Access to new medicines in Sweden

A review of patients' access to new medicines approved by EMA in 2014-2016 and the share of replaceability among non-available medicines

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Preface

- Each year, EFPIA presents its Patients W.A.I.T. Indicator analysis[1] of the rate of availability of new medicines (i.e. with a substance previously not available in the EU) that received EMA approval in a rolling 3-year cohort in 26 Europan countries.

- This report was commissioned by LIF, De Forskande Läkemedelsföretagen, in an effort to understand and further develop the findings of the Patients W.A.I.T Indicator analysis that are applicable to the Swedish setting.

- This report uses the 2017 Patients W.A.I.T. Indicator results as the starting point, and assesses the rate of availability of the 146 new medicines (i.e. available, non-available or unknown [N/A]) in Sweden up until May 1st, 2018.

- This report begins by outlining the background to – and objectives of – the analysis, followed by a presentation of the definitions of availability used and the resulting rate of availability of medicines and time to market in Sweden. The remainder of the report focuses on the non-available medicines. Specifically, the reasons for non-availability, and whether replacement options are available. Lastly, it provides summary information relating to the non-available non-replaceable medicines, and an assessment of which of these are available in Denmark, Finland, and Norway. All results are reported on an aggregated level.

- Input from County Council representatives in Stockholm and Skåne, based on a presentation - and discussion - of interim results are incorporated into the analysis. Other than this, no clinical experts have been consulted in this project.

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[1] Machin, Claire (2018). *EFPIA Market Access Delays Analysis*, Date: 14/03/2018, Version: Final

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Background

- EFPIA's Patients W.A.I.T. Indicator for new medicines (i.e. substance that has not been previously available in Europe) within a 3 year cohort, estimates for 26 European countries:

    1. The rate of availability, measured by the number of medicines available to patients in each country *(for most this is the point at which the product gains access to the reimbursement list)* compared to the total number of approved new medicines

    2. The average time to market for available medicines from marketing authorization to patient access

- The 2017 Patients W.A.I.T. Indicator analysis, based on a sample of 146 products approved by EMA between January 2014 to December 2016 – (46 in 2014, 53 in 2015, 47 in 2016), provides a snapshot of the rate of availability and time to market at the December 2017 cut-off date.

- The results indicate that 55% of the included products are available to Swedish patients (while 34% are non-available, and 11% are unknown*), on average 281 days after market authorisation.

- Due to a high level of medicines categorised as unknown in Sweden, and an interest in further understanding which medicines are non-available, LIF initiated a project to deep-dive into the results.

* The main reason for the relativley large proportion of unknown medicines is that these are hospital drugs without a NT recommendation.

Objectives

- Perform a more detailed review of the Swedish W.A.I.T. Indicator 2017 results:

1. Review and update the SWE W.A.I.T. Indicator 2017 Excel file:
   i. Update availability status of available and non-available medicines if necessary
      - Using later cut-off date (1 May 2018)
      - Taking into account the specificities of vaccines and medicines indicated in communicable diseases
   ii. Assign an availability status to medicines classified as unknown
   iii. Calculate rate of availability and time to market, according to alternative definitions

2. Deep-dive into medicines that are classified as non-available:
   i. Evaluate whether one or more replacements exist and are available in Sweden
   ii. Present summary information for non-available non-replaceable medicines
   iii. Comparison with Denmark, Finland, and Norway

Rate of availability in Sweden

- Definitions
- Results

Definition of availability – Definition 1 (similar to EFPIA's European Patients W.A.I.T. Indicator definition)

- The medicines approved by EMA are classified as **available if** they are currently marketed in Sweden (primarily assessed through **FASS*), and**
  1. Have received a positive reimbursement decision / recommendation, i.e. if there is, per 1 May 2018:
     i. a positive TLV reimbursement decision (non-hospital drugs), or
     ii. a positive NT recommendation (hospital drugs)

  or

  2. Are indicated in the treatment of a communicable disease (i.e. reimbursement decision/recommendation is not needed to be classified as available)

- Medicines that do not fulfill the above definition are classified as **non-available†**.

* Note. 145 of 146 medicines were identified in FASS, while one was not. This medicine is not marketed in Europe.
† Except for vaccines, which are classified as unknown.

Definition of availability – Definition 2 (adjusted)

- The medicines approved by EMA are classified as **available if** they are currently marketed in Sweden (primarily assessed through **FASS), and**
  1. Have received a positive reimbursement decision / recommendation, i.e. if there is, per 1 May 2018:
     i. a positive TLV reimbursement decision (non-hospital drugs), or
     ii. no negative NT recommendation but medicine has relevant sales* (hospital drugs)

  or

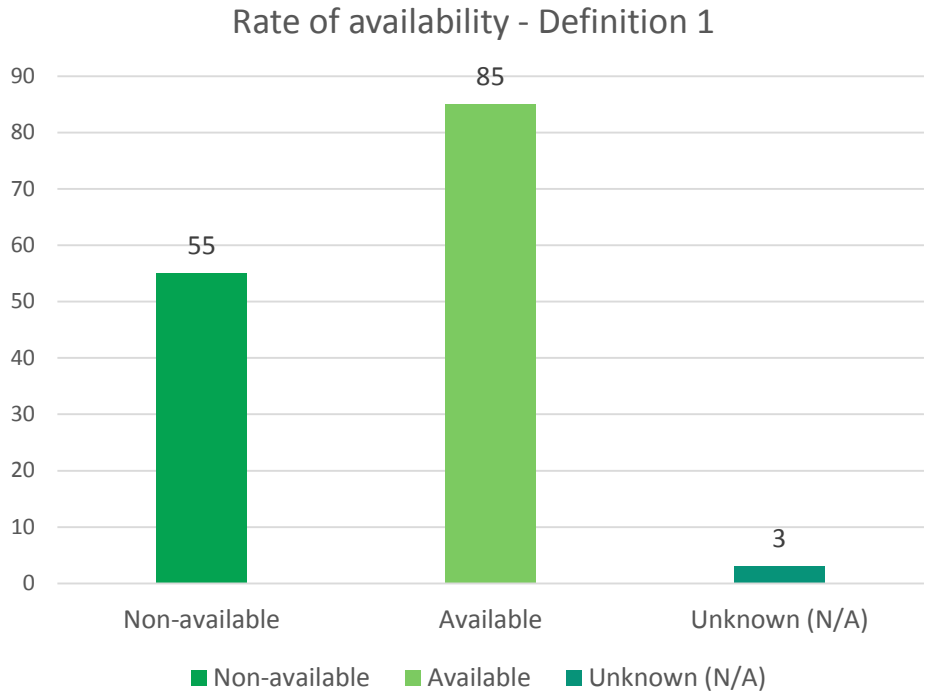
  2. Are indicated in the treatment of a communicable disease (i.e. reimbursement decision/recommendation is not needed to be classified as available)

- Medicines that do not fulfill the above definition are classified as **non-available†**.

* Based on a rough estimation of number of patients treated in relation to the number of patients included in the eligible population (using data on number of packages sold).
† Except for vaccines, which are classified as unknown.

Results, Definition 1: availability of new medicines in Sweden

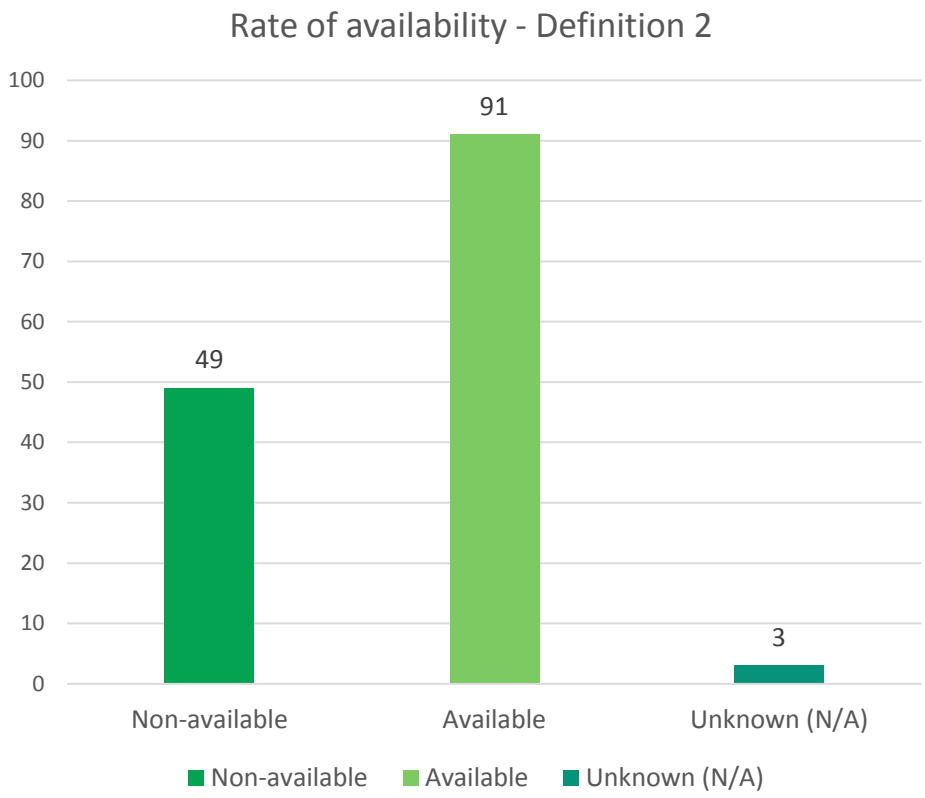
- Definition 1: positive NT or TLV, or communicable disease.
- 146 new medicines received EMA approval in 2014-2016. Of these, three were excluded from the analysis; two have been de-authorized, and one is only possible to administer in Italy.
- Thus, a total of 143 medicines were included in the assessment, of which:
  - 55 were assessed as being non-available
  - 85 were assessed as being available
  - 3 were classified as being unknown (vaccines)
- A total rate of availability of 59% was estimated*
- A rate of non-availability of 38% was estimated



* Please, refer to the Appendix for a complete review of how availbility statuses were assigned to medicines with unknown status, and any updates made to medicines classified as available or non-available in the SWE W.A.I.T. Indicator 2017 analysis.

