

Mapping the antibiotic market in Denmark, Finland, Norway and Sweden – focus on clinically important antibiotic with a risk of insufficient availability

Summary

PLATINEA and the Public Health Agency of Sweden have mapped the antibiotic market for clinically prioritized antibiotics that have been assessed as having a risk of insufficient availability in the Nordic region. Experts from Denmark, Finland, Norway and Sweden contributed. The analyses focused on the analytical dimensions market isolation, product range variety, market fragmentation and supply risk, which indicate challenges to the availability and sustainable provision for specific formulations of listed antimicrobial substances. In addition a by-country analysis was performed. The present mapping is intended as a basis for decision-makers to identify possible measures to strengthen the Nordic antibiotic markets. The results disclose noticeable differences in products available and considerable market fragmentation between the Nordic countries despite similar low levels of antibiotic resistance and likely similar medical needs, and indicates great potential for harmonization. A comprehensive analysis of the market may be of value in order to identify market challenges for specific clinically prioritized formulations of medicinal products.

Background

Access to recommended antibiotics, including many older antibiotics, is crucial to being able to treat infections effectively while slowing down the emergence and spread of antibiotic resistance in individuals and society. Shortages of important medicinal products where alternative treatments are suboptimal, are frequently seen for products mainly used in small markets and with vulnerable supply chains. Unfortunately, currently clinicians and patients in the Nordic countries and elsewhere face increasing episodes of shortage situations as well as permanent withdrawals from the market of important antibiotic products threatening a sustainable supply. This is a particularly serious problem for paediatric formulations. A prerequisite to address this issue is a thorough analysis of the antibiotic market in the concerned region. Therefore, in this report we map and analyse the antibiotic market in the four largest Nordic countries, as a way to support other measures aimed to increase the resilience of the market and supply of important antibiotic products.

Absence of the preferred treatment can affect the patients and society at different levels. While shortages of *substances* and *formulations* often are referred to as most critical, this survey also focuses on different *strengths* and *package sizes* of a given product, which can be of great importance to the patient, and from an antimicrobial stewardship perspective.

The Nordic countries have relatively low levels of antibiotic resistance, which allows narrow-spectrum antibiotics to be used. Each of these countries are commercially small markets and prices of older products are often low. Despite likely similar medical needs, the Nordic countries occasionally use different but similar substances and many times different strengths and package sizes of identical substances for treating the same type of infection, further fragmenting already fragile markets. The Nordic countries experience repeated shortages and this study is an attempt to highlight some of the market challenges that may be contributing to this.

This survey aims to map the antibiotic market in the Nordic region, here represented by Denmark, Finland, Norway and Sweden with a focus on medically prioritized products that are at risk of insufficient availability in one or several Nordic countries. The objective is to produce a basis for authorities and politicians, as well as for decision-makers in healthcare and companies, to be able to identify opportunities for harmonization and synergies. A more coordinated antibiotic market in the Nordic countries could potentially lead to more resilient supply and thus a more sustainable access.

Collaboration within Platinea and with Nordic countries

A working group in [PLATINEA](#) in collaboration with the Public Health Agency of Sweden conducted an analysis to map the availability of antibiotics considered clinically important and having a vulnerable supply, such as being exposed to frequent shortages or perceived to have risk for deregistration, in the four largest Nordic markets, namely Denmark, Finland, Norway and Sweden. Iceland was not included in this mapping partly due to that it is a very small market and practice a simplified registration system enabling an easier access to drugs registered in EU countries. The data were collected from April to October 2023. The original information source to identify the products marketed in each country was MIDAS, a system collecting detailed sales data. However, sales data are not displayed in our analysis, due to confidentiality and because the aim of our survey was simply to identify which products are sold in each country, not their sales volumes. Representatives (clinical experts) from each included country were repeatedly given the opportunity to correct and supplement, and to comment on whether the product (1) was formally registered and marketed, or prescribed on a named patient basis (not included in the present survey), and (2) was considered critical to have access to.

