White Paper

Reporting of Medicine Shortages in Europe

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Executive summary

This document assess the reported drug shortages of a representative sample of EU countries (11 countries covering top-5 European markets, the Nordics, and Central & Eastern Europe). IQVIA analysis of the existing publicly available data suggests:

SHORTAGE DEFINITIONS ARE AMBIGUOUS AND INCONSISTENT ACROSS COUNTRIES

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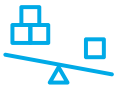
Publicly available shortage data is not comparable across European countries due to inconsistent shortage definitions across countries' shortage reporting databases. 8/11 countries studied are aligned to just half of the EMA definition, and differences in content of shortages reports and notification can be as low as 1%.



SHORTAGES ACROSS EUROPE VARY 10-FOLD, BUT NOT ALL 'SHORTAGES' ARE CREATED EQUAL

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Based on the number of SKUs / unique packs, the number of active shortages per country (November 2019) varies significantly across the 11 studied countries, but based on the variable definitions, cross-country comparison has limitations.

ACCORDING TO CURRENT DATA, THERE ARE NO PAN-EUROPEAN SHORTAGES

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Only 5 products are in shortage across >5 countries, and considering the issues in reporting, some multi-country shortages can be excluded due to reasons such as removal from the market or being older generation products. In other cases, there may be shortages to which we are unaware due to poor reporting.

OVER 80% OF SHORTAGES ARE GENERIC PRODUCTS WITH ALTERNATIVE MANUFACTURERS

Page 8

Pharmacist authority to interchange varies between markets due to different local regulation and payer decisions. It remains unclear if an interchangeable product are available with inventory. Swedish data suggests that many SKUs have zero sales and are likely to be 'not available' but are not reported.

HALF OF THE TOP-20 PHARMA COMPANIES REPORTED ≤5 PACKS IN SHORTAGE

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Companies with a narrow portfolio and newer products had less shortages, and major generic manufacturers with portfolios >450 molecules were responsible for the majority.

INVENTORY DATA IS A SOLUTION TO 'TRUE' SHORTAGES

Page 11

Current shortage lists are based on a manufacturer's internal visibility, and rely on vetting of shortages by the national authorities. The public shortage lists are shown to include significant numbers of these shortages, and solutions are available to have safe, and transparent inventory at an exchange group level as a solution.

Background and methodology

Shortages are a significant issue in Europe. The Organisation for Economic Co-operation and Development (OECD), the European Commission, the World Health Organisation (WHO) and the European Medicines Agency (EMA) have all included medicines shortages in their top priority areas for medicines in 2020, highlighting the importance to population health. However, they are not a new phenomenon and the number of drugs in short supply continues to rise in European states, according to trade associations.[1,2]

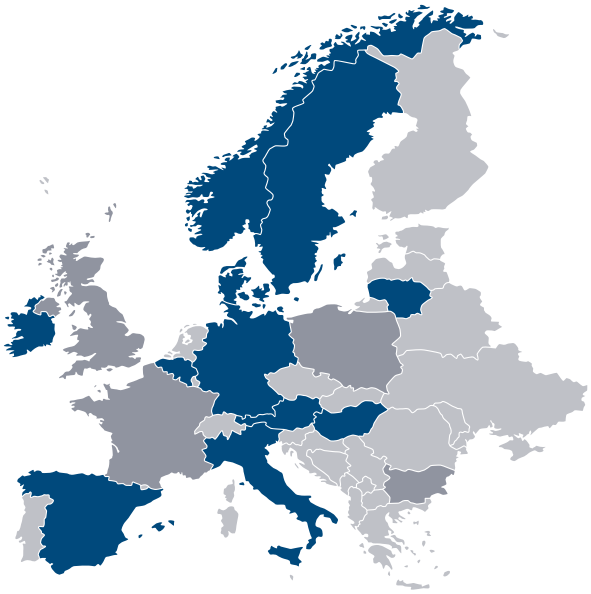
Previous publications have focused on the causes of drug shortages such as production problems, lack of raw materials, logistic issues, supply factors, and parallel trade.[3] Recent work has dealt with the need for a common definition of drug shortage and calls for the European Commission to undertake action on the shortage situation.[4]

The main focus of this IQVIA analysis is to investigate existing shortage reporting and what can be learnt by comparing different European countries. IQVIA assessed and compared the reported drug shortage lists from 11 countries with an acceptable level of data quality (see Figure 1). Publicly available shortage data was normalised in order to create uniformity between the different countries, which involved an adjustment to equate one shortage to one Stock Keeping Unit (SKU).

As there was a significant inconsistency on how each country presented the information, an 'active shortage list' was created to include drugs that started being in shortage in the market from the 1st January 2019 and the issue was not resolved by 31st August 2019. These are a representative sample of European countries where different factors affect availability: price level, price mechanism, generic substitution system, distribution system, parallel trade and market size. The available information was then bridged to include an ATC class, protection status, generic product information, and exchangeability using IQVIA MIDAS data.

As a consequence, the data analysed does not contain shortages from parallel trade as the sources are based on the official, marketing authorisation holder-reported shortages to the competent authority. Access to the pharmacy reported shortage listings has not been made transparent, and as such our analysis excludes parallel export blockage lists. The paper therefore cannot comment on the impact of parallel trade, as it cannot be seen.

Figure 1: Table showing European countries with suitable shortage / discountation lists included in the study



Country studied	Rationale/segment
Germany	Major EU5 market
Spain	Major EU5 market
Italy	Major EU5 market
Denmark	Nordic market
Sweden	Nordic market
Norway	Nordic market
Hungary	Eastern European markets
Lithuania	Eastern European markets
Austria	Strong shortage data
Belgium	Strong shortage data
Ireland	Strong shortage data

Notable exclusions

France	Main list is pharmacy reported, as opposed to the MAH data available), access to the underlying data was not available
UK	Poor data quality (alerts / memos), or an alternative export ban list which is unsuitable for comparison
Bulgaria	Poor data quality (alerts / news on shortages only)
Poland	Poor data quality for shortages, the list available is used to manage parallel export via prior authorisation not to generate visibility to shortages

Source: IQVIA Global Supplier & Association Relations

Comparison of public shortage reports

No resources are currently available to easily compare shortage reports or the data within them. IQVIA has collated the publicly available documents to determine cross-country variability and discuss the major differences.

The definition of shortage is not consistent across countries' shortage reporting databases. Calls for a clear definition have been around for almost 10 years[5,6,7] despite this few countries have an explicit and official definition for shortage reporting. In 2019, the EMA proposed a common definition which aims to be comparable across countries, however it leaves room for international interpretation (Figure 2).

