

Recent issues on stable supply of APIs in Europe

Tokyo, April 2023
Marieke van Dalen, Aspen Oss B.V.
For APIC

Contents of this presentation

- Introduction
- Shortages: a global issue
- The missing link
- Strategies in Europe to decrease shortages
- Conclusion

Introduction

- Marieke van Dalen
- Working for Aspen Oss API in the Netherlands, an API producing site.
- Over 35 years of experience in the regulatory field
- Board member of APIC, a Technical European Industry Association, based in Brussels, with focus on APIs from a quality and regulatory perspective.
- APIC is the API observer in the ICH and is a recognized discussion partner for many authorities including Anvisa, EDQM, EMA and the FDA.

Shortages: a global issue

All around the world countries and regions are struggling with medicine shortages. In most regions there are frequent updates as to which medication is in shortage.

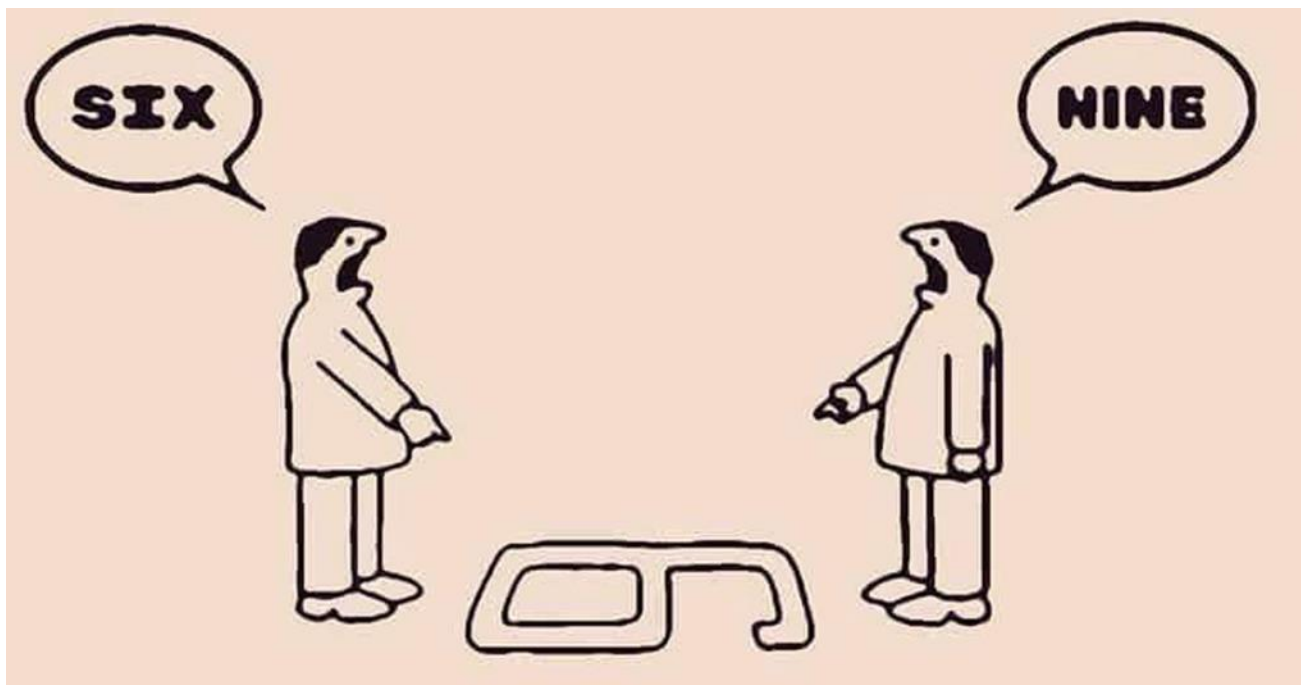
There are no figures on which API's are in shortage.

Nevertheless, a shortage of medication is often related to a disruption in the supply chain.

Shortages: a global issue

What is the global API supply chain?

It probably depends on who answers the question..



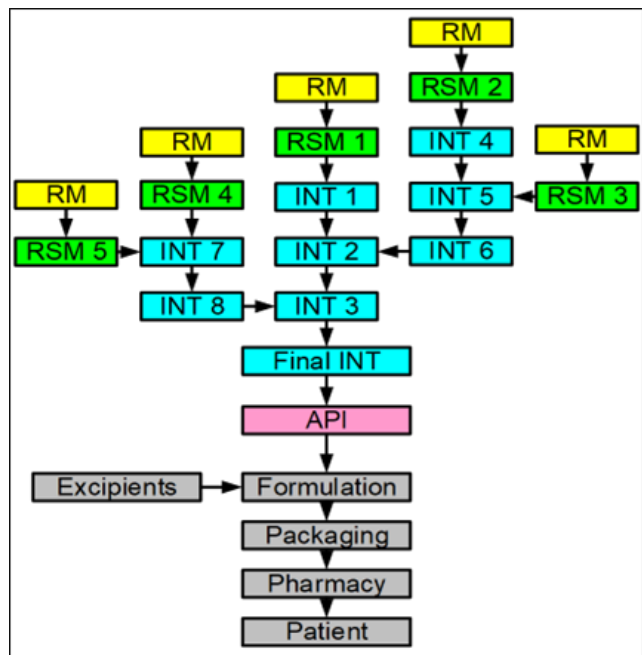
Shortages: a global issue



The patient probably only knows where to get the medicine, and who produces it. The patient has no knowledge of API manufacturers, excipients, raw materials...