Results, Adjusted Definition 2: availability of new medicines in Sweden

- Definition 2: positive TLV, non-negative NT and sales, or communicable disease.
- A total of 143 medicines were included in the assessment (and 3 were excluded):
  - 49 were assessed as being non-available
  - 91 were assessed as being available
  - 3 were classified as being unknown (vaccines)
- A total rate of availability of 64% was estimated*
- A rate of non-availability of 34% was estimated



* Please, refer to the Appendix for a complete review of how availbility statuses were assigned to medicines with unknown status, and any updates made to medicines classified as available or non-available in the SWE W.A.I.T. Indicator 2017 analysis.

Results, Average rate of availability – comparison across different definitions/data cuts

- The rate of availability in the SWE W.A.I.T. Indicator 2017 was estimated to 55%.
- Taking into consideration the new data cut (allowing for decisions up until 1 May 2018), reducing the number of unknowns (N/A), and making smaller adjustments, the rate of availability when applying Definition 1 increased somewhat to 59%.
- Including medicines with non-negative NT recommendations and sales as available, according to Definition 2, the rate of availability increased further to 64%.

Classification	SWE W.A.I.T. Indicator 2017 (Cut off date Dec 2017)	Definition 1 (Positive NT or TLV, or communicble disease)	Definition 2 (Positive TLV, non-negative NT and sales, or communicable disease)
Non-available	50	55	49
Available	81	85	91
Unknown (N/A)	15	3 (vaccines)	3 (vaccines)
Excluded	0	3 (de-authorized, Italy)	3 (de-authorized, Italy)
Total included*	146	143	143
Average rate of availability	55%	59%	64%

*Note. The total number of included medicines differs across the three analyses; 3 medicines are excluded in the updated analyses. However, performing of sensitivity analyses shows that excluding or including these medicines have limited impact on the results.

For the 91 available medicines (Definition 2) the majority also seem to reach patients

- Sales data from 2017 and the first four months of 2018, for each of the 91 medicines classified as available, have been used as a proxy to assess whether they are also accessible to patients.

- The share of medicines matching each of the following criteria was estimated:
  - Any sales in 2017 and/or 2018 (at least one package sold)
  - Sales in 2017 ≥ 5 packages/month
  - Projected sales 2018 ≥ 5 packages/month

- The results in the table to the right show that most medicines had at least low levels of sales in 2017 and 2018.

- In 12% of medicines, sales were below 5 packages per month in 2017. An analysis of forecasted sales indicates similar levels in 2018: 13%.

- Although the 5 packages/month-threshold was somewhat arbitrarily chosen, and further analyses could provide additional insights into the availability of those medicines fulfilling Definition 2, these results indicate that a positive TLV/NT decision enables, but does not guarantee actual access to patients. Additional access hurdles, such as regional recommendations/lists and guidelines may exist.

91 available medicines – Sales criteria	N	Share
Non-zero sales in 2017	89	98%
Non-zero sales in 2018	89	98%
Sales in 2017 ≥ 5 packages/month	80	88%
Projected sales in 2018 ≥ 5 packages/month	79	87%

Time to market in Sweden

- Definition
- Results

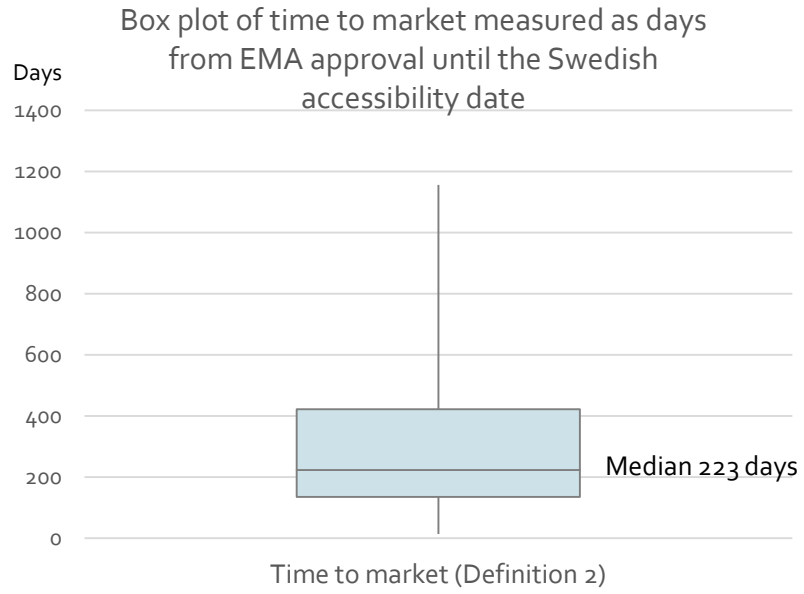
Definition of time to market

- Time to market is calculated, for all available medicines, as the number of days between the market authorisation (MA) date and the Swedish accessibility date, where the accessibility date equals:
  1. The date of positive TLV reimbursement decision (non-hospital drugs), **or**
  2. The date of positive NT recommendation (hospital drugs), **or**
  3. The 15th of the month of the first record of sales if the medicine
     i. Has received no negative NT recommendation and has relevant sales (hospital drugs) or
     ii. Is indicated in a communicable disease

Results, Average time to market – comparison across different definitions/data cuts

- The average time to market in Sweden was estimated to 281 days (~9 months) in the SWE W.A.I.T. Indicator 2017 analysis.
- Re-classifying available medicines according to Definition 1 and 2 leads to a slightly longer time to market (+20 days) as well as a higher share of medicines (~27-28%) with a time to market exceeding one year.
- On average, about 10 months from EMA approval to medicine becoming available to patients was estimated for both definitions*.
- 25% of available medicines were estimated to have a time to market > 422 days, whereas 25% have a time to market of less than 136 days (Definition 2).

Time to market (TTM) in days	SWE W.A.I.T. Indicator 2017 (Cut off date Dec 2017)	Definition 1 (Positive NT or TLV, or communicble disease)	Definition 2 (Positive TLV, non-negative NT and sales, or commmunicable disease)
Average	281	299	297
Minimum	46	14	14
25th percentile	N/A	133	136
Median	216	218	223
75th percentile	N/A	423	422
Maximum	1156	1156	1156
Percentage of medicines with TTM > 365 days	22%	28%	27%



*Note. The time to market analysis does not assess the underlying reasons for the delay, such as e.g. MAH waiting to submit documentation or authority delays. Neither does the analysis take into account whether the indication(s) approved by TLV/NT, making the medicine classified as available, correspond to the indication(s), which the medicine was granted EMA approval for initially.

Deepening the understanding of the medicines with the shortest and the longest time to market

- Considering high variation in time to market and an interest to further understand the characteristics of both fast and slow examples, an analysis of these medicines was made.

- The parameters investigated and summarized include:
  - Setting (hospital drug, non-hospital drug or communicable disease)
    - Potential inclusion in "Nationellt ordnat införande av nya läkemedel" for hospital drugs
  - Orphan status, and potential condititional approval by EMA
  - NT/TLV assessment of severity of the disease (if available)
  - If assessment is based on a CUA or CMA
  - If there is a tripartite agreement between the MA holder, the county councils and TLV
  - Indication made available, as compared to indication originally approved by EMA (for those medicines with the longest time to market)
  - Limited reimbursement / recommendation in Sweden
  - Year of EMA approval

Medicines with the shortest time to market - successful access stories

- 15 medicines with short identified time to market (14 to 79 days) were assessed.