By comparing the EMA definition to the publicly listed definitions of a shortage on national registries we are able to show the level of variability between methods (Figure 3). We are aware that national groups record and interpret data post-reporting, but by highlighting this we can show:

1. **A lack of transparency in data gathering,** and;
2. **The issues with analyses that have been published using this imprecise science.**

The definition of shortage itself can be broken down into 4 constituent parts, each of which have different levels of variability.

THERE ARE FOUR CENTRAL COMPONENTS TO THE EMA'S DEFINITION TO WHICH COUNTRIES SHOULD COMPLY

1. Key term: The 'key term' is a concept which takes the phraseology used by the national registry and compares to both the EMA definition, and to other European markets. Phrases used leave room for interpretation, but countries often add nuance to their definitions with subcategories which is likely to be a useful tool in interpreting the real impact on patients.

2. Owner of notification: All countries align to this segment of the definition. In Hungary, patients and other supply chain players can report a shortage directly. In Lithuania, parallel exporters can report a shortage, and in Spain the public documentation permits health authorities to report a shortage (although this is an option, not an obligation). This could be beneficial in acknowledging that other reasons for shortages exists, adding clarity to the situation, however the added complexity would likely counteract this. In situations where multiple generic players operate, the value of multiple notifications

Figure 2: Definition analysis of EMA common shortage definition

Source: IQVIA Global Supplier & Association Relations. EMA/674304/2018; https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guidance-detection-notification-shortages-medicinal-products-marketing-authorisation-holders-mahs_en.pdf

Notes: See appendix for details of countries' shortage definitions for reporting[9]

becomes highly complex and as such alternative notification is valuable.

The most insightful option is based on whether pharmacies are able to get access to the medicines. This is used in Spain, France, and the Netherlands. In several countries (Poland, Bulgaria, UK) information about inventory is collected by a Government body to have a more objective picture of the situation.

3. Criteria: In Lithuania, Norway and Sweden, marketing authorisation holders are asked to report based on a different 'criterion': supply issues rather than shortages. This means demand is not considered at the time of notification in these countries. Products which are either no longer required by patients or are outdated treatments could therefore be recorded as being in shortage. However, this interpretation may be done post-reporting and publication of shortages may not consider these products within their national list, as demand is unknown, and transparency unavailable.

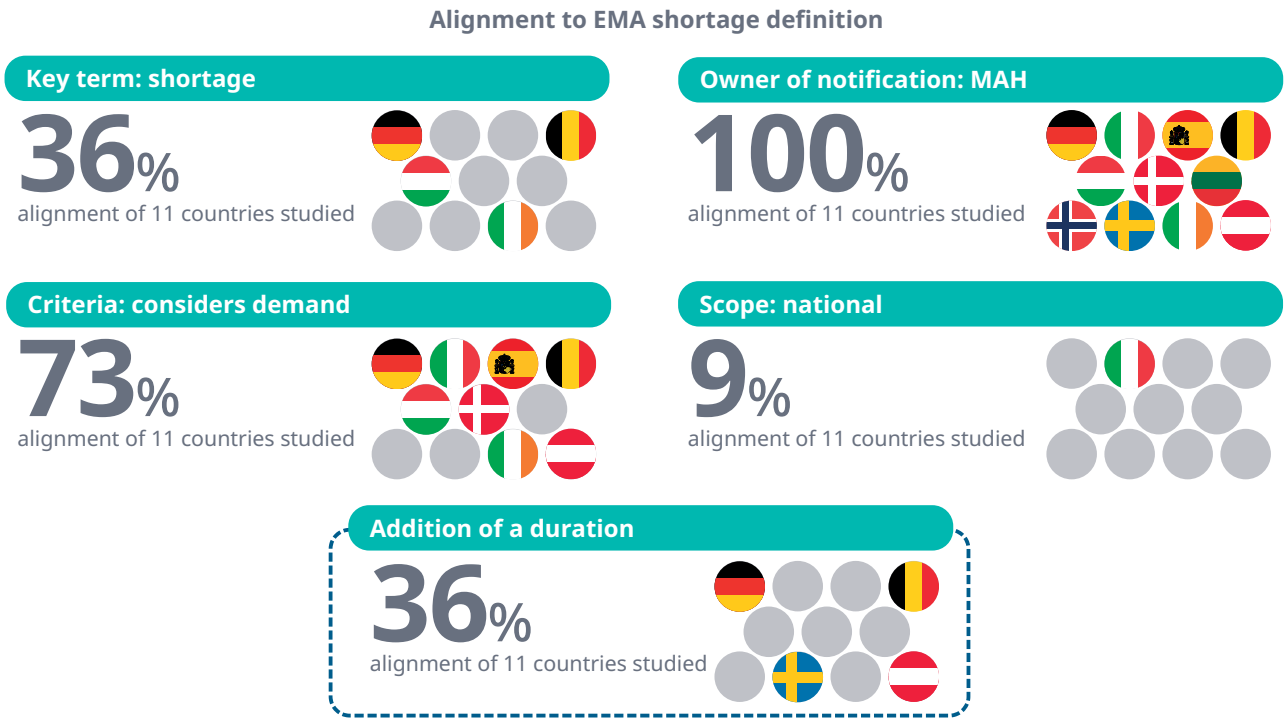
4. Scope: Countries rarely explicitly define the 'scope' of whether a shortage issue is national or local, however Spain specifies if can be either, meaning regional issues are also reported. Four countries include additional, supportive scope details, such as duration of shortage, to bolster the EMA broad definition (Austria, Belgium, Germany and Sweden). The importance of ensuring that the shortage is national is to remove the potential for the shortage to be due to misallocation within a country or between separate wholesalers.

Duration is not noted within the EMA's official definition and is easily confused with the deadline within which to report a notification (discussed in more detail on page 5). Only a handful of countries stipulate a duration to which a shortage must be in place for it to be classified as a true shortage. The value of this addition is that it ensures a medicine is not a temporary shortage, backlog within the system that is easily rectified through use of parallel trade, additional wholesalers, or regional communication.

