(s) listed at TLV
- 8 MAHs were locally present in Sweden
- A large share of medicines had high disease severity and/or orphan designation status

Non-available non-replaceable new medicines available in Denmark – descriptive information*	N=18	%
Drug characteristics		
Oncology medication	2	11%
Hospital drug	8	44%
Orphan drug	12	67%
Non-oncology and orphan	11	61%
Disease severity and treatment options		
High disease severity	11	61%
Existing treatment is symptomatic	7	39%
MAH characteristics	**N=16**	**%**
MAHs with local presence	8	50%
MAH experience with the Swedish reimbursement system		
0 reimbursed medicines	6	38%
1-9 medicines	5	31%
10-19 medicines	1	6%
20+ medicines	4	25%

* A medicine may have several of these characteristics, meaning that the numbers will not sum to 100%

Discussion and conclusion

Discussion – Rate of availability in Sweden

- A majority of new medicines (68; 59%) with EMA approval in 2017-2019 were classified as available in Sweden
- Orphan drugs were associated with a lower rate of availability than non-orphan drugs (35% vs. 70%)
  - The lowest rate of availability was seen among non-oncology orphan drugs
  - The lower rate of availability observed among orphan drugs in this study may reflect the difficulties in balancing costs and benefits, and the lack of robust data for assessment
  - Due to small patient populations, the MAHs of orphan drugs often face challenges in conducting randomised clinical trials. The low availability of these medicines might be an indication that the Swedish HTA system is not designed to optimally handle submissions lacking robust evidence from clinical trials
- Over time across the three-year rolling cohorts in the period 2014-2019, the rate of availability has been rather constant at ~60-70%, this entire period was subject to the new way of working with agreements and the NT-council
- Among 14 non-available new medicines marketed by Lif members, the most common reasons for non-availability were having an ongoing or withdrawn application or the WTP in Sweden being too low
- The analysis of sales data showed that a majority of available new medicines seemed to reach patients. This indicates that a positive NT recommendation or TLV decision enables, but does not guarantee actual access to patients
  - Some medicines not classified as available were privately available, however, sales of these medicines were limited

Discussion – Time to market in Sweden

- Among the available medicines, the overall TTM was estimated to 7.9 months
  - Like in previous reports, a positive trend towards shorter TTM was observed, in combination with a lower percentage of new medicines having a TTM exceeding one year
  - Over time, the variance in days to market has decreased but remains large, ranging from 23 to 872 days
- The ten medicines with the shortest TTM were available within 1-2 months
  - This includes primarily medicines indicated in communicable diseases or which had received positive TLV decisions based on a CMA (comparable effect at the same or lower price as available comparators), indicating a quick and easy process
- The ten medicines with the longest TTM were available within 514-872 days (1.4-2.4 years)
  - A majority (70%) of the medicines were indicated in a disease area with high disease severity
  - CUAs were used in most TLV applications, showing rather sensitive ICERs leaving room for TLV to challenge the medicines' cost-effectiveness
- Non-orphan drugs were on average associated with a shorter TTM than orphan drugs (197 vs. 416 days), while no big differences were seen based on oncology indication
  - Orphan non-oncology medicines had the longest TTM, and non-orphan non-oncology medicines had the shortest TTM
  - This might be due to several factors, among others that the NT council have to wait for TLV to conduct a HE evaluation
- Decisions made by TLV were associated with ~1 month shorter TTM than recommendations made by the NT council
  - Medicines reimbursed by TLV with a national price agreement on average had a shorter TTM of ~1.7 months compared to those without
- Among the 17 new medicines in the Lif member survey with TTM >270 days, a majority experienced long administration times due to different views on HE data, evaluations or cost-effectiveness or other reasons (most notably, slow requests for evaluations from the NT council). Meanwhile, some MAHs waited with submitting their reimbursement applications, mainly due to other reasons such as awaiting material (data/models) for the submission
  - An adjusted TTM was calculated, indicating that the average TTM among these medicines was 308 days rather than 462 days and that 53% of these medicines had a TTM >270 days