- The top 5 (a time to market between 14 and 30 days) are medicines indicated in communicable diseases, for which reimbursement decision/recommendation is not needed to be classified as available.
  - No additional review of these has been made
  - Supports the "obvious" that medicines not requiring a national HTA assessment are introduced faster

Medicines with the shortest time to market - successful access stories

- The 10 top 6-15 medicines are hospital and non-hospital drugs with a time to market between 46 and 79 days. Of these:
  - **2**/10 are hospital drugs and **8**/10 are reimbursement drugs
  - **2**/10 are orphan diseases
  - **7**/10 are assessed to have a high – very high disease severity, and **3**/10 unknown
  - **5**/10 submitted a CMA, and **5**/10 a CUA:
    - The CUA reported ICERs range between 58 000 and 1 370 000 SEK
    - 60% of ICERs below 500 000 SEK
  - **5**/10 received limited reimbursement / recommendation in Sweden compared to EMA indication(s)
  - **4**/10 have been part of jointly coordinated tripartite agreements, and **1**/10 has been part of a national procurement process under the Swedish Public Procurement Act
  - **4**/10 received EMA approval in 2014, **4**/10 in 2015, and **2**/10 in 2016
- Both hospital drugs were included in the "Nationellt ordnat införande" process
  - Prior work likely done already before EMA approval date
- 8 drugs with positive TLV decisions, of which:
  - 4 are indicated in hepatitis C, all with tripartite agreements in place

Examples of quickly available medicines:

- Medicines indicated in communicable diseases
- Medicines with high disease severity
- Reimbursement drugs assessed by TLV, in an area where other similar drugs have recently been assessed

Deep-dive into the medicines with longest time to market

- 10 medicines were initially included, but one was omitted from the analysis due to lack of further information (only recommended while awaiting a TLV HE assessment; no details provided)

- 9 medicines with a time to market between 670 and 913 days were assessed:
  - **3**/9 are hospital drugs and 6 are reimbursement drugs
  - **1**/9 with conditional approval by EMA (a hospital drug)
  - **3**/9 are orphan drugs (only reimbursement drugs)
  - **6**/9 are assessed to have a high-very high disease severity, and 3 unknown
  - **4**/9 submitted a CMA, **5**/9 a CUA:
    - The CUA reported ICERs range between 760 000 and 2 000 000 SEK
    - 60% of ICERs above 1 000 000 SEK
  - **7**/9 received limited reimbursement / recommendation in Sweden
  - **4**/9 have been part of tripartite agreements
  - **3**/9 received EMA approval in 2014, **3**/9 in 2015, and **3**/9 in 2016

- All 3 hospital drugs were part of the "Nationellt ordnat införande" process
  - All with reported ICERs above 1 000 000 SEK

- 6 reimbursement drugs with positive TLV decisions, of which:
  - 3 are orphan diseases

- All received approval for the same indications as approved by EMA

Examples of medicines with long TTM:

- Reimbursement drugs indicated in orphan diseases
- Indicated in diseases with high-very high severity
- Majority of ICERs estimated > 1 000 000 SEK

Non-available medicines in Sweden

- Reasons for being classified as non-available

Selection of non-available medicines for further analysis

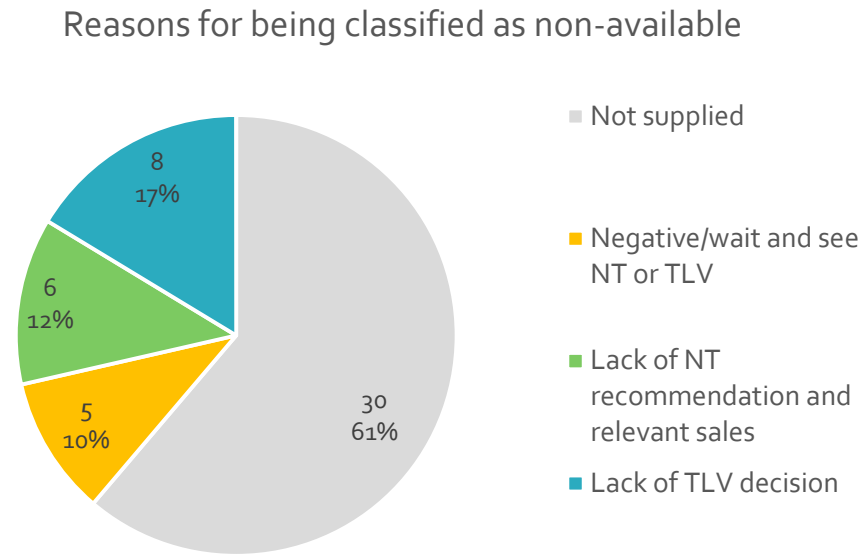
- Definition 2 is assessed to capture the rate of availability in Sweden most accurately
  - Based on a discussion with Stockholm and Skåne County Councils
  - Recognizing that it incorporates hospital drugs with a non-negative NT recommendation, and some level of reasonable sales, as available

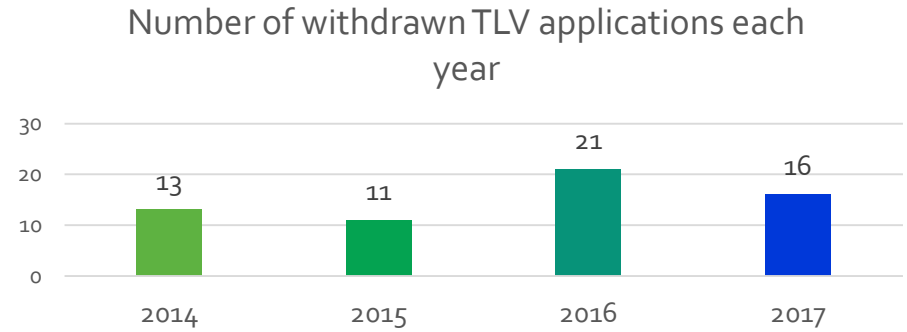
- Thus, the remaining analyses describing the non-available medicines are based on the 49 medicines classified as non-available according to Definition 2.

Non-available medicines (Definition 2) – Reasons for being classified as non-available

- 49 medicines are classified as non-available.

- They have been classified as non-available in this analysis because:
  - 30 are currently not supplied in Sweden, with no further information on potential HTA process/decision
    - Could incorporate medicines with withdrawn TLV applications (e.g. if negative decision recommended by TLV office. See figure for number of applications withdrawn/year; could be multiple for same product, so not directly comparable)
    - And/or cases where the MA holder has not attempted to apply for reimbursement, or even launch their product in Sweden at all
  - 5 have a negative/wait and see decision/recommendation from NT or TLV:
    - 1 with negative TLV decision
    - 3 with negative NT recommendations
    - 1 is not recommended for use, until more data are available
  - 14 are registered as supplied, but 6 of these are lacking a NT recommendation and have no relevant sales, and 8 are lacking a TLV decision
    - Potentially in processing
    - Or withdrawn / never applied for reimbursement





Non-available non-replaceable medicines in Sweden

- Methods
- Summary information
- Comparison with Denmark, Finland, and Norway

Non-available medicines (Definition 2) – Methods to assess replaceability

- 49 medicines are classified as non-available in the analysis.

- In an attempt to understand what type of medicines these are and the potential consequences of them not being available in Sweden, a **pragmatic effort** to assess if they are "replacable" has been made.

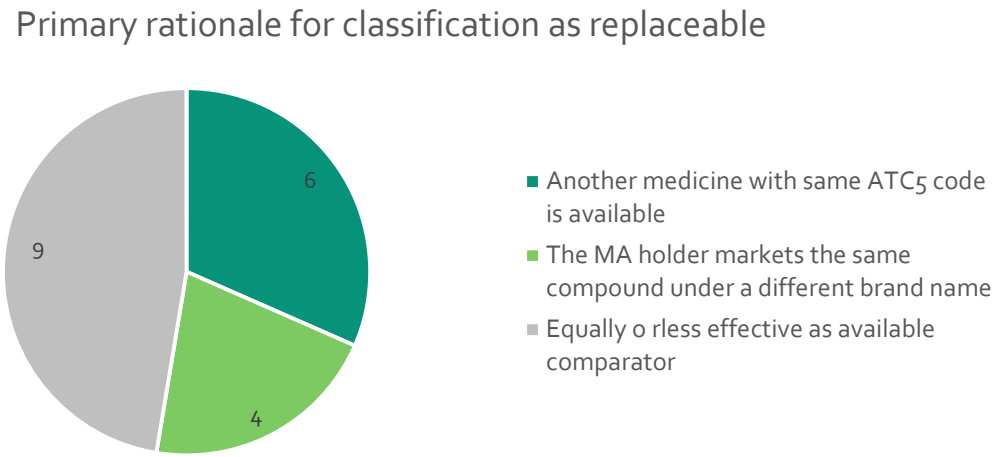
- Medicines with unique features (indication, limited treatment options/unmet medical need, mode of action, tolerability profile, route of administration, and efficacy) believed to provide relevant added patient value were tabulated from the following sources of information:
  1. Identifying whether >1 other medicine is registered in FASS as "currently supplied" with same active substance (ATC 5 level)*
  2. Reviewing the following documentation for assessment of uniqueness:
     i. EMA's EPAR summary for the public, and SPC
     ii. TLV and NT reports, if available
     iii. Swedish clinical guidelines, if (i) - (ii) do not contain sufficient information
     iv. Other sources, if (i) – (iii) do not contain sufficient information

* Recall that the 146 medicines with EMA approval in January 2014 - Decemeber 2016 were "new medicines" (i.e. with substance previously not available in the EU). However, this report analyses if there are other medicines with same full ATC5 code available in Sweden up until 1 May 2018 (up to 3 years and 5 months post the MA date of the first included medicine). Thus, altough a medicine was introduced as a new subtsance when receiving EMA approval, new medicines with same active substance may have entered the market since then, and these are captured in this report and included in the assessment of replaceability.