8/11 COUNTRIES STUDIED ARE ALIGNED TO 50% OF THE EMA DEFINITION

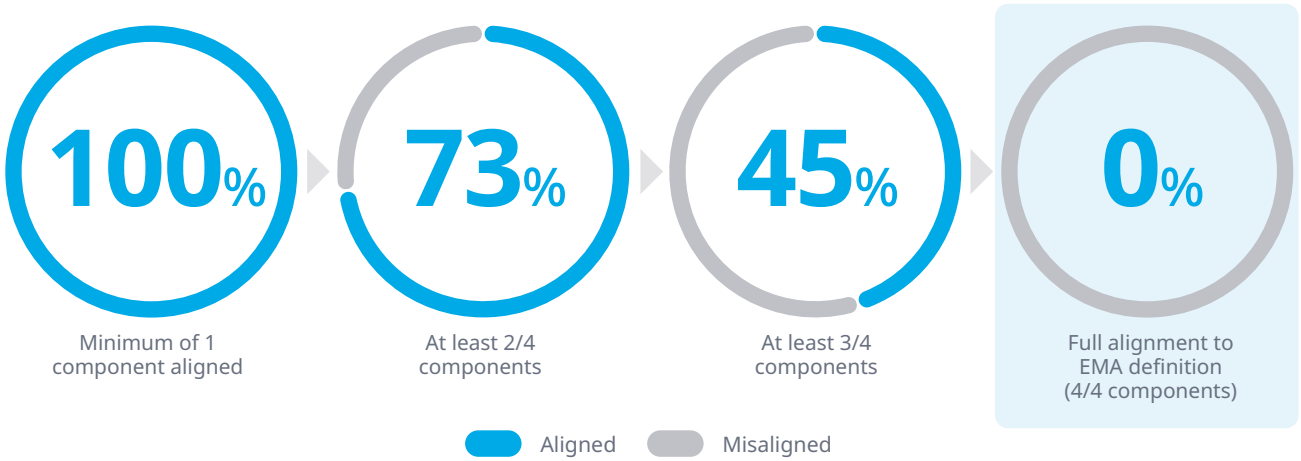
No country is 100% aligned to the EMA definition, with the majority of countries (8/11 studied, 72%) aligning to only 2 out of 4 of the definition's components. Given that the introduction of the shortage definition has been in place for less than a year, this is expected to improve subject to the alignment of competent authorities.

Figure 3A: Alignment of country shortage definitions for reporting to common EMA shortage definition



Source: IQVIA Global Supplier & Association Relations. See appendix for details of countries' shortage definitions for reporting[8]

Figure 3B: Alignment of country shortage definitions for reporting to common EMA shortage definition



Source: IQVIA Global Supplier & Association Relations. See appendix for details of countries' shortage definitions for reporting[8]

DIFFERENCES IN CONTENT OF SHORTAGES REPORTS AND NOTIFICATION CAN BE AS LOW AS 1%

Once a shortage (based on the above definitions) has been determined, and further layer of variability occurs in the content of the reports which are sent to the national bodies to inform them of such an issue.

The EMA suggest that the notification should be done in 'no less than 2 months before the interruption in the placing on the market of the product' or as early as the shortage is confirmed.[9] They proposed a template for the notification of shortage which includes 11 segments where minimum information should be provided to the competent national authority: *Product name, National Authorisation code, /EMA Authorisation number, human/veterinary medicine, pharmaceutical form, strength, date of beginning of shortage, expected end date of shortage (if applicable), reason for shortage, risk assessment of impact of shortage and email of contact person.*

In Sweden, the adherence to this requirement is estimated to be 1% according to the recent report from Swedish Medical Products Agency.[10] When extracting this information from the published shortage lists, low adherence to the recommendation is found. Most of the countries comply well in reporting the name of drug, form, strength and the beginning of the drug shortage. In many countries studied, there is no reported reason for the shortage, often limited details are provided, and there is rarely a risk assessment. It would therefore be unfair to draw solid conclusions based on the 'reported cause' of shortages when so few have detailed reporting via this public dataset.

Denmark, Norway and Italy include a large quantity of information within the publicly available lists making easier the evaluation and resolution of the problem. However, the missing piece to the published shortage reports is a proposal for an alternative medicine that could be used which is critical for the patient's outcome and for the supply chain. Sweden is an outlier here in that it publishes alternative products in case a drug is missing from the market.

By contrast, Poland, Czech Republic, Spain and Italy publish the prior notification lists for exportation. This does not reflect 'true' shortages but is more representative of possible future shortages. This way of defining shortages often results in an export ban in anticipation of a shortage and is likely to result in inaccurate figures.

Observations on shortage data in Europe

As shown through our comparison of definitions and the quality of content within shortage reports, data is highly variable across European markets. There is no formal way to normalize for this variation, and as such the data on shortages should be regarded as limited/ low quality.

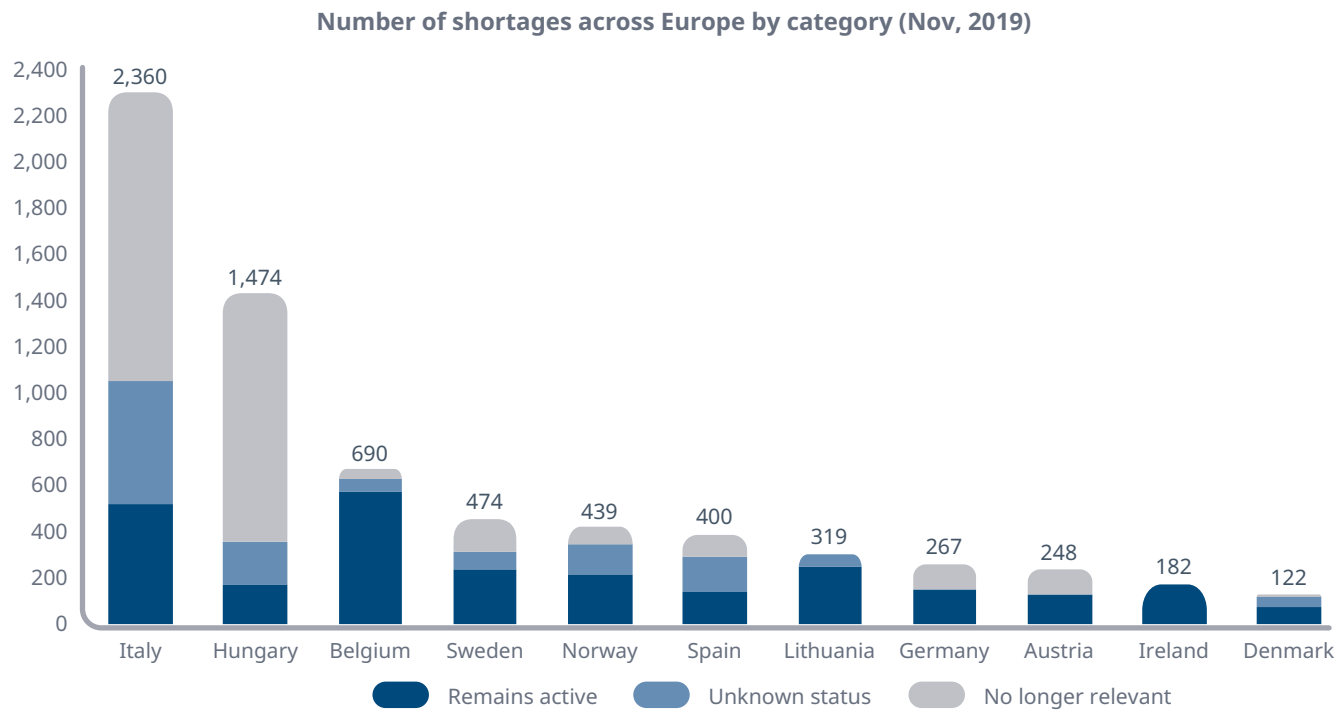
In order to highlight this, IQVIA cleaned the data as much as possible by a) relating one shortage to one SKU, and b) focusing on the 'active shortage list' (shortages started after the 1st of January 2019 and not being resolved by 31st of August 2019). Without doing this, the shortages range from 100 to over 2,300 within European countries. From this, IQVIA analyses determined a number of valuable insights that have not yet been shown in the context of the shortage discussion. The following analysis focuses on the "active shortage list" of the 11 representative countries and notes 5 observations.