Discussion – Non-replaceable medicines

- Overall, 38 new medicines were classified as non-available non-replaceable. Of these, 22 (58%) were not supplied in Sweden
- All included medicines in the present study were believed to add value to patients by EMA (determined as effective and safe, and granted MA)
- In this study, an additional threshold to differentiate the added value of medicines based on their unique features in comparison to other existing treatment options was employed
  - The level of uniqueness and the potential value added to Swedish patients by non-available non-replaceable new medicines varied among the medicines. Some medicines were indicated in disease areas where no treatment alternatives existed while others contributed with smaller improvements
  - 10 (21%) medicines were classified as replaceable (at least one medicine with the same ATC5 code was available or no unique feature was identified)
  - 38 (79%) medicines were classified as non-replaceable, and their non-availability might have negative consequences for Swedish patients. An in-depth assessment of these drugs and the intended population would be valuable to better understand the patient value foregone for not having access to these drugs
- An alternative approach to calculating the rate of availability, adding non-available replaceable medicines to the available medicines, shows that the alternative rate of availability has been rather constant at ~70-80% across the four three-year rolling cohorts during the period 2014-2019
- Many of the non-available non-replaceable new medicines were oncology medications, orphan drugs and/or indicated in diseases with high severity
- The comparative analysis of non-available non-replaceable medicines with the three other Nordic countries showed that a sizeable share (N=18; 47%) of the non-available non-replaceable medicines were available in Denmark. Finland and Norway had a bigger overlap with Sweden: only 6 (16%) were available in both Finland and Norway

Discussion – Limitations

- Limitations of assessing products rather than indications approved
  - This study did not consider that a medicine may have several indications. The present study did not take into account conditional reimbursements/recommendations limiting use to sub-set of approved indications. As such, availability might be limited although the medicine is classified as available

- The analysis of availability is conducted based on outcomes from national HTA processes rather than actual uptake. Access might be limited by factors such as regional recommendations/lists, guidelines, local conditions for diagnosis, physicians' prescribing habits and other factors. As such, the definition of availability in the present study may overestimate the actual perceived rate of access for patients. The present study attempted to control for this by analysing sales data

- This study primarily used publicly available information. In an attempt to assess what underlying factors affected availability and TTM, the study was complemented with answers from a survey sent to Lif members
  - Among 42 medicines not being supplied in Sweden or lacking a decision from the decisionmakers, 16 had MAHs that were Lif members and answers were submitted for 14
    - Of the remaining 26 medicines, 21 had MAHs that were not locally present in Sweden and lacked experience of the Swedish reimbursement system
    - As a sizeable proportion of MAHs in the non-availability survey were not members of Lif, had local presence or experience from the HTA system, we may still be missing underlying factors such as perceived complexity of the HTA processes deterring entry, or lack of interest in the Swedish market
  - Among 21 medicines having a long TTM (>270 days), 17 had MAHs that were Lif members and answers were submitted for all 17

- Access to new medicines is a joint effort by MAHs and decisionmakers. This study did not analyse areas of improvement or evaluate what a reasonable level of availability may be. The aim of this study was to document the situation at the study cut-off date, hightlight gaps and enable informed discussions on both sides on how to continously improve patients' access to medicines in Sweden

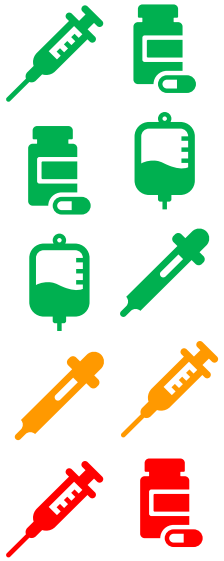
Conclusions

- 6 of 10 new medicines authorised by EMA in 2017-2019 were available in Sweden
  - A vast majority seemed to reach Swedish patients
  - Availability was generally lower for orphan drugs

- The TTM was on average 7.9 months
  - Yet generally longer for orphan drugs, especially for orphan non-oncology drugs
  - A relative improvement in TTM of new medicines was observed compared to earlier reports; however, there is still large variation with access times exceeding 2 years
    - More efficient processes are needed to minimise adverse consequences to Swedish patients due to slow or lacking access to new medicines, in particular for medicines indicated for the treatment of orphan diseases and diseases with high severity where treatment options are limited
  - The Lif member survey showed that TTM can improve as a result of joint efforts by MAHs and decisionmakers, i.e., MAHs can prepare documentation to apply at the date of EMA approval and the NT council can request HE evaluations from TLV sooner rather than later

- 4 of 10 new medicines were non-available in Sweden
  - A majority were not supplied in Sweden
  - From a company perspective among Lif members marketing medicines that were not supplied or had not received a decision/recommendation, the main reason underlying non-availability was awaiting a decision or a recommendation, followed by having withdrawn their application and experiencing a too low WTP from decisionmakers
  - 2 of 10 were assessed to be replaceable
  - 8 of 10 were assessed to be non-replaceable (no reasonably similar replacement option exists), assessed to be associated with an added value for patients
  - Almost half of the non-replaceable non-available medicines were available in Denmark