Non-available replaceable medicines

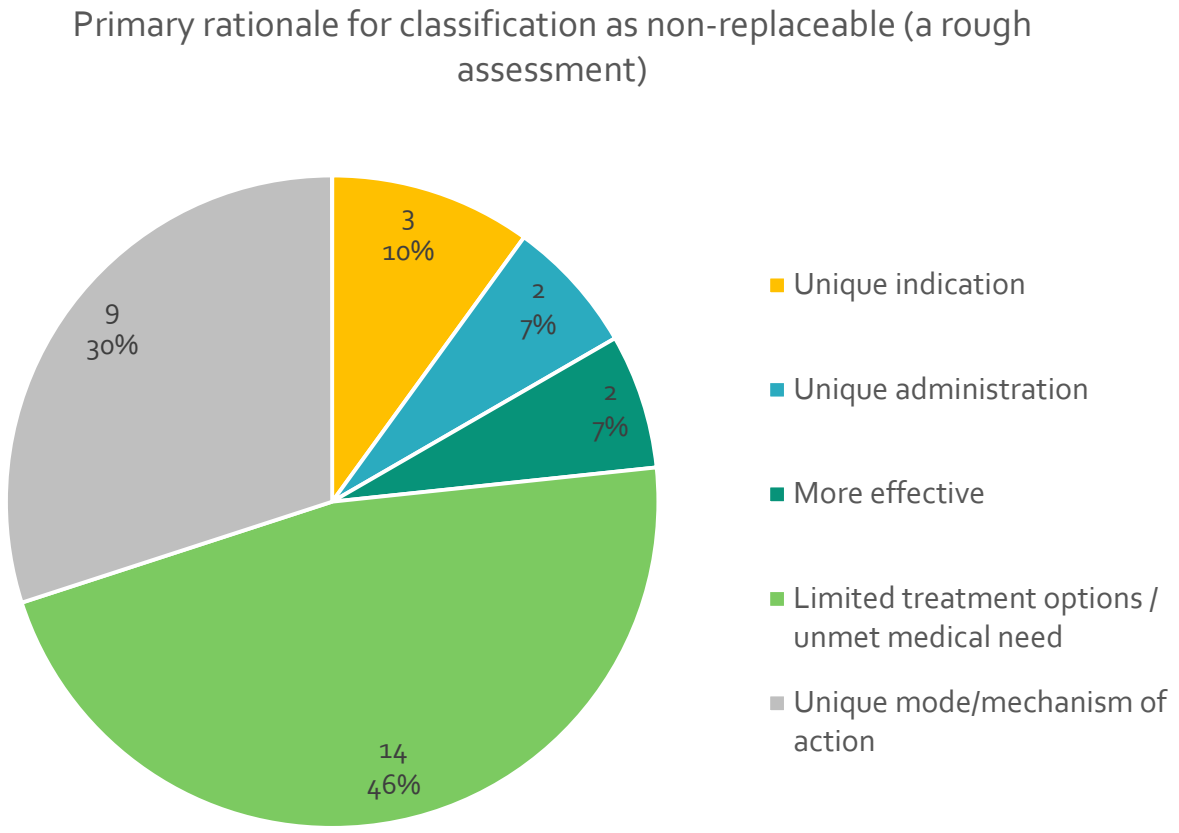
- Applying the approach on the previous slide, of the 49 non-available medicines, 19 (39%) are assessed as replaceable, and 30 (61%) as non-replaceable.

- The primary rationale for classifying medicines as replaceable includes:
  - In 6 cases, another medicine with the same ATC5 code is available in Sweden (at time of launch or later date), but with slightly different mechanism of action, administration form or strength
  - In 4, the MA holder markets the same compound under a different brand name
    - If these 4 medicines are excluded from the analysis, the total sample of EMA approved medicines is reduced to 139, which would increase the rate of availability somewhat to 91/139 = 65%
  - In 9, it was found primarily to be equally or less effective as an available comparator



Non-available non-replaceable medicines – identified based on primary unique feature

- 30 medicines were assessed to be non-replaceable, based on the pragmatic approach described in previous slides
  - Of these, 13 (43%) are currently not supplied in Sweden.
- 5 parameters of uniqueness were taken into account
  - Most medicines classified as non-replaceable were so based primarily on information supporting an unmet medical need and limited other treatment options (46%)
  - A unique mode of action/mechanism, indicating value for certain subgroups of patients refractory to other options and/or with tolerability problems, was the second most prevalent reason for non-replaceability (30%)
  - Additional unique features include indication, mode of administration and improved efficacy
- Note that only the primary rationale is counted; although some medicines have additional unique features



Non-available non-replaceable medicines – describing according to a set of summarizing parameters

- An attemtp was made to further classify the non-replaceable medicines, according to the following parameters, thereby enabling a descriptive summary of them:
  1. Drug characteristics
     - A medicine was classified as a hospital drug if there was a public NT case for it and/or IV administration and/or SPC states that clinical staff is required for administration. All other medicines were classified as non-hospital drugs.
  2. Subjective level of severity of disease and existing treatment options
     - Severity of disease was estimated as high for all included oncology products.
     - Severity of disease for the other indications and information on existing treatment options were elicited from public sources of information, such as EPAR summaries and Swedish clinical guidelines, and if necessary other sources of information were consulted. No clinical experts were involved in the assessment.
  3. Number of unique MA holders, and local presence in Sweden
     - Local presence was assessed in FASS. If FASS indicated no local presence in Sweden, local presence was further assessed by examining if the company is registered on a Swedish address.
  4. MA holder experience with the Swedish reimbursement system
     - Experience was measured as number of medicines included in the Swedish reimbursement scheme.
  5. ATC1 code, indicating disease area (see next slide)

Non-available non-replaceable medicines - summary information	N	%
Drug characteristics		
Oncology medication	9	30%
Hospital drug	14	47%
Orphan drug	14	47%
Non-oncology and orphan	10	33%
Disease severity and treatment options		
High disease severity	19	63%
Existing treatment is symptomatic	11	37%
MA holder characteristics		
Unique MA holders	27	90%
MA holders with local presence	19	70%
MA holder experience with the Swedish reimbursement system		
0 reimbursed medicines	11*	41%
1-9 medicines	8	30%
10-19 medicines	4	15%
20+ medicines	4	15%

* Includes the 8 MAH with no local presence in Sweden.

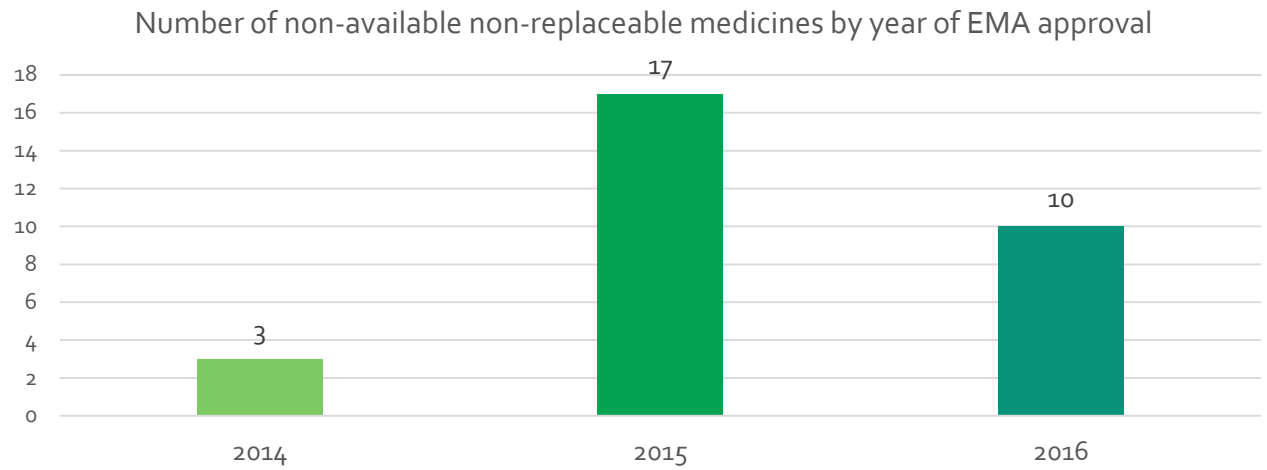
Non-available non-replaceable medicines – by therapeutic category (1st level of ATC classification)

- The table below shows the ATC1 code distribution among the 30 non-available non-replaceable medicines and includes some additional descriptive comments to make it more concrete what type of medicines are concerned.