1. SHORTAGES ACROSS EUROPE VARY 10-FOLD, BUT NOT ALL SHORTAGES ARE CREATED EQUAL

The number of shortages varies between countries from 120 to over 1,000 products if all shortages are truly active (Figure 4). The length of the shortage could only be evaluated in 7 of the countries from the data in the shortages list due to the fact that countries do not consistently report a predicted "end date" of the shortage. The variability is very high, and although it is uncommon to see shortages of critical medicines for over 2 years, there are numerous instances where shortages over 2 years long are reported. This figure will be highly influenced by the definition of shortages and how countries comply with the regulation, and the frequency of reporting.

A further complication is the blurred line between discontinued and temporary out-of-stock drugs. For example, Italy and Hungary include SKUs which were reported to be in shortage in 2014 with a planned resolution in 2020, reflecting a (temporary) withdrawal from the market than an actual shortage. This means that a shortage in one country is rarely equivalent to a shortage in another country.

Figure 4: Publicly available shortages across study cohort of 11 EU markets, broken down by status



Source: "IQVIA Global Supplier & Association Relations analysis of publicly available shortage reporting databases
Notes: No longer relevant determine by being on the list for >2 years, versus unknown / not provided dates, or recently added shortage medicines (shortages that started after 2019 and remain unresolved).

2. ACCORDING TO CURRENT DATA, THERE ARE NO PAN-EUROPEAN SHORTAGES

Figure 5 shows that a very limited number of products have a general shortage issue across Europe. In most of these cases the background is known and is quality-problem oriented. However, it would be expected to see these shortages in almost all countries, highlighting the issue of incomplete reporting. The high number of single country or very few country shortages infers that the source of the problem may be planning related, but this analysis has not validated the sales of the products in other countries.

The case of ranitidine is a perfect example of how shortage reporting is confounding the true situation. Ranitidine has been requested to be withdrawn in Europe and US in 2020, removing all prescription and over-the-counter (OTC) ranitidine drugs from the market formally due to the presence of low levels of an impurity called N-nitrosodimethylamine (NDMA).[11,12] The recall began in 2019 with OTC products first, and it is clear this product is not a true shortage but is counted in the statistics as such. It is therefore unsurprising that it is unavailable in 10 of our 11 countries studied.

Figure 5: Top-15 molecules noted upon publicly available shortage lists by number of countries where they are in shortage

	MOLECULE	NUMBER OF COUNTRIES	NUMBER OF SKUS
>5 countries	ranitidine	10	43
	losartan	7	40
	valsartan	6	31
	ibesartan	6	25
	clotrimazole	6	16
≤5 countries	paclitaxel	5	28
	alendronate	5	16
	quetiapin	5	15
	olmesartan	4	37
	telmisartan	4	20
	venlafaxin	4	18
	naproxen	4	18
	ibuprofen	4	13
	pregebalin	3	24
	methotrexate	3	14

Source: IQVIA Global Supplier analysis of publicly available shortage reporting databases

"The number of shortages varies between countries from 120 to over 1,000 products if all shortages are truly active"

3. THE MAJORITY OF SHORTAGES ARE GENERIC PRODUCTS WITH ALTERNATIVE MANUFACTURERS

In order to understand the impact of shortages, it is important to understand their patent status. This would infer whether potential other manufacturers would be able to resolve a shortage reported by a marketing authorisation holder. Our breakdown of the patent status of medicines (Figure 6) reported as shortages is vital in viewing the impact:

i. Only 1% – 8 % of the SKUs reported in shortage are 'Protected' drugs

Products with patent protection, and therefore with no direct alternative, represent a small proportion of total reported shortages, and lower than many would expect. Manufacturers have high financial incentive to secure the availability of these products, and therefore manufacturing for both API and finished products is likely well controlled. Parallel export is said to be a major reason for these protected product shortages, yet there are many confounding factors that make drawing such a conclusion potentially unreliable:

a) The method of shortage reporting (MAH-reported) record instances of 'restricted availability' rather than 'no availability' for such products, which could underestimate the numbers;

b) An export ban or pre-approval required list is mitigating the shortage problems in countries that utilise this strategy, however countries with a very high per capita export, like Norway, and no export ban list show few shortages in this segment.

c) Depending on market, these products can have parallel import available as alternative. Of the patented protected products, 2 molecules are reported as having shortages in >2 of the 11 countries, which shows that such shortages could be resolved in many cases by responsible practices by parallel exporters.