- These findings raise the question of Sweden's attractiveness as an early launch country for new medicines, in particular for orphan drugs, and whether quicker and less complex reimbursement processes and/or lower price pressure could attract more MAHs, e.g., those lacking knowledge of the Swedish reimbursement system, to improve patients' access to new medicines in Sweden



Abbreviations

Abbreviation	Abbreviated term	Abbreviation	Abbreviated term
ATC	Anatomical Therapeutic Chemical classification system	**Lif**	The research-based pharmaceutical industry
CMA	Cost-minimisation analysis	**MA**	Marketing authorisation
CUA	Cost-utility analysis	**MAH**	Marketing authorisation holder
EFPIA	European Federation of Pharmaceutical Industries and Associations	**NT**	New Therapies council
EMA	European Medicines Agency	**SPC**	Summary of product characteristics
EPAR	European public assessment report	**TLV**	The Dental and Pharmaceutical Benefits Agency
HE	Health economic	**TTM**	Time to market
HTA	Health technology assessment	**W.A.I.T**	Patients Waiting to Access Innovative Therapies
ICER	Incremental cost-effectiveness ratio	**WTP**	Willingness to pay

Appendix

Definitions

Feature	Description
Definition of hospital drugs	A medicine was classified as a hospital drug if: • There existed a public NT case for it, and/or • The medicine was administrated IV (without possibility to self-inject at home), and/or • The summary of product characteristics (SPC) stated that clinical staff was required for administration. Medicines that did not fulfill this definition were classified as non-hospital drugs
Definition of availability	A medicine was classified as available if it was supplied in Sweden (listed as supplied in FASS), and per 22 December 2020, either had received: • A positive TLV reimbursement decision (non-hospital drug), or • A positive NT recommendation (hospital drug), or • Lacked an NT recommendation but was assessed to have a relevant level of sales based on a rough estimation of number of patients treated in relation to the size of the patient population (hospital drug), or • Was indicated in the treatment of a communicable disease (i.e., a reimbursement decision/NT recommendation was not required) Medicines that did not fulfill this definition were classified as non-available.
Definition of private availability	A medicine was privately available if it was supplied in Sweden (listed as supplied in FASS), and per 22 December 2020 was available for purchase at www.apoteket.se. This does not necessarily mean that the patient paid for the medicine privately.

Definition of TTM	TTM was calculated, for available medicines, as the number of days between the EMA approval date and the date of patient access in Sweden, where the date of patient access in Sweden was defined as either:
	• The date of positive TLV reimbursement decision (non-hospital drug), or
	• The date of positive NT recommendation (hospital drug), or
	• Day 15 of the month of first-ever sales in Sweden if the medicine:
	  • Lacked NT recommendation but had a relevant level of sales (hospital drug), or
	  • Was indicated in a communicable disease
	If a medicine had more than one date of patient access, the first date was chosen.

Methods, selected clarifications

Feature	Description
Study cut-off date	22 December 2020
Sample size	In total, the EFPIA W.A.I.T survey included 238 new medicines approved for authorisation in the EU by EMA in 2014-2019. One medicine, authorized in 2016, was excluded as it was only administered in an Italian hospital. An additional medicine, authorised in 2018, was excluded due to a withdrawn NA. This resulted in a sample size of 236 new medicines for the period 2014-2019 and 116 new medicines for the period 2017-2019.
Comparability with previous studies	The same definition of availability was used in this study as in the previous study (2016-2018), however: • As the inclusion/exclusion criteria were updated by EFPIA in the 2019 W.A.I.T. Indicator cohort compared to the 2017 and 2018 cohorts, the possibility to compare the results over time is somewhat limited • The 2014-2016 study had a different cut-off date (May 2018) compared to the thre more recent studies (5 December 2018, 9 December 2019 and 22 December 2020 for the 2015-2017, 2016-2018 and 2017-2019 studies, respectively) • The two first studies (2014-2016; 2015-2017) included vaccines in the analysis set; in the present study (2017-2019), as well as the 2016-2018 study, vaccines were excluded

Analyses of sales	Sales data, on the national level, for the first eleven months of 2020, were used as a proxy to evaluate 'actual access to patients' to the new medicines that were classified as available and privately available, respectively
	• If sales was unknown, sales were assumed to be zero
	• Actual access was evaluated using four sales criteria:
	  • Any sales at all, representing the lowest threshold
	  • 5 packages/month to represent a fair proxy for availability not only limited to a single care episode or single region practice
	  • 21 and 105 packages/month, respectively, were applied to illustrate a higher level of distribution of – and access to – the medicine (somewhat arbitrarily chosen to correspond to the number of Regions in Sweden)