ATC1 codes represented	N	Description of indication and severity of disease
Antineoplastic and immunomodulating agents	10	All are indicated in second or third line cancer treatment. 5 are orphan drugs. All assessed as addressing disease with high severity.
Alimentary tract and metabolism	5	Four are orphan, and 2 are pediatric, all with high or varying degree of severity. 1 non-orphan indicated in weight management, with non-high severity.
Blood and blood forming organs	3	2 are indicated in bleeding disorders, one of which is orphan, and 1 is an enzyme deficiency disorder. 2 have high severity, 1 has varying to high severity.
Dermatologicals	3	All are indicated in skin diseases. 1 is orphan and has varying severity, 2 are non-orphan with non-high severity.
Antiinfectives for systemic use	2	Antibiotics, assessed to treat bacterial infections with potentially high severity
Nervous system	2	Orphan sleeping disorders, one with varying degree of severity and one with non-high severity.
Sensory organs	2	Both are used in eye surgery. One is orphan and has high severity, one is non-orphan with non-high severity.
Other ATC1 codes	3	1 is indicated in the ATC1 ”respiratory disease”-group, is pediatric with a varying to high degree of severity. 1 is indicated in the ATC1 ”genito-urinary system”-group with non-high severity. 1 indicated in the ATC1 ”musculo-skeletal system”-group with high severity.

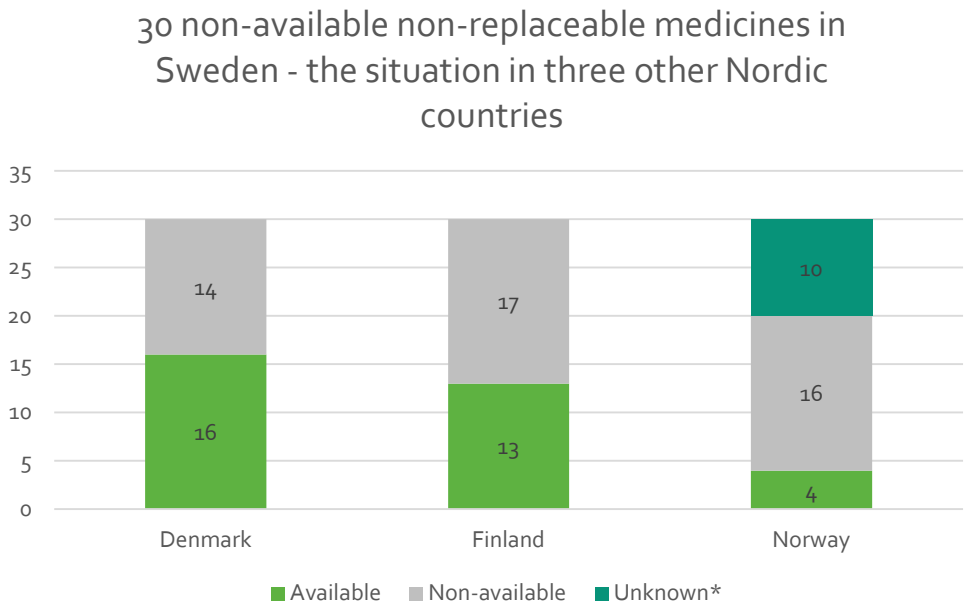
Non-available non-replaceable medicines – By year of EMA approval

- The graph depicts number of non-available non-replaceable medicines by year of EMA approval.
  - Most of the medicines received EMA approval in 2015 (N=17; 57%).
  - 10 (33%) of the medicines received approval in 2016.
  - Only 3 (10%) received approval in 2014
- The temporal differences could have a number of underlying reasons
  - Potentially including changed behaviours of MA holders, or expectations/experiences of the system
  - Or simply that additional time increases the likelihood of becoming available



Non-available non-replaceable medicines – Comparison with Denmark, Finland, and Norway

- According to the 2017 Patients W.A.I.T. Indicator, Denmark, Finland, and Norway reported an ovearll rate of availability of 79%, 68%, and 53%*, respectively (Sweden 64% in the updated analysis).
- Based on the W.A.I.T. files for these three countries, approximately half of the 30 non-available non-replaceable medicines in Sweden are available in Denmark, and Finland, while 1/10 is available in Norway (partly due to high unknow status):
  - Denmark: 16 (53%)
  - Finland: 13 (43%)
  - Norway: 4 (13%)*
- Further, 12 medicines are assessed as non-available in all three countries, and 2 are available in all three countries.
- Overall, the comparison shows that Sweden has a potentially higher rate of availability than Norway (although many unknowns), somewhat lower than Finland, and notably lower than Denmark.
- However, it seems that different medicines are available in different markets.



*Note. Norway has classified 19% of the 146 medicines as unknown. 10 of these are included among the 30 medicines that are classified as non-available non-replaceable in Sweden.

A description of 16 non-available non-replaceable medicines available in Denmark

- To facilitate the understanding of potential lost value to Swedish patients, the 16 non-available non-replaceable medicines that are available in Denmark have been analyzed.

- These assessed as non-available in Sweden because:
  - 2 are currently not supplied in Sweden, with no further information on potential HTA process/decision
  - 2 have received a negative NT recommendation
  - 12 are registered as supplied, but 4 of these are lacking a NT recommendation and have no relevant sales, and 8 are lacking a TLV decision
    - Potentially in processing
    - Or withdrawn / never applied for reimbursement

16 non-available non-replaceable are available in Denmark – Summary information	**N**
Drug characteristics	
Oncology medication	7
Hospital drug	8
Orphan drug	9
Non-oncology and orphan	5
Disease severity and treatment options	
High disease severity	12
Existing treatment is symptomatic	6
MA holder characteristics	
Unique MA holders	14
MA holders with local presence	14
MA holder experience with the Swedish reimbursement system	
0 reimbursed medicines	3
1-9 medicines	4
10-19 medicines	3
20+ medicines	4

Non-available non-replaceable – 5 examples

- 5 example medicines that are not available to Swedish, but to Danish - as well as in some cases also to Finnish and Norwegian - patients, are described below, to provide some more substance to the analysis:

Drug 1:
- Hospital drug
- Orphan
- Oncology indication
- High severity
- Available in 2 other Nordics

Drug 2:
- Reimbursement drug
- Orphan
- Pediatric enzyme deficiency disorder
- High severity
- Available in 2 other Nordics

Available in Finland

Drug 3:
- Hospital drug
- Orphan
- Pediatric enzyme deficiency disorder
- High severity
- Available in 2 other Nordics

Drug 4:
- Reimbursement drug
- Pediatric respiratory disease of the lungs
- Varying - high severity
- Available in 2 other Nordics

Available in Norway

Drug 5:
- Reimbursement drug
- Oncology indication
- High severity
- Available in Denmark only