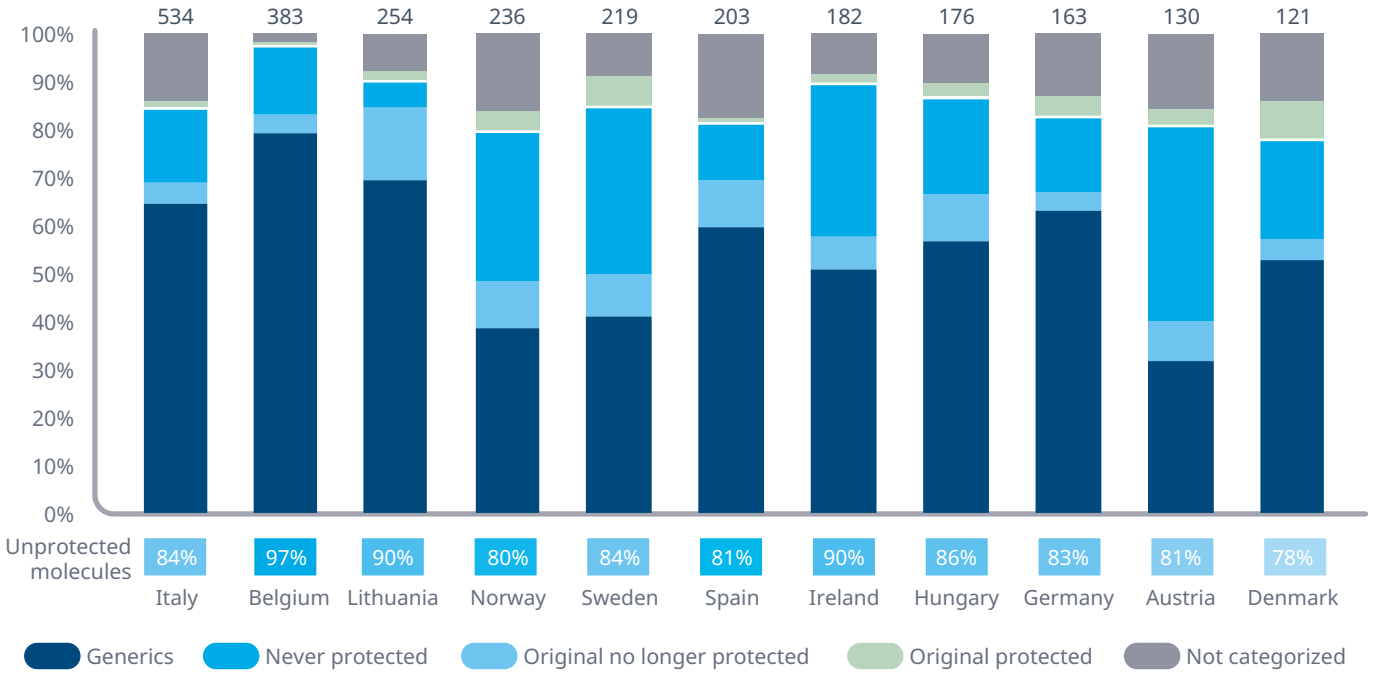
ii. 5% - 40% of the reported SKUs are 'No Longer Protected' original products

70% of these 'no longer protected, original products' have alternative generics or parallel import products. Most of these products are not the same between markets (only 4 molecules were missing in more than 5 countries) and can in some cases account for small volumes but create true patient problems when they do not have an alternative.

iii. More than half (52% - 79%, dependent on country) of the SKUs in shortage are generic products

In this category there is likely significant under-reporting due to manufacturer compliance, but in the majority of cases the results show that these drugs reported as in shortage can be interchanged for the same product manufacturer by an alternative manufacturer. The majority generics in shortage are 'multisource products' (i.e. with an alternative available), either the original product or a generic alternative.

Figure 6: Number of SKUs in shortage on a country level, categorized by their protection status



Source: : IQVIA Global Supplier & Association Relations analysis of publicly available shortage reporting databases
Notes: The countries are ordered by the total number of SKUs missing from the market.

From a medical point of view, these shortages are harder to interpret for seriousness. The fact that there are multiple manufacturers producing this product means that, if the product is available, then there should be no patient harm (excluding delays to treatment). However, there is a considerable risk however when the alternative product does not have the capacity to cover the need and/or when the alternative manufacturer does not report diligently. This links back to the importance of aligned definitions and quality of reporting, and the value of visibility to inventory.

iv. Payer driven restrictions for substitution can aggravate the situation.

Netherlands and Germany have tendering per Insurance Company and Sick Fund. This generates a situation where multiple products need to be available for the same contract and it seems to generate more reported shortages. Denmark and Sweden tender but with very short tender period of 2-weeks each month. Manufacturers only tender if they already have stock and it appears that this system generate very few shortages.

Crucially, a manufacturer does not have visibility to the inventory of other manufacturers who make the same molecule. It makes resolution complex, and also means that a shortage recorded in this instance is not a true shortage. Swedish data suggests that many SKUs have zero sales and are likely to be 'not available' but are not reported; this is good practice to vet the shortage list appropriately. Visibility to inventory from a competent authority, which would show the molecule supplied by another manufacturer, would be a highly desirable and remove a non-issue that is created by nuances of the EMA's definition.

4. CARDIOVASCULAR AND NERVOUS SYSTEM PRODUCTS ARE MOST FREQUENTLY IN SHORTAGE ACROSS EUROPEAN COUNTRIES

The main therapeutic classes affected by shortages seem to be consistent between the different countries (Figure 7). ATC C (Cardiovascular) is the most prevalent in the 11 countries. This can be due to several different factors; the primary factor being the ripple effect of a shortage in a class of medicines such as antihypertensives, where prescribers will simply shift directly to another product with similar mechanism of action. It is likely that this is causing direct impact at the patient level.

ATC N (Nervous system) is the second most affected medicinal group. This includes antiepileptic,

Figure 7: SKUs in shortage by ATC class in each country's market

COUNTRY	ATC C CARDIOVASCULAR	ATC N NERVOUS SYSTEM	ATC L ANTI-NEOPLASTIC	ATC A ALIMENTARY TRACT & METABOLISM	ATC J ANTI-INFECTIVES	ATC M MUSCULO-SKELETAL
Italy	134	91	75	47	51	15
Belgium	103	83	36	38	26	36
Lithuania	56	30	33	27	32	18
Spain	36	51	29	25	20	11
Norway	32	46	5	27	24	32
Ireland	63	24	12	15	21	11
Sweden	14	58	7	21	24	21
Germany	13	56	21	18	18	8
Hungary	55	28	5	18	15	12
Denmark	11	24	34	10	14	6
Austria	27	14	12	22	17	5
Total	**544**	**505**	**269**	**268**	**262**	**175**

Source: IQVIA Global Supplier & Association Relations analysis of publicly available shortage reporting databases
Notes: Principal medicine groups experiencing shortages among the European Market.
At the bottom we have the sum of SKUs missing from each medicine group.

Low High

antipsychotic and antidepressant drugs. These medications are often more difficult to be interchanged as patients with mental illnesses rely a lot on the placebo effect and an alternative may affect the treatment.