Agreement analysis	An in-depth analysis was conducted to evaluate if TTM differed depending on whether the medicine was subject to a national price agreement between the marketing authorisation holders (MAH) and regions. Information regarding national price agreements was extracted from: • www.janusinfo.se; Quantify also e-mailed Sveriges kommuner och regioner (SKR) and received a confirmation that no agreement for medicines approved in the period 2017-2019 had expired • TLV's reports entitled 'Prognos av besparingar från sidoöverenskommelser' regarding prognoses of savings from tripartite agreements published in 2017-2019

Methods, selected clarifications

Feature	Description
Agreement analysis	An in-depth analysis was conducted to evaluate if TTM differed depending on whether the medicine was subject to a national price agreement between the marketing authorisation holders (MAH) and regions. Information regarding national price agreements was extracted from: • www.janusinfo.se; Quantify also e-mailed Sveriges kommuner och regioner (SKR) and received a confirmation that no agreement for medicines approved in the period 2017-2019 had expired • TLV's reports entitled 'Prognos av besparingar från sidoöverenskommelser' regarding prognoses of savings from tripartite agreements published in 2017-2019
Lif member survey	A survey was sent to MAHs that had at least one medicine that was non-available (due to not being supplied or not having a TLV decision/NT recommendation) or had a long TTM (>270 days, i.e., TLV's statutory 180 days + 90 days of additional time for complements within the application) and who were members of Lif in order to understand factors underlying non-availability and long TTM. MAHs with non-available medicines were asked to choose between the main factor being: ❑ We do not have the resources (or presence) to launch the product in Sweden ❑ The willingness to pay is too low in Sweden ❑ There are too few patients in Sweden needing the product ❑ We have at one or more points in time withdrawn the reimbursement application ❑ We have an ongoing reimbursement application/hospital drug evaluation ❑ Other, please specify: _____ MAHs with medicines with long TTM were asked to choose between the main factor being: **Long processing time at the deciding decisionmaker, due to:** ❑ Different views on health economic data/assessments or cost-effectiveness ❑ Long-spun tripartite negotiations ❑ Other, please specify: _____ ***or*** **We initially waited with applying for reimbursement after the EMA approval, due to:** ❑ We initially lacked resources (or presence) to launch the product in Sweden ❑ The willingness to pay was too low in Sweden ❑ There were initially too few patients needing the product ❑ Other, please specify: _____ **MAHs with medicines with long TTM were also asked for an application date (year, month, day if possible). Imprecise answers, such as "July 2019" were set to the middle of the period, i.e., 2019-07-15. These answers were used to calculate an adjusted TTM, defined as the number of days between EMA approval and application date**

Methods, selected clarifications

Feature	Description
A pragmatic effort to assess replaceability	Publicly available documentation of the non-available medicines was analysed to identify unique features (limited treatment options/unmet medical need, indication, mode of action, route of administration, and efficacy) believed to provide relevant added patient value. The most distinctive feature was highlighted as primary (pragmatically assessed), although some medicines may have additional unique features. The public sources of information used were: FASS, EMA's European public assessment report (EPAR) summary for the public and/or SPC, TLV and NT reports (if available), Swedish clinical guidelines and other public sources of information (if relevant). Off-label use of medicines in the assessment of replaceability was not considered. A medicine was considered replaceable if: • At least one other medicine with same active substance (ATC-5 level) was considered available according to the above mentioned criteria, or • No unique feature could be found compared to other medicines that were already considered available with the same indication All other medicines were classified as non-replaceable.

Descriptive statistics of non-available non-replaceable medicines	Non-available non-replaceable medicines were described according to the following parameters:
	• Drug characteristics
	• Level of severity of disease (assessed by Quantify, without consultation of clinical experts), based on:
	  • The level of severity reported by NT or TLV in public reports/documents
	  • The level reported or indicated by EMA's EPAR assessment
	  • Estimated as high for all oncology products
	  • Reported as N/A if disease severity varied
	• Whether existing treatment options were symptomatic, elicited from public sources of information
	• Number of unique MAHs, and local presence in Sweden
	  • Local presence was assessed in FASS. If FASS indicates no local presence in Sweden; further assessed by examining if MAH was registered on a Swedish address
	• MAH experience with the Swedish reimbursement system
	  • Experience was measured as the number of medicines included in the Swedish reimbursement scheme at the analysis cut-off date

Comparison with three Nordic countries	The data used for the comparison with the three Nordic countries was elicited from the individual country's W.A.I.T. tabulation file reported into the new European 2020 Patients W.A.I.T. Indicator, collected and assessed by the respective countries' branch organisations (independently from Quantify) • Definitions of availability differs somewhat across the countries, meaning that the comparison should only be seen as an indication of difference in availability and should be interpreted with caution

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