The starting point of the present survey was those substances/ formulations/ strengths that the Public Health Agency of Sweden had already officially classified as [Category A](#), that is, products with a high risk of shortages and/or withdrawal, based on low sales volume, and judged to cause major clinical consequences if not available. After building a comprehensive database, the excel file was shared with the other participating countries who were invited to add additional substances/formulations they considered as critical and vulnerable, that is would match the Swedish Category A list. Clinically prioritized antibiotics corresponds to those recommended as first choice for treatment of major infection types, or considered essential for a small patient cohort. For each substance/formulation, all marketed strengths and package sizes were stated.

The additional products proposed by the other countries helped create a final excel file, containing information on specific antibiotic products (substance, formulation, strength and package size), as well as in which countries each product is being sold. Next to the Swedish team performing the analysis, representatives for each of the other countries (Denmark, Finland and Norway) were appointed in consultation with the Swedish Medicines Agency. Thus, all formulations of the antibiotic substances finally included in the document for analyses, were considered as clinically prioritized with perceived risk for insufficient availability.

We applied the following key dimensions in our analysis in order to identify market challenges for specific formulations of listed antimicrobial substances; *1) Market isolation*, that is, the substance, formulation, or package size is marketed in only one of the four countries or, if the formulation is marketed in multiple countries, at least two package sizes are marketed in only one country; *2) Product range variety*, that is, an antibiotic substance is marketed in the Nordic region in a large number of strengths or pack sizes for each formulation (in this survey, clinically unmotivated was defined as 5 and more strengths or 7 package sizes per formulation); *3) Market fragmentation*. For antibiotic formulations marketed in multiple countries and with at least 3 package sizes in total, high market fragmentation refers to when more than 50% of these package-sizes are marketed only in a single country. And *4) Supply risk*, i.e. only one market authorization holder (MAH) markets a given formulation in the Nordic region (Supplement 2).

This quantitative analysis was then combined with a clinical assessment by three infectious disease doctors representing three large regions in Sweden, who highlighted 1) substance or formulations that were considered to be clinically prioritized in the Nordic countries but not necessarily in the rest of Europe, and 2) prioritized and with vulnerable availability in any of the Nordic countries but globally widely sold products. The substances were also compared against the [WHO classification of Access, Watch and Reserve](#).

The survey was related to a government assignment to three Swedish authorities, the Public Health Agency, the Medicinal Product Agency and The Dental and Pharmaceutical Benefits Agency (TLV), [Strengthen access to older antibiotics](#), which was completed in November 2022 and on two Norwegian reports published [June 2019](#) and [March 2022](#).

Results

We identified a total of 36 antibiotic substances marketed in the Nordic region, available in a total of 68 formulations, with various number of strengths and package sizes. All are detailed in a complex database, here called "the master file" (Supplement 1). For each substance, the master file includes a sheet with all formulations that were considered prioritized and vulnerable from a medical and accessibility perspective in at least one of the countries at the time of the mapping. These listed products were marketed in at least one of the four countries and are listed with all respective strengths and pack sizes, including substance name and

information of MAHs. As the antibiotic market constantly evolves, the master file reflects the situation in October 2023. Parallel imported products and companies were excluded from our analysis, since this type of sales is considered more uncertain and tend to diminish when financial conditions are less favourable.

Supplement 1. Masterfile.



Masterfile Nordic
survey.xlsx

In order to get a better overview of the four selected Nordic antibiotic markets, results from the master file were synthesized into a compiled table focussing on the analytical dimensions of market isolation, product range variety, market fragmentation and supply risk, which indicate challenges to the availability and sustainable provision of the various products (Supplement 2).

Supplement 2



Compiled data of
the Nordic antibioti

Of the 68 formulations of substances categorized as prioritized in the Nordic countries, 19 was considered as relatively small products from a global perspective or with only one MAH providing a given registered formulation in the Nordic region, according to the clinical evaluation described in the Method section. Seven of these 19 are oral suspensions, mainly aimed for small children. These 19 formulations are presented in Table 1, including data regarding market isolation, product range variety, market fragmentation and supply risk.