Although some medicinal classes are more commonly affected across European countries, a limited number of products face shortages across several markets. A primary supply problem for one product in a class can increase the demand for alternative products, leading to shortages due to increased demand. We can also see that it is not the same drugs, or the same manufacturers driving shortages in different countries.

5. HALF OF THE TOP-20 PHARMA COMPANIES REPORTED ≤5 PACKS IN SHORTAGE

The majority of top European pharma companies have few SKUs in shortage (Figure 8). As shown previously, the majority of shortages are generic products, and therefore companies with the highest reported numbers are unsurprisingly large generic manufacturers with broad portfolios based in primary care. In the study sample, the top 3 generic companies (Mylan, Sandoz and Teva) together accounted for around 25% of all SKUs in shortage.

Generic companies often have portfolios which are much broader than the portfolios of an innovative manufacturer. For example, the top-10 generics manufacturers by Rx sales in 2020 have an average of over 400 molecules within their portfolios,[15] not considering the multiple product / form / strength combinations that are produced. It should also be noted that throughout this paper we have shown areas of under-reporting from other segments, nuances with wording, and therefore would advise against drawing a conclusion that shifts onus onto generic manufacturers. As we have seen throughout this paper, the reported shortage data requires a much more nuanced conclusion.

As we analysed the data it became clear that the available shortage data have several weaknesses. The existing reporting of shortages based on MAH reports is not indicative of the reality.

We identified the following key issues – see Figure 9 below:

Figure 8: Number of SKUs in shortage for top-20 European pharma companies

NUMBER OF SKUS IN SHORTAGE	NUMBER OF COMPANIES
≤5	10
>10	2
>25	4
>50	3
>100	1

Low High

Source: IQVIA Global Supplier & Association Relations analysis of publicly available shortage reporting databases
Notes: Company names have been removed for confidentiality, and for the reasons discussed before regarding reporting bias. Ranked by European sales Q4 MAT 2019.

Figure 9: Key issues with shortage reporting

Under-reporting

It is likely that some manufacturers of multi-source products are not reporting shortages in all cases, and parallel importers are not obliged to report them.

Over-reporting

Many countries have very long shortage lists; partly due to discontinued products being reported as shortages when they should be considered a separate issue, or regulation leading to precautious over-reporting.

Incompleteness

The fact that the majority of the countries have not put in place a strict regulation for drug shortage reporting results in a significant inadequacy of information that further complicates the resolution of this problem.

Source: Global Supplier & Association Relations analysis. See appendix for further details.[14]

The future of the shortage issue

DESPITE POOR DATA, BEST-IN-CLASS COUNTRIES DO EXIST AND LEARNINGS CAN BE TAKEN

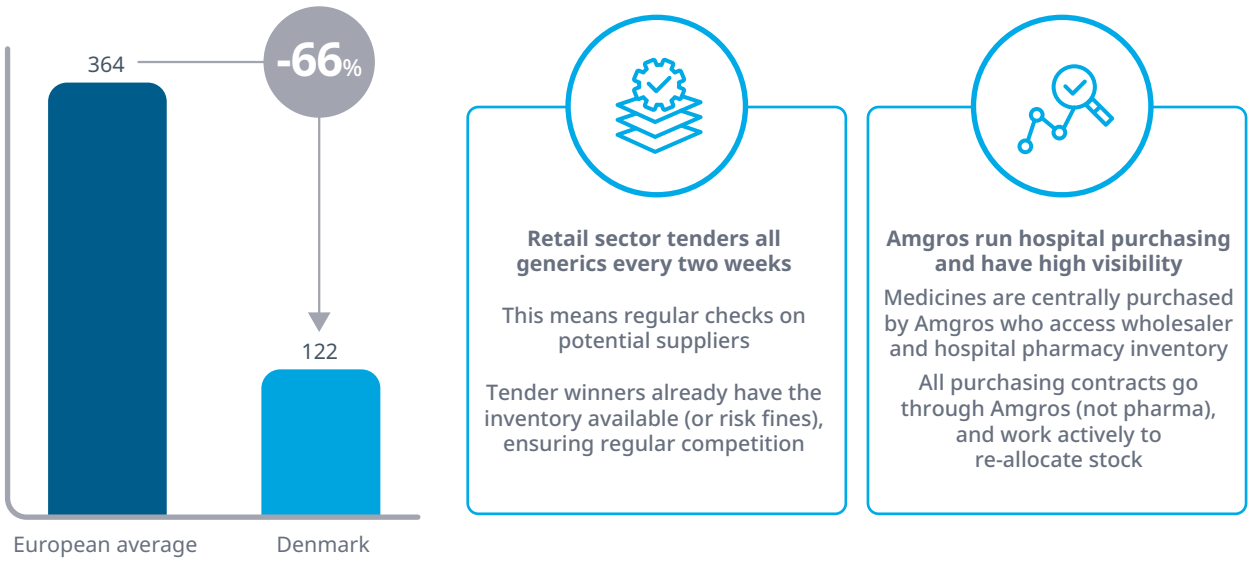
Even if shortages are a problem in many countries, some countries such as Denmark appear to be managing supply more efficiently, and as such the patient burden is minimal. Denmark has one of the lowest level of shortages (Figure 10). This indicates that the way of identifying potential shortages, ordering, and follow-up has a significant impact. In Denmark, Amgros manages the supply, and are active in system-wide management with two critical points:

1. **Provision of suppliers with an estimate of the expected demand at SKU-level**
    - Estimates are adjusted when the hospitals expect significant changes in demand, and suppliers are asked to confirm supply capability according to the latest estimate.
2. **National-level follow-up on all backorders**
    - Investigation of inventory levels versus expected volume during the backorder period (normally hospital pharmacies inventory cover 2-week consumption, for critical products inventory should cover 8 weeks), checks on availability of alternative products, if an alternative is needed, and dialog with the Danish Medical Agency in those cases where medicines require importation.