Available in Denmark

Summary and discussion

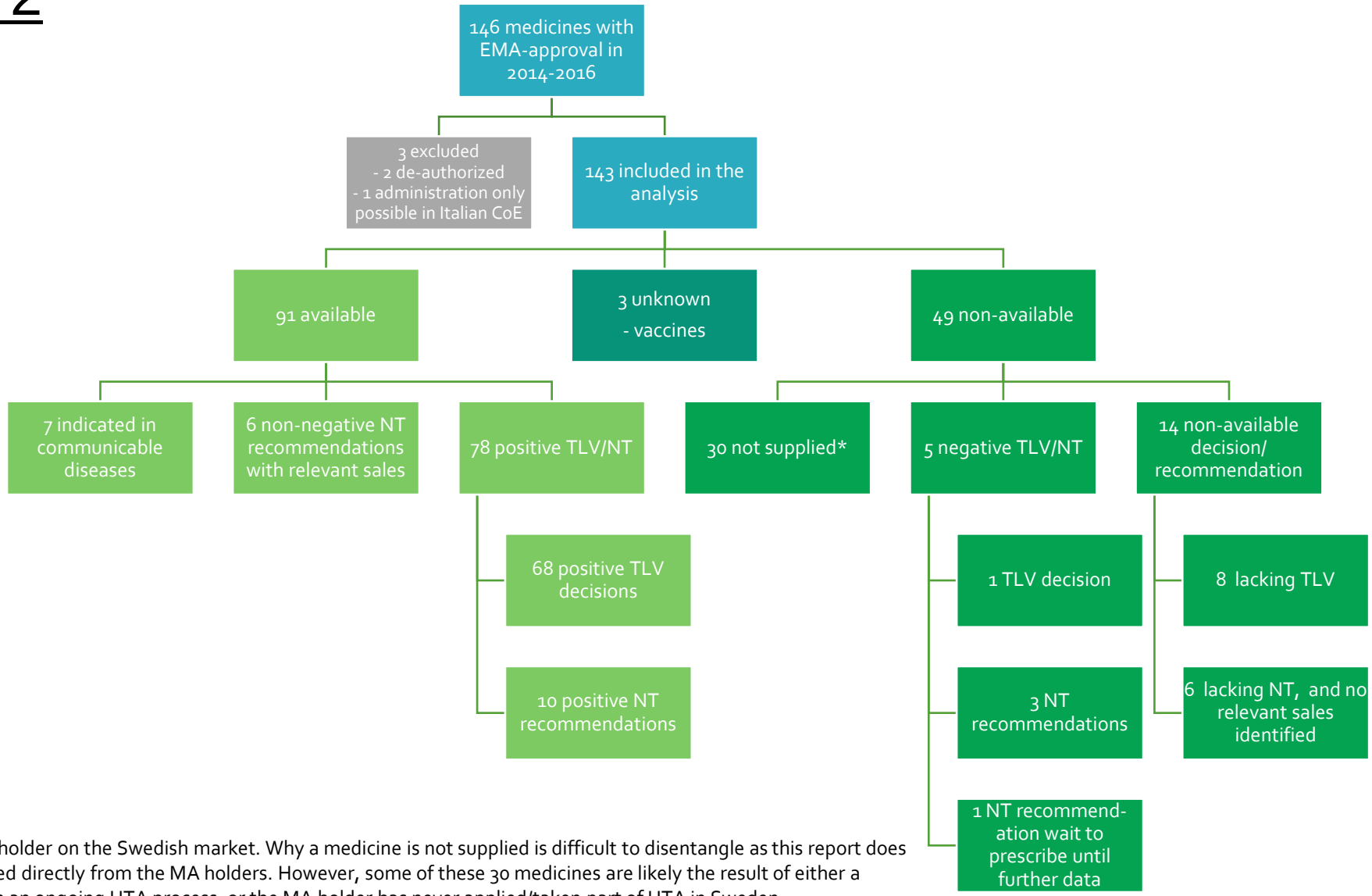
Summary – Rate of availability

- This report is the result of an effort to understand and further develop the findings from the 2017 Patients W.A.I.T Indicator analysis, which showed that 55%, 34%, 11% of the 146 new medicines were available, non-available, and unknown, respectively in Sweden.

- This report applied a later cut-off date (May 1st, 2018) and the following definition of availability on the sample of the 146 medicines:
  - Available if positive TLV, or non-negative NT and relevant sales, or communicable disease; a sligthly broader definition, which should better reflect the Swedish specific situation for hospital drugs.

- Using the revised definition, the analysis of availability of new medicines in Sweden was updated (see the flow chart on later slide for more details):
  - 3 medicines were excluded due to de-authorization and considering that one was only possible to administer in Italy
  - 143 medicines were included in the analysis. Of these, 91 were assessed as available, 3 as unknown, and 49 as non-available
  - The rate of availability was estimated to 64%.
  - On average, it took 10 months from EMA approval to medicine becoming available to patients (range 14 to 1156 days; median 223 days)

Summary - Flow chart summarizing the assessment of the 146 EMA-approved medicines regarding availability – Definition 2



*These are not supplied by the MA holder on the Swedish market. Why a medicine is not supplied is difficult to disentangle as this report does not incorporate information obtained directly from the MA holders. However, some of these 30 medicines are likely the result of either a withdrawn TLV application, being in an ongoing HTA process, or the MA holder has never applied/taken part of HTA in Sweden.

Summary – Non-available, non-replaceable

- 49 medicines were identified as non-available in the analysis. Among these:
  - 19 were classified as replaceable, as other options with same ATC5 code or with equal or better efficacy are available in Sweden, and
  - 30 were classified as "non-replaceable" as they were assessed to have one or more unique features associated with increased value to patients; most commonly these medicines were addressing a disease area with limited other treatment options (46%) or providing a unique mode of action/mechanism (30%).

- Main summary information about the non-available non-replaceable medicines show e.g. that:
  - 1 in 3: Oncology medications
  - 1 in 2: Orphan
  - 1 in 3: Non-oncology medications and orphan
  - 2 in 3: High disease severity
  - 1 in 2: Available in Denmark

- The 30 identified medicines were represented by 27 unique market authorisation holders, whereof about 60% have one or more other products in the reimbursement system and 70% a local office in Sweden.

Discussion – methods and definitions

- Acknowledging the limitations of assessing products rather than indications approved
  - The EMA W.A.I.T. Indicator looks at new EMA approved medicines. Those that meet Definition 2 in this study are included as available. Hence, the analysis does not take into account that each medicine may have several different indications, and that these may be treated differently by the HTA authorities. E.g. conditional reimbursements/recommendations, limiting use to sub-set of indications, is disregarded in this analysis.

- Outcome from national HTA process are used to define availability
  - However, additional regional and local hurdles such as formulary lists may limit actual presribing.
  - A rough assessment using sales data as a proxy for actual patient use, was conducted for the 91 available medicines. In a majority of cases, these do seem to reach the patients, at least at low levels. Still, 1 in 10 had sales below a "low-sales"-threshold (5 packages/month), indicating that a positive TLV/NT decision enables, but does not guarantee, actual access to patients.

Discussion – methods and definitions

- Lack of details around underlying reasons
  - This analysis takes only publicly available information into account, which means that e.g. information about withdrawn TLV applications, or if a MAH at all has attempted to achieve access in the Swedish market is lacking. The results can therefore not assess to what extent additional efforts from the state and regions could improve access to new medicines further.

- High number of non-supplied medicines
  - A relatively high number, on average 10 per year, of non-available medicines assessed as having unique features which could benefit patients, were found to not even be supplied in Sweden.
  - These medicines were represented by a wide range of companies, some of them without local offices in Sweden, but most semingly familiar with the Swedish system (local branch office and/or already other medicine in the reimbursement system).
  - There is no information on the underlying reasons for not supplying these medicines. Additional research to understand whether it is e.g. unsuccessful attempts at gaining access, perceived complexity of the HTA processes deterring entry, or simply no interest in the Swedish market, would be useful.

Discussion – methods and definitions

- What is a reasonable level of availability?
  - Without going into details around the individual medicines, analysing information such as the calculated cost per QALY gained, price, and uncertainty of the cases, it is difficult to say what level of availability actually rimes with the value-based framework that is applied in Sweden; and what a good target should be.
  - A comparison with other Nordic countries shows that Sweden has a potentially higher rate of availability than Norway (many unknowns), somewhat lower than Finland, and notably lower than Denmark.

- On the same lines, the time to market analysis does not assess the underlying reasons for the timings
  - Such as e.g. if long processes are due to MAH waiting to submit documentation, authority delays or polarised price expectations
  - Compared to the UK, Germany, and Denmark, about twice the time is estimated for a medicine to become available in Sweden. But these are, on the other hand, best in class in Europe.
  - The national ”ordnat införande av läkemedel” process was introduced in Sweden in January 2015, to among others faciliate patients’ access to medicines. It is perhaps a bit too soon to evaluate the effectiveness of this, and it requires additional data. However, this report supports that the vision to have a recommendation/decision available at 3 months post EMA approval is far from reached, as less than 25% of medicines in this assessment were estimated to be available within that stipulated timeframe.

Conclusion

Conclusion

- Althogether, this re-analysis of the W.A.I.T. Indicator for Sweden, shows that almost 2/3 of medicines approved by EMA in 2014-2016 have become available to Swedish patients by May 1st, 2018, which is mostly in line with the situation in the other Nordic markets.

- The majority of the the non-available medicines were assessed as having unique characteristics, not easy to replace, and hence, their non-availability may to a varying extent be associated with negative consequences for Swedish patients.

- A high variation in time to market was recorded, indicating that there may be room for improvement to accelerate selected processes. Long access times may e.g. be attributed to high-cost/high ICER.

- However, good examples were also identified, where time to market was obtained in less than three months. Especially communicable diseases and high-severity reimbursement medicines where similar cases had previously been assessed or managed within a three party negotiation, seem to have short access times.

- Access to new medicines is a joint effort by MAHs and authorities. This report neither analyses who could improve, nor what a reasonable level of availability is; but it aims to document the current situation, hightlight gaps, and enable informed discussions on both sides, on how to continously improve patients' access to medicines in Sweden.