Table 1. Clinically prioritized formulations of substances in the Nordics categorized as having a vulnerable availability

Substance	Formulation	No of countries (Market isolation)	No of strengths (Product range variety)	Package-sizes per formulation (Product range variety)	Unique package-sizes in a single country (Market isolation)	Countries with one MAH per formulation	No of MAH in the Nordics (Supply risk)
Amoxi/Clav	IV	1	1	1	1	DK	1
Bensylpenicillin	IV	4	6	6	3	DK, NO	3
Cefadroxil	Oral susp	1	1	1	1		2
Cefadroxil	T/K	1	2	4	4		3
Cefuroxim	T/K	1	1	2	2		2
Ciprofloxacin	Oral susp	1	1	1	1		4
Dicloxacillin	T/K	2	2	4	1	NO	4
Doxycycline	Oral susp	1	1	1	1	SE	2
Phenoximethylpenicillin	Oral susp	4	3	5	2	FI, NO	4
Phenoximethylpenicillin	T/K	4	10	41	33	FI	11
Flucoxacin	Oral susp	1	1	1	1	SE	1
Flucloxacilin	T/K	3	4	11	3	FI	2
Cloxacillin	IV	4	2	3	1	FI, SE	5
Linezolid	Oral susp	1	1	1	1	SE	1
Nitrofurantoin	T/K	3	2	5	1	DK, NO	3
Nitrofurantoin , Vit C	T/K	1	1	3	3	FI	1
Pivmecillinam	T/K	4	2	10	2		2
Rifampicin	Oral susp	1	1	1	1	SE	1
Trimetoprim-sulfamethoxazole	IV	1	1	1	1	SE	1

Analysis of the mapping

Several market challenges were identified. By combining the analyses described above, we identified the following (Supplement 2):

Market isolation

Almost 50% of the 68 formulations are characterized by market isolation, in the sense that they are available only in one country (11 products), or, if marketed in multiple countries, at least two among multiple package sizes are available in only a single country (21 formulations). These products characterized by “isolated” markets comprise 32 unique formulations of 23 listed substances. Although considered as clinically prioritised in the Nordic countries, about half of these are considered being small products in a global perspective (Table 1), which potentially aggravates the isolation of these markets.

Of a total of 15 oral suspensions listed in the current survey, 10 are categorized as exposed to market isolation, further emphasizing the vulnerability of paediatric formulations.

Product range variety and Market fragmentation

High product range variety among the four Nordic countries was observed. The analysis revealed three formulations marketed in at least five strengths (amoxicillin, phenoxymethylpenicillin and bensylpenicillin) in 5-41 pack-sizes each, and 10 additional formulations marketed in 7-12 different package sizes per formulation.

Large market fragmentation among the Nordic countries, according to the definition above, was seen for 7 substances/formulations (amoxicillin/clavulanic acid, ampicillin, cephalexin, ciprofloxacin, erythromycin, phenoximethylpenicillin, and gentamicin).

Furthermore, common tablet strengths of amoxicillin, phenoxymethylpenicillin, flucloxacillin and pivmecillinam have an unexpected fragmented market, related to number of pack-sizes marketed in the four countries (10-41). At the same time, concerning phenoxymethylpenicillin, only Sweden has the stronger strength of oral suspension registered, as well as the small tablet aimed for children.

Supply risk

Of the 68 listed substances/formulations, 12 formulations are marketed by a single MAH across Denmark, Norway, Finland and Sweden, making them especially vulnerable for shortages. Seven of these 12 substances are classified as “Access” by the WHO. However, 28 substances (in 51 formulations) of the in total 36 substances listed by the Nordic countries in the current survey, are clinically considered as also globally important and wide-spread and are therefore not threatened in a longer perspective. Short- and medium term shortages in our countries cannot be ruled for nine of these 51 formulations in a situation of global shortages, since these nine formulations are marketed by a single MAH in all our four countries, which make their availability vulnerable.

By-country analysis

In some cases, different but relatively interchangeable substances are used in the different countries, for example cephalexin is used in Denmark, Finland and Norway, while Sweden uses cefadroxil. In Denmark and Norway, dicloxacillin is marketed, which is not available in Sweden or Finland where flucloxacillin is used. It was also noteworthy that some formulations of

certain substances are not marketed at all in some of our countries. For example, there is no formulation for intravenous use of metronidazole in Finland; in Denmark, parenteral and oral formulations of trimethoprim-sulfamethoxazole or parenteral vancomycin are not marketed; and moxifloxacin, rifabutin and intravenous preparations of trimethoprim-sulfamethoxazole are missing in Norway. Amoxicillin-clavulanic acid for intravenous use is only marketed in Denmark. Two substances that particularly stand out are amoxicillin and phenoxymethylpenicillin, for which there is a high fragmentation regarding strengths, especially for the solid oral formulation. Both substances are widely marketed in the four countries, by a total of 14 and 11 MAH, respectively. Amoxicillin tablets are marketed in a total of five strengths and in 19 package sizes, nine of which are only available in a single country. Phenoxymethylpenicillin tablets are marketed in a total of 10 strengths and in 41 different package sizes, of which 33 in only in a single country.