Our work suggest that the best-in-class approach in combatting shortages is a combination of:

- Good forecasting of demand on the level of groups of interchangeable products
- Visibility of inventory across stakeholders with appropriate commercial sensitivity
- Devolved, or clear responsibility for an organisation to lead the initiative

Figure 10: Danish system case study summary



Source: IQVIA Global Supplier & Association Relations analysis of publicly available shortage reporting databases

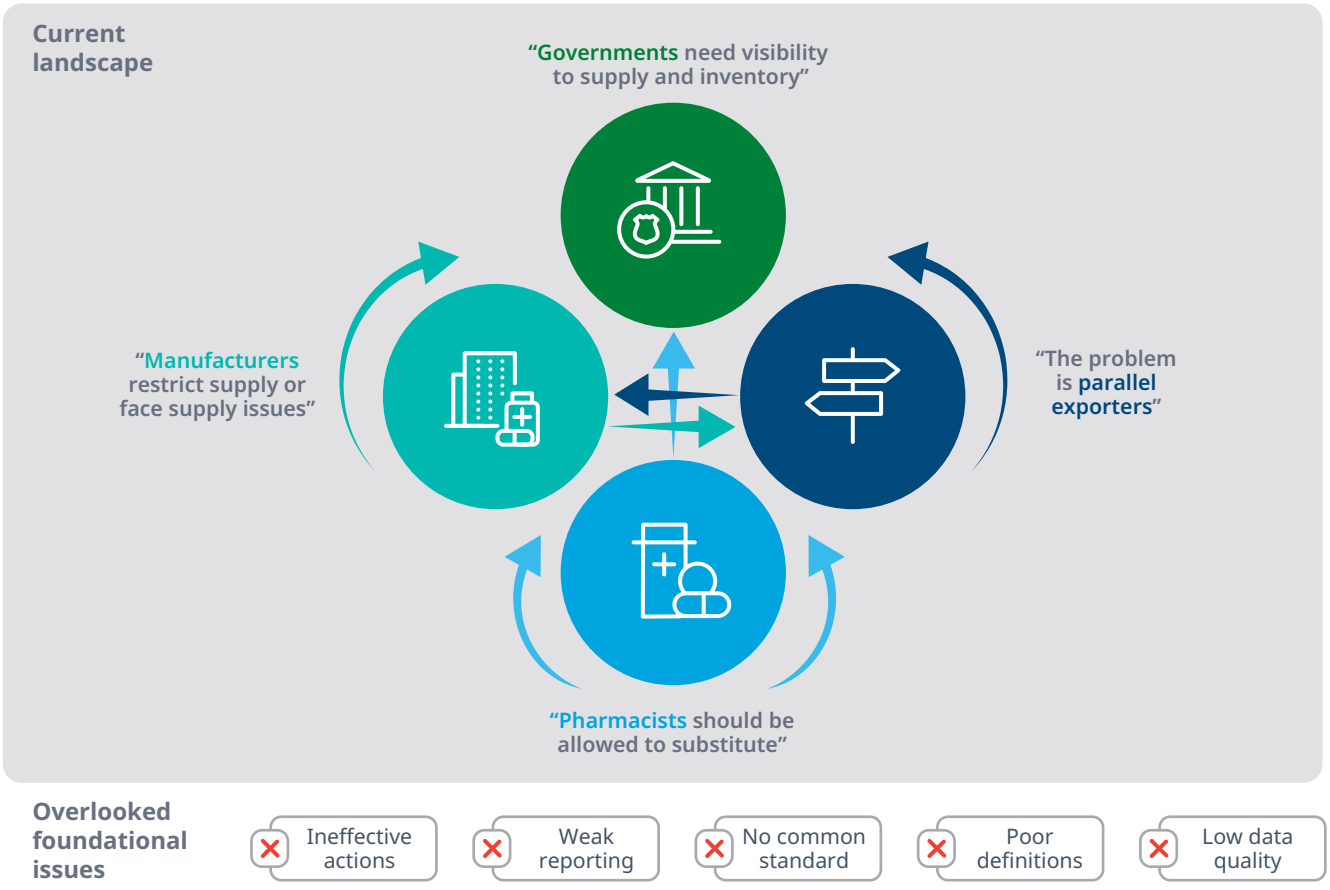
THE DATA DOES NOT YET SUPPORT RELIABLE INSIGHTS INTO CAUSES, INSTEAD HIGHLIGHTING AREAS FOR IMPROVEMENT

Previous work into the cause of shortages has been entirely dependent on the perspective of the stakeholder publishing and has resulted in additional complexity in determining true causes. Comparing these various position statements over recent years shows that a 'blame-game' is in process within the supply chain. Based on the insights on the quality of the shortage data, we cannot conclusively put a position of blame on any stakeholder. In reality, the variety of shortage perspectives is built upon a number of 'foundational issues' which are responsible for the differing, yet valid perspectives (Figure 11).

Our findings therefore suggest that the situation is more complex. For example, if a product is inter-changeable, then which manufacturer is responsible for resolving the shortage? If it is a single source product, does the manufacturer have the right information and is the product economically viable?

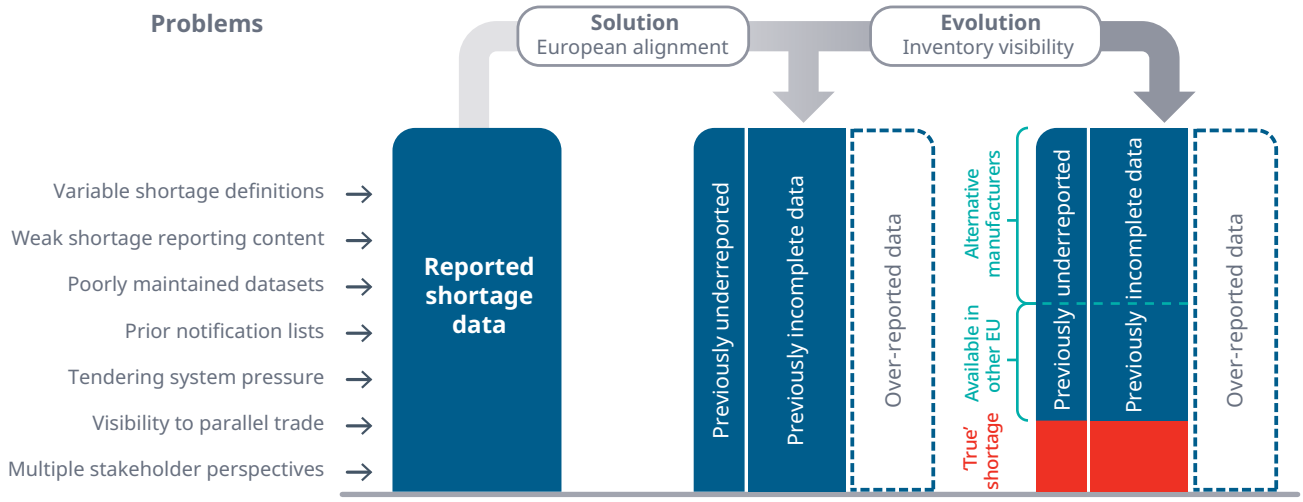
At present, our analysis shows we are battling against a 'blurred view' of the shortage issue which is driven by a number of confounding factors (see illustration in Figure 12). To remove the blurred lines between markets, there is an undeniable need for European alignment / harmonisation in requirements as called for by numerous key stakeholders.[15,16] This would allow the quality of the data on shortages to increase dramatically, and support resolutions into root causes. However, transparency of inventory would be a valuable tool in the fight against shortages by giving a competent authority visibility to the 'true' shortages and ensuring that the shortage list can be cleaned with