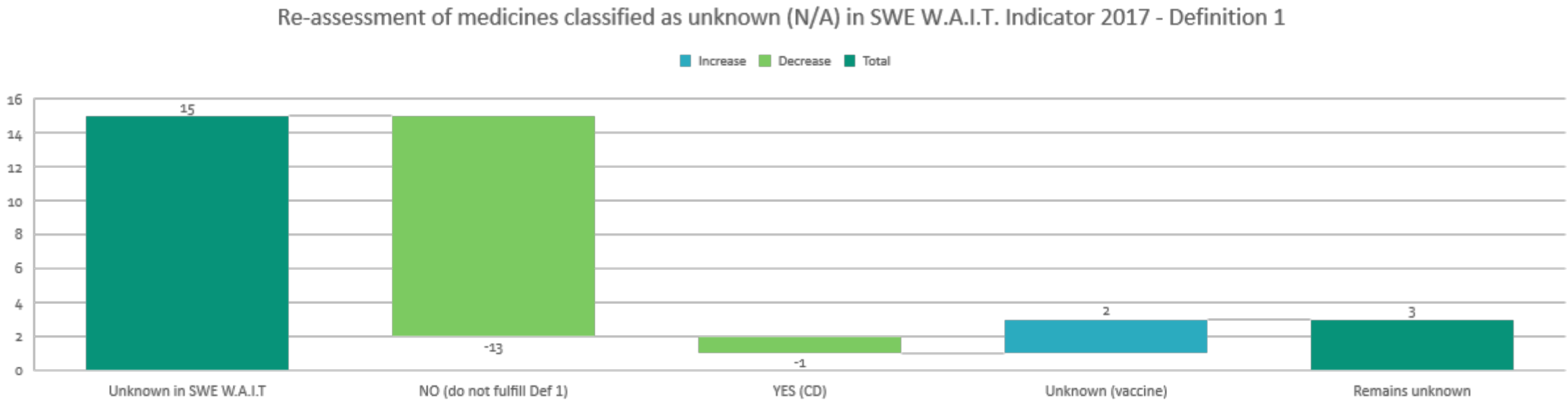
Appendix: The process of assigning availability statuses to the 143 included medicines, using the SWE W.A.I.T as a starting point

- Assigning availability statuses to medicines with unknown status
- Re-assessment of medicines classified as available and non-available

Comparison vs W.A.I.T: Assigning an availability status to medicines classified as unknown (N/A) in SWE W.A.I.T. Indicator 2017 – Definition 1

- The following updates of medicines' availability statuses were made when applying Definition 1:
  - 15 medicines previously classified as having an unknown status:
    - 13 re-classified as non-available (do not fulfill Definition 1),
    - 1 as available (communicable disease, indicated in HIV)
    - 2 as unknown (vaccines)

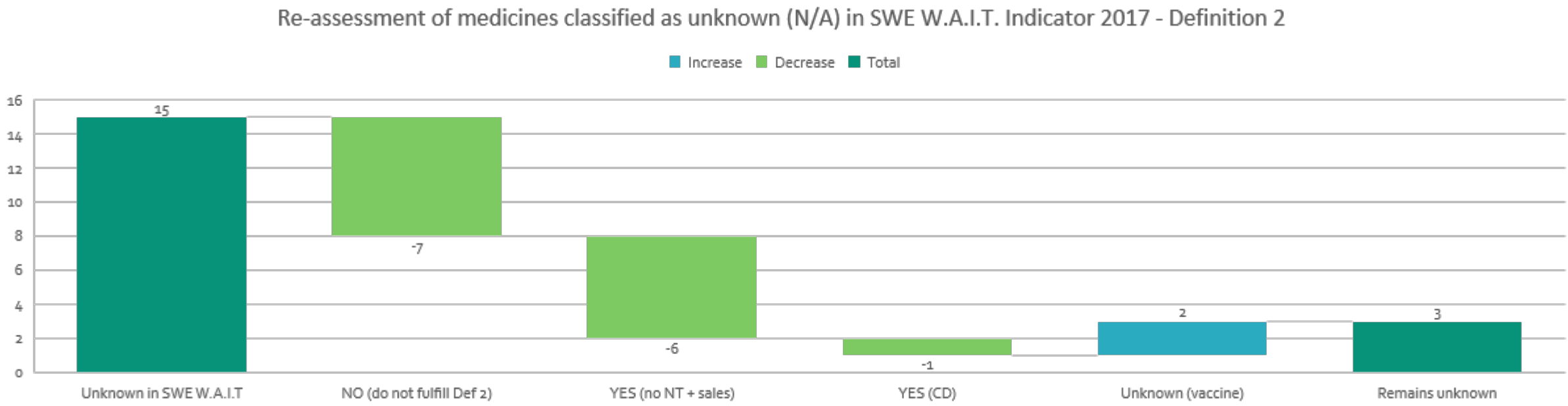
  - This results in only 3 medicines remain classified as unknown (all vaccines).



Abbrevation: CD = Communicable disease, Def = Definition

Comparison vs W.A.I.T: Assigning an availability status to medicines classified as unknown (N/A) in SWE W.A.I.T. Indicator 2017 – Definition 2

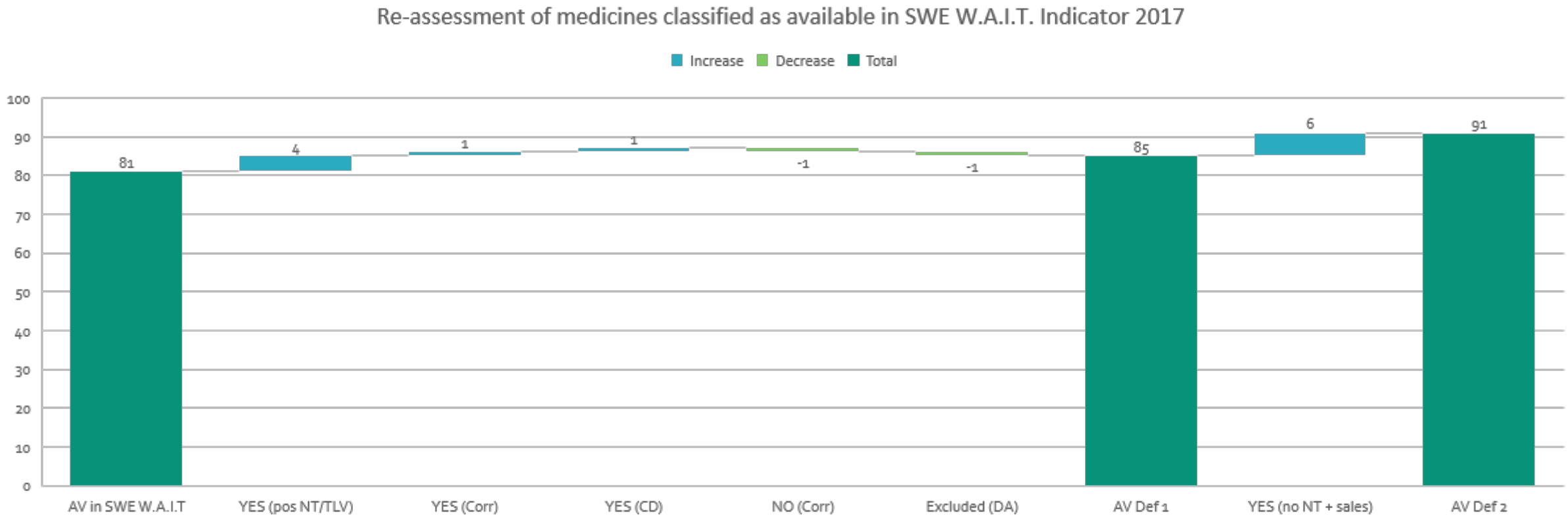
- The following updates of medicines' availability statuses were made when applying Definition 2:
  - The difference compared to Definition 1 on the previous slide is that 6 are classified as available as there is no negative NT recommendation and relevant sales.
  - Only 3 medicines remain classified as unknown (all vaccines)



Abbrevation: CD = Communicable disease, Def = Definition, No NT + sales = Non-negative NT and relevant sales

Comparison vs W.A.I.T: Re-assessment of medicines classified as available in SWE W.A.I.T. Indicator 2017