Cefixime is not marketed in any Nordic country, but the need for this substance is expressed by experts both in Norway and in Sweden.

Denmark and Norway rely on a named-patient based prescribing for a number of products, with an emphasis on paediatric formulations, which is considered both unsafe for patients and resource-intensive. For example, in Norway, doctors are referred to a named-patient based prescription of levofloxacin and moxifloxacin, and of intravenously administered trimethoprim-sulfamethoxazole, as well as of doxycycline, both for intravenous administration and oral suspension. Access to tuberculosis drugs is also very limited in Norway, who also stresses the critical vulnerability of benzylpenicillin, a corner-stone for infection treatment with a high risk for insufficient supply.

Discussion and conclusions

The present survey of the antibiotic market in the Nordic region demonstrates that several products, often narrow-spectrum antibiotics, potentially face availability challenges due to fragmented markets and a vulnerable supply in the region. Urgent measures to increase the sustainability of access to important antibiotic products are needed, which calls for joint efforts from Nordic policy-makers and authorities. We introduce new concepts for analysis of access to marketed antibiotic products in a multi-country region with similar resistance pattern, such as market isolation, product range variation, market fragmentation and supply risk. This analytical approach aims to clarify the current situation and thereby support further actions to address this problem.

The mapping shows that access to important and vulnerable substances, formulations, strengths and package sizes of older antibiotics varies in the Nordic countries. In general, availability to children's formulations is often a problem, which was particularly highlighted by both Denmark, Norway and Sweden.

This survey was performed by a multisectorial collaboration platform consisting of competences from academia, authorities, industry and healthcare. Independent representatives from Denmark, Finland and Norway were involved in the survey. This approach ensured that views from the different sectors and countries were reflected throughout the process.

Notable is that the classification of prioritized products with vulnerable supply was not explicitly and jointly defined across the involved countries, but relied on the [Swedish priority list](#). This left open to a somewhat subjective judgement of which products to include in the survey. However, we also opted to let each country decide to include products nationally considered prioritized and vulnerable. Another limitation is that the present survey mirrors the situation in October 2023.

Differences in strengths and package sizes are strongly related to differences in practice guidelines including treatment durations for common infections. An example of fragmentation in strengths and package sizes that is highly related to treatment traditions is that phenoxymethylpenicillin tablets are marketed as milligram (mg) in Norway, Sweden and partly in Denmark, while as international units (IU) in Finland and Denmark.

As the Nordic countries have similar levels of antibiotic resistance as well as similar demography and infection panorama, harmonisation of treatment guidelines across the Nordic region would be highly desirable. This could be a route to a less fragmented antibiotic market, by reducing unnecessary product range variety and the occurrence of packages sold only in a single market. A possible way to improve the current market isolation may be to implement co-Nordic or electronic package leaflets, which would simplify sharing of products within our countries when needed. An even more powerful approach to strengthen availability to prioritized antibiotic products in the Nordics, could be to agree upon a co-Nordic regulatory system for older, nationally approved antimicrobials or medical products in general. This would render any product nationally approved in any of the Nordic countries, regularly permitted for marketing in the other countries. This approach would pave the way to larger and more attractive markets, but would require substantial amendments in current national regulations for medicinal products. However, the risk of unwanted withdrawals from the market because an MAH would face undesired competition should be considered.

In conclusion, this survey highlights the weaknesses of small markets like the antibiotic market in the Nordic countries. A comprehensive analysis of the market including key dimensions, such as market isolation, product range variety, market fragmentation and supply risk, may be of value in order to identify market challenges for specific clinically prioritized formulations of medicinal products.