Figure 11: Illustration showing the differing perspectives on the cause of shortages according to public statements



Source: Global Supplier & Association Relations perspectives
Notes: Arrows are illustrative of public statements on the cause of shortages in published documents by trade associations between 2018 - 2020

Figure 12: Illustrative example of the issues with current reported shortage data



Source: Global Supplier & Association Relations perspectives

greater accuracy. Alternative measures are available to show exchange group level transparency of inventory which would shield what an individual wholesaler or manufacturer would be able to see within an exchange group, to avoid issues related to competition.

This highlights the complexity of drawing valuable conclusions on the quality of data and variable definitions we have available through the publicly available, marketing-authorisation holder reported shortage data, which is the best cross-country comparison available at present.

Conclusion

Our work suggest that the best-in-class approach in combating shortages is a combination of good forecasting of demand on the level of groups of interchangeable products, visibility of inventory across stakeholders with appropriate commercial sensitivity, and devolved, or clear responsibility for an organisation to lead the initiative.

References

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3 GIRP Reflection Paper: Medicine Shortages in Europe and their Impact on Patients; http://girp.eu/sites/default/files/documents/girp_medicine_shortages_reflection_paper.pdf

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8 Shortage database reporting definitions (see Figure 13 on opposite page)

9 EMA/674304/2018; https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guidance-detection-notification-shortages-medicinal-products-marketing-authorisation-holders-mahs_en.pdf

10 Läkemedelsverket, Swedish Medical Products Agency; Dnr: 4.3.1-2019-068169 Läkemedelsverket, 2020-01-30

11 FDA; https://www.fda.gov/news-events/press-announcements/fda-requests-removal-all-ranitidine-products-zantac-market

12 EMA; https://www.ema.europa.eu/en/medicines/human/referrals/ranitidine-containing-medicinal-products

13 IQVIA MIDAS Corporation data, ranked by sales value, Q1 2020 (accessed August 2020)

14 Notes: Discontinued products (which have been withdrawn from the market) are normally discontinued due to lack of economic viability for the manufacturer and this needs to be looked on separately – is there a viable alternative, is the product really needed from a medical point of view and is the price too low.
An additional reason for over-reporting is that some counties (Netherlands, Italy) have applied regulations that manufacturers must report upcoming supply chain issues at an early stage (2-3 months in advance) or face fines. This regulation could lead to a precautious over-reporting of drugs, that may encourage the pharmacists to stock up on specific products and subsequently cause a true shortage.

15 FIP addressing global medicines shortages; https://www.fip.org/Medicines-shortages

16 GIRP press release, 2019: Addressing the root causes of medicines shortages; https://www.efpia.eu/media/413378/addressing-the-root-causes-of-medicines-shortages-final-051219.pdf

Figure 13: Shortage database reporting definitions

COUNTRY	SCOPE OF SHORTAGE REPORTING	MEDICAL AGENCY
Austria	A notification must be made by the MAH when a prescription-only medicine has or is expected to have limited availability (the product can no longer be supplied continuously and in sufficient quantities by pharmacies in Austria) for more than four weeks or no availability (the product can no longer be dispensed by pharmacies in Austria) for more than 2 weeks	*BASG; https://www.basg.gv.at/en/companies/online-services/guidance-notes/faq-meldung-vertriebseinschraenkung?sword_list%5B0%5D=shortage
Belgium	A temporary shortage is when the MAH cannot deliver the product to meet demand within 3 working days	*FAMHP; https://www.famhp.be/en/items-HOME/unavailability_of_medicinal_products
Denmark	The MAH must report any supply difficulties that they deem risk affecting the treatment of patients in Denmark	Laegemiddelstyrelsen; https://laegemiddelstyrelsen.dk/da/godkendelse/kontrol-og-inspektion/alvorlige-forsyningsvanskeligheder/
Germany	A supply shortage is an interruption of delivery that is expected to exceed 2 weeks, or a significantly increased demand that cannot be adequately met	Bundesinstitut fur Arzneimittel und Medizinprodukte; https://www.bfarm.de/DE/Arzneimittel/Arzneimittelzulassung/Arzneimittelinformationen/Lieferengpaesse/_functions/Filtersuche_Formular.html?nn=11296612
Hungary	A shortage is any discontinuation of adequate supply, when the MAH is unable to maintain steady supplies	*OGYEI; https://www.ogyei.gov.hu/hiany_bejelentes
Ireland	A shortage is when the supply of a medicinal product is inadequate to meet the needs of the patient	HPRA; http://www.hpra.ie/homepage/medicines/medicines-information/medicines-shortages
Italy	A temporarily deficient drug is when a medicine cannot be found throughout the country, as the marketing authorization holder cannot temporarily guarantee an appropriate and continuous supply	AIFA; https://www.aifa.gov.it/en/web/guest/farmaci-carenti
Lithuania	Marketing authorisation holders and holders of parallel import authorizations are requested to provide information on temporary and permanent supply disruptions of medicinal products	VVKT; https://vvkt.lt/index.php?3520160586
Norway	The MAH must notify the authority if the product ceases to be placed on the market, either temporarily or permanently	Statens Legemiddelverk; https://legemiddelverket.no/english/regulatory-affairs/notification-of-marketing-interruption-of-a-medicinal-product-in-norway-including-withdrawal
Spain	A supply problem is a situation in which the available units of a medicine in the pharmaceutical channel are less than the national or local consumption needs.	AEMPS; https://www.aemps.gob.es/distribucion-de-medicamentos/problemas-de-suministro-de-medicamentos/?lang=en
Sweden	Notifications must be made when residual listings (lack of deliveries) are expected to exceed 3 weeks, or when residual listings are shorter then 3 weeks but may entail patient safety risks.	Läkemedelsverket; https://www.lakemedelsverket.se/sv/behandling-och-forskrivning/forskrivning/restnoteringar

* indicates definitions supplemented by agency correspondence
Source: IQVIA Global Supplier & Association Relations analysis 2020; Q4 2019 data

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