Shortages: a global issue

From an API manufacturer's point of view, we also have a lot of focus on the first part of the supply chain.



The missing link

- Obviously, the supply chain involves all these steps and contributors.
- If any of the players in the scheme is not able to provide their material (regardless of whether this is a starting material, an intermediate in the API production, an API, an excipient), this may lead to a shortage.

The missing link

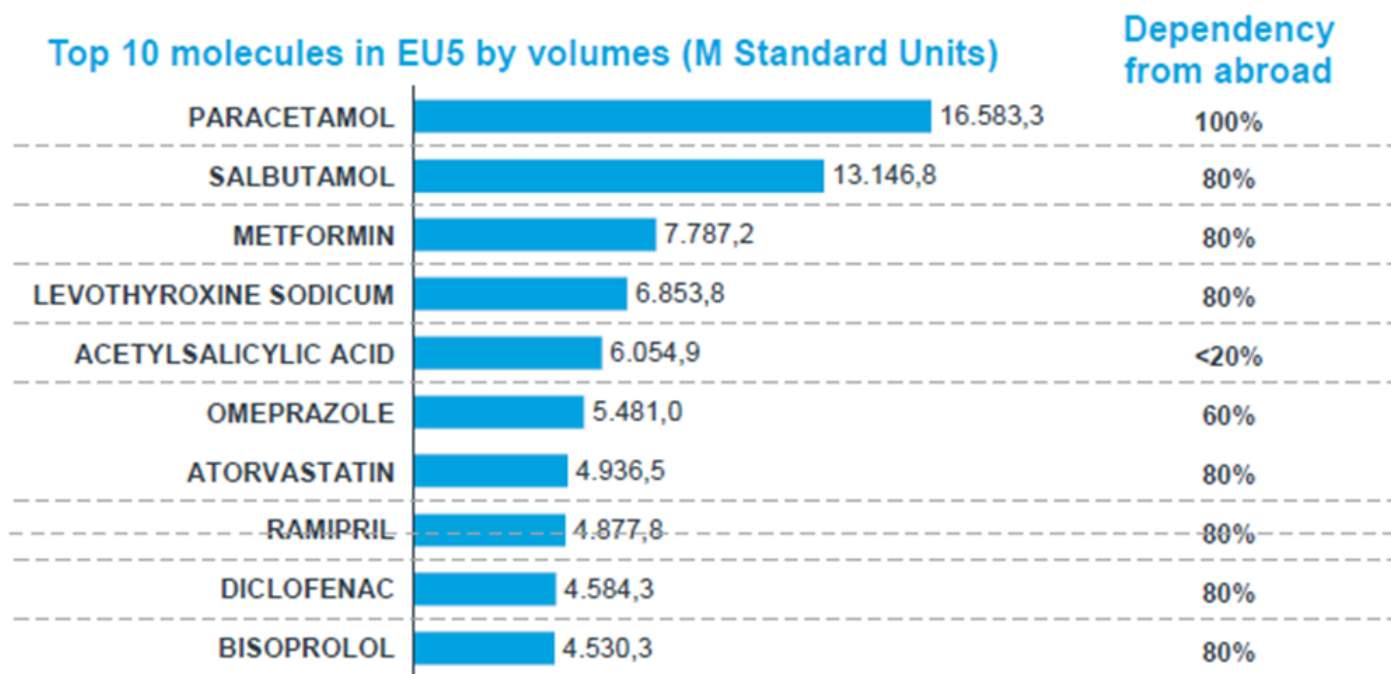


The missing link

One of the things that the Covid pandemic clearly showed is the dependency of e.g. Europe and the US on “out of the region” manufacture.

It is estimated that approx. 70% of the APIs used in Europe originate from India and China. Main reason for that is obviously the price. The lower price is a result of a.o. lower wages and less stringent SHE requirements.

The missing link



The missing link

What is not shown in these figures is the dependency on e.g. regulatory starting materials for API production. Even if API production is performed in Europe, the starting materials are often still coming from China.

In case of global disruption of supply chains, this means that could still lead to shortages.