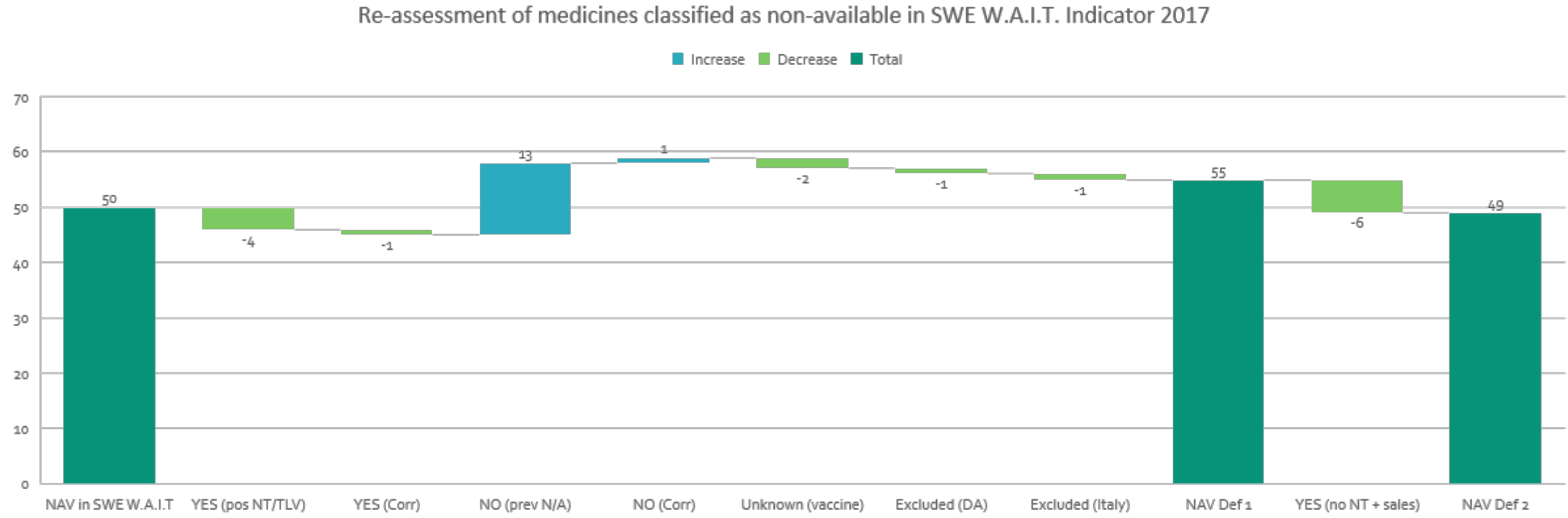
- A re-assessment of available medicines results in small changes due to a new cut-off date (1 May 2018) and adjusted Definition 2 for hospital drugs:



Abbrevations: AV = Available, CD = Communicable disease, Corr = Corrected, DA = De-authorized, Def = Definition, No NT + sales = Non-negative NT and relevant sales, Pos = Positive

Comparison vs W.A.I.T. : Re-assessment of medicines classified as non-available in SWE W.A.I.T. Indicator 2017

- The re-assessment of non-available medicines also results in small changes due to new cut-off date (1 May 2018) and adjusted Definition 2 for hospital drugs:

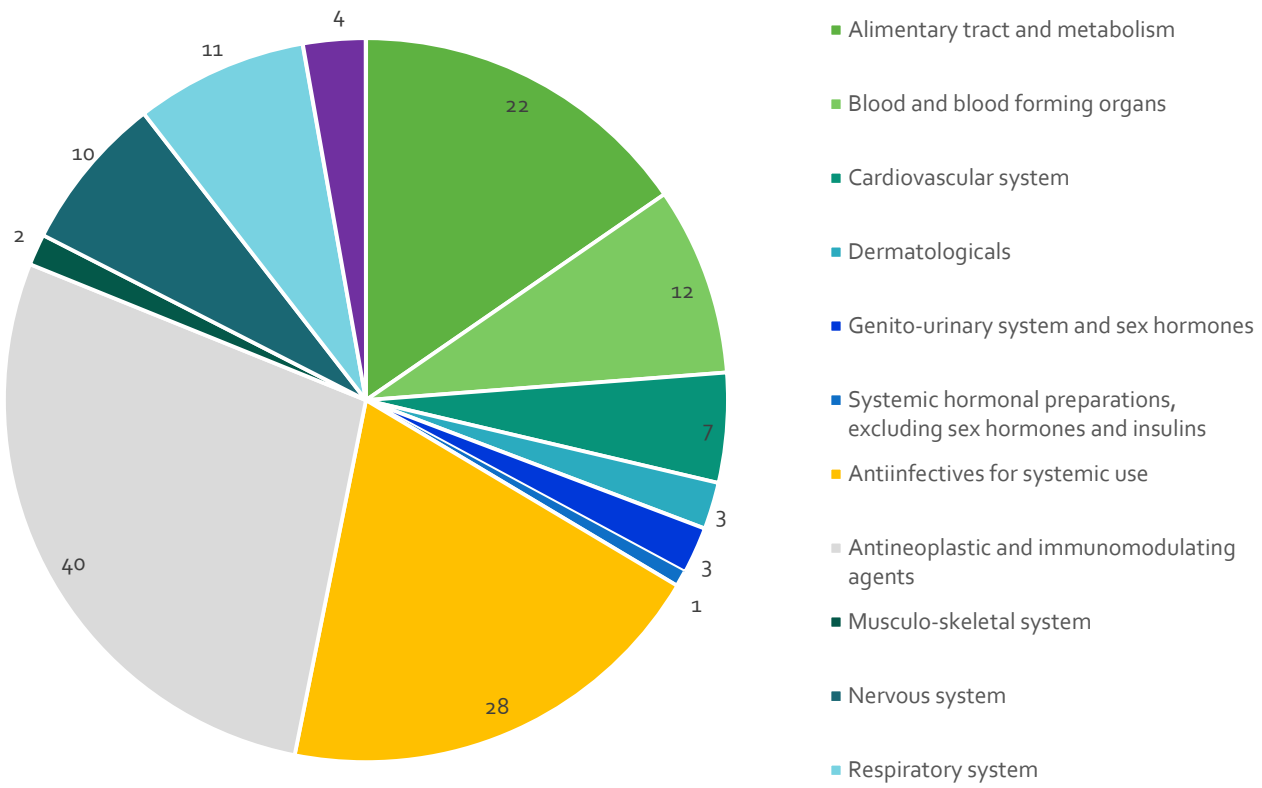


Abbrevations: NAV = Non-available, CD = Communicable disease, Corr = Corrected, DA = De-authorized, Def = Definition, N/A = Unknown, No NT + sales = Non-negative NT and relevant sales, Pos = Positive, Prev = Previously

Appendix: ATC1 codes as determinants of availability – an exploration of the Swedish data sample (143 medicines)

The sample of 143 EMA approved drugs – categorisation per ATC1 code

- Antineoplastic and immunomodulating agents is the most common category of new drugs
  - This category includes a substantial share of new oncology products
- Anti-infectives for systemic use is also a prevalent category in receiving marketing approvals.



*Note the "Antiparasitic products, insecticides and repellents" and "Various" groups have been omitted from the pie chart, as none of the 143 included medicines belong to these two groups.

ATC1 codes as determinants of availability

- A recent report[2] commissioned by the European Commission, analyses launches of medicines in the European Member States based on level 1 ATC codes, and shows that availability varies quite greatly across this categorization;
  - The medicines with the highest level of availability belong to the ATC1 category "Antineoplastic and immunomodulating agents".
    - These are often cancer medicines, and launch in ≥50% of the EU member states within 2 – 3 years from market authorization (MA).
  - The medicines with the lowest level of availability belong to "Dermatologicals", skin care products.
    - Launch in <1/4 of the member states even after 15 years MA.
- This report has reviewed each of the available and non-available medicines (following Definition 1), and identified which ATC1 category they belong to, to see if this resembles the findings of the EC Report, see the results on the next slide.

[2] European Commission (2018). *Study on the economic impact of supplementary protection certificates, pharmaceutical incentives and rewards in Europe,* Written by Copenhagen Economics, Final Report, May 2018

ATC1 codes as determinants of availability – Availability in Sweden (Definition 2) vs the European Commission Study

- The table to the right compares the availbility rate in Sweden with the European Comission (EC) study by ATC1 codes
- The results are more or less is in line with the European Comission results for 10 of 12 ATC1 codes.
- However, for some of the categories, there are only a few included medicines. Thus, results should be intepreted with caution.

ATC1 code*	European Comission results (launch probability)†	Distribution of 143 medicines with EMA approval	Available in Sweden	Non-available in Sweden	In line with EC study results?
Alimentary tract and metabolism	1 (reference group)	22	55%	45%	Yes
Blood and blood forming organs	1.9	12	58%	42%	Yes
Cardiovascular system	1.3	7	100%		Yes
Dermatologicals	0.3	3		100%	Yes
Genito-urinary system and sex hormones	1.5	3		100%	No
Systemic hormonal preparations, excluding sex hormones and insulins	2.1	1	100%		Yes
Antiinfectives for systemic use	2.0	28	82%	7% (excl. 11% unknown, vaccines)	Yes
Antineoplastic and immunomodulating agents	2.7	40	68%	33%	Yes
Musculo-skeletal system	1.2	2	50%	50%	Yes
Nervous system	1.7	10	40%	60%	No
Respiratory system	1.1	11	64%	36%	Yes
Sensory organs	1.0	4	50%	50%	Yes

* Note. The "Antiparasitic products, insecticides and repellents" and "Various" groups have been omitted from the pie chart, as none of the included medicines belong to these two groups.
† The launch probability is the probability of launch compared to that of the reference group. For example, the launch probability of the "Blood and blood forming organs"-group is on almost twice as great as that of the "Alimentary tract and metabolism"-group.