Strategies in Europe to decrease shortages

One of the consequences of the complicated supply chain is of course that a disruption early in the supply chain will only be visible after a long time at the pharmaceuticals level. Production of API's may already take up to 1 year.

It is thus of importance that all players are informed and aware of any disruption at the earliest possible stage in order to enable them to mitigate the risks.

In Europe the coordinating role lies with EMA. The Single Point Of Contact (SPOC) approach makes it easier for industry to notify the official bodies.

Strategies in Europe to decrease shortages

Within EMA, the Executive Steering Group on Shortages and Safety of Medicinal products (MSSG) has been set up to ensure a robust response to medicine supply issues caused by major events or public-health emergencies.

The Medicine Shortages Single Point of Contact (SPOC) Working Party is responsible for monitoring and reporting events that could affect the supply of medicines in the European Union (EU).

Strategies in Europe to decrease shortages

The SPOC Working Party is responsible for the following activities:

- Monitoring any event that is likely to lead to a major event or a public-health emergency that could affect the supply of human medicines in the EU
- Reporting these events to EMA's MSSG
- Drawing up lists of the main therapeutic groups of human medicines that are used in emergency care, surgeries and intensive care, to inform the preparation of the critical medicines lists in order to respond to a 'public health emergency' or 'major event', at the request of EMA's MSSG

Strategies in Europe to decrease shortages

SPOC Working Party activities:

- Drawing up lists of human medicines that are critically important during a major event ('the major event critical medicines list') and during a public-health emergency ('the public-health emergency critical medicines list'), at the request of EMA's MSSG
- Monitoring the demand and stock levels of critical human medicines
- Reporting any critical shortages of human and veterinary medicines and potential alternatives to EMA
- Providing advice on medicine shortage-related issues to EMA and the European Commission
- Cooperating on shortage-related issues with international regulators

Strategies in Europe to decrease shortages

So, the SPOC workgroup supports the MSSG in getting information in a timely matter.

The MSSG then of course has a number of responsibilities:

- establishing lists of the main therapeutic groups of human medicines that are being used in emergency care, surgeries and intensive care;
- establishing lists of critical medicines that need to be monitored for supply issues during a major event or a public-health emergency;
- monitoring the supply and demand of critical medicines to identify any potential or actual shortages of these medicines;

Strategies in Europe to decrease shortages

MSSG responsibilities:

- providing recommendations and coordinating activities that aim to prevent shortages or mitigate their effects;
- advising the European Commission on whether medicine shortages and other ongoing or imminent events should be recognised as 'major events';
- evaluating information on the quality, safety and efficacy of medicines affected by public-health emergencies and other major events, and consider the need for urgent and EU coordinated actions;
- providing recommendations on actions to be taken at EU level relating to medicine shortages and the quality, safety and efficacy of medicines, to the European Commission and to EU Member States.

Strategies in Europe to decrease shortages

An example of a current shortage: at present there is a shortage of a number of antibiotics on the European market. These supply issues also affect countries outside the EU, and EMA has exchanged key information with other international regulators. Various measures have been implemented at Member State level to ensure that patients can receive appropriate treatment.

Strategies in Europe to decrease shortages

The national competent authorities in the EU are encouraged to make use of the regulatory flexibilities available, such as allowing the exceptional supply of certain medicines or presentations that may not be authorised in a particular Member State or granting full or partial exemptions to certain labelling and packaging requirements to ensure that patients can receive appropriate treatment. In addition, MSSG supports temporary national measures such as unit dose dispensing and compounding.

Next to this, the SPOC group engages with companies to provide regulatory support to increase supplies.

Strategies in Europe to decrease shortages

The regulatory flexibility approach was also used during the Covid pandemic.

It was possible to file changes (e.g. to increase production or to introduce a different API supplier) without having full validation data available. Obviously these data then needed to be provided at a later date, but assessment could already be done.

Of course this was limited to Covid related products/APIs.

Strategies in Europe to decrease shortages

The regulatory flexibility approach was also used during the Covid pandemic.

It was possible to file changes (e.g. to increase production or to introduce a different API supplier) without having full validation data available. Obviously these data then needed to be provided at a later date, but assessment could already be done.

Of course this was limited to Covid related products/APIs.

Next to EMA. Also EDQM was using a regulatory flexibility approach, which enabled them to prioritise submission/changes for Covid related APIs.

Strategies in Europe to decrease shortages

Also the European Commission is thinking about the problem and solutions. One of the things they are considering is reshoring API production to Europe. Easier said than done, as this will require huge investments and re-introduction of some technologies. On top of that, it will probably be very difficult to produce APIs in Europe for prices that are competitive when compared to Asia.

Conclusion

- Shortages are a global problem and difficult to predict because of the very complex supply chains.
- With appropriate reporting systems in place, shortages can be predicted and thus sometimes be avoided.
- Health authorities can play an important role when shortages are there: regulatory flexibility is one of the ways to achieve this.

