

# MEDICINE SHORTAGES IN EUROPE AND THEIR IMPACT ON PATIENTS A Reflection Paper

## Executive summary

It is without question that the availability and continuous supply of medicines is the cornerstone of a healthy society and therefore a key priority for European healthcare systems.

Despite increasing medicines shortages there is still a lack of understanding on their actual causes and robust solutions for resolving the problem have yet to be found.

Numerous plausible explanations have been put forward as reasons for medicines shortages. It seems that the reasons differ from country to country and from product to product. However, on a closer look it is clear that there are some common underlying causes which seem to influence medicines shortages.

This paper aims to initiate a discussion and is based on the viewpoints of full-line wholesale distributors and their perspectives on the causes of shortages, the impact and potential solutions.

Our initial reflection reveals the following to be among the key underlying root causes of shortages:

- The Falsified Medicines Directive mandates that Active Pharmaceutical Ingredients (APIs) imported into the EU must comply with European Good Manufacturing Practice guidelines (GMP) which will have a knock-on effect on the sourcing of 'approved' APIs for the production of medicines. The unavailability of APIs leads to production and supply disruptions.
- Lack of market attractiveness from an economic perspective for certain (older) medicines results in manufactures stopping production of certain low income generating products and / or from international reference pricing regimes (leading to a downward spiral of prices).
- Unforeseen disruptions or extraordinary demand due to bad weather, force majeure or viral outbreaks can result in shortages of certain products which suddenly see a rapid increase in volume demand;
- The on-going economic crisis and consequential austerity measures are resulting in reduced incentives to market such as price reductions and margin cuts.
- System failures such as the apparent race by payers to the lowest price possible without due consideration to the impact on other markets or to the supply chain participants.
- Stringent supply quotas imposed by pharmaceutical manufacturers on pharmaceutical full-line wholesalers with the attempt to steer the supply of medicines on the national markets. When supply quotas are imposed without flexibility and understanding of changes in the market they can be a reason for medicines shortages instead of avoiding them.

The paper also reflects on those impacted most by shortages and yields one clear conclusion – patients are the most affected by medicines shortages! Furthermore, pharmacists as healthcare professionals must spend valuable time sourcing medicines instead of caring for their patients.

Having considered some of the root cause of shortages and those impacted by them the paper looks at some possible pragmatic solutions to addressing the problems:

- Combating production-related shortages with the support of the European Medicines Agency (EMA) is key to preventing, mitigating and managing shortages of important medicines caused by manufacturing/GMP compliance problems.

- The European Commission and national authorities should adopt actions to support the continuation of products through market attractiveness for older medicines.
- Disruptions of supplies and unexpected demand of medicines can be combated through preparedness programmes and buffer stocks established at European and / or national level.
- Shortages due to austerity measures and the economic crisis could be partially resolved by supporting the real contribution the supply chain operators make to the economics of the sector in terms of pre-financing (function of pharmaceutical manufacturers and full-line wholesalers) the supply of medicines.
- System failures can be dealt with through the effective monitoring and enforcement of Article 81, paragraph 2 of the Directive 2001/83/EC which refers to a joint obligation of pharmaceutical manufacturers and wholesalers to “ensure appropriate and continued supplies of medicinal products to pharmacies and other persons authorised to supply medicinal products to the public so that the needs of patients in the Member State in question are covered”. The introduction of a Public Service Obligation (PSO) on wholesale distributors combined with the right of the wholesaler to be supplied by pharmaceutical manufacturers, including the enforcement of these obligations, is an efficient way to mitigate supply related shortages.
- In order to combat unjustified supply quotas, stakeholders in the supply chain should aim for increased collaboration, transparency, responsibility and accountability.

## Introduction

The continuity of supply and guaranteed availability of medicines are key priorities of the European healthcare systems. Ensuring the availability of medicines for patients is therefore reflected in the EU legal framework governing the pharmaceutical sector, requiring supply chain partners to comply with it in accordance with Article 81 of Directive 2001/83<sup>1</sup>. However, medicine shortages and unavailability have become an increasing problem in recent years. Due to the lack of availability of medicines, full-line wholesalers encounter difficulties ensuring the continuous supply of the full range of medicines to pharmacies. Recent studies have shown that medicines shortages not only adversely affect therapy and cause poorer treatment outcomes, but also compromise or delay medical procedures, lead to medication errors and to the use of less desirable, often more expensive, alternative medicinal products<sup>2</sup>.

Healthcare professionals are increasingly alarmed about the effects that unavailability of medicines has on patients and the significantly increased resources required for sourcing the medicines for their patients<sup>3</sup>. Shortages have seen a growth in number and complexity across Europe. Supply chain partners along with national and European authorities seek ways to end, prevent and solve this issue. Still, the measures adopted so far have not proved to be very effective at eliminating unavailability of medicines.

Today, more and more European Member States are facing shortages and discussions have been taken up not only at national level, but also on European level, but solutions are not easily found. The issue is as complex as the reasons for shortages of medicines are manifold and there is no quick fix by a single measure.

Medicines shortages are not only a European, but also an international problem. In the US, the Food and Drug Administration (FDA) has been working on reducing medicines shortages for over 7 years. According to the FDA, in the US, the number of medicine shortages has annually tripled from 2005 to 2010.<sup>4</sup> Quality problems at the manufacturing facility resulting in disruptions in supply were the leading cause of shortages, accounting for 43% of all shortages, followed by other delays in manufacturing or shipping (15%) and a shortage of the

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<sup>1</sup>Directive 2001/83, Article 81, par 2: “The holder of a marketing authorisation for a medicinal product and the distributors of the said medicinal product actually placed on the market in a Member State shall, within the limits of their responsibilities, ensure appropriate and continued supplies of that medicinal product to pharmacies and persons authorised to supply medicinal products so that the needs of patients in the Member State in question are covered.”

<sup>2</sup> [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Other/2012/11/WC500135113.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/11/WC500135113.pdf)

<sup>3</sup> [http://www.ashp.org/DocLibrary/Policy/DrugShortages/ASHP\\_shortage\\_guide09.pdf](http://www.ashp.org/DocLibrary/Policy/DrugShortages/ASHP_shortage_guide09.pdf)

<sup>4</sup> <http://www.fda.gov/downloads/aboutfda/reportsmanualsforms/reports/ucm277755.pdf>

active pharmaceutical ingredient (API; 10%)<sup>5</sup>. The FDA worked with manufacturers on reducing shortages and identified means to diminish the dangers of products with quality problems.

### **Why do medicines shortages occur?**

Until now, no clear answers could be given as to what triggers medicine shortages. Numerous reasons have been put forward, but they differ from country to country and from product to product. However, several dynamic forces appear to influence the lack of medicines such as the globalisation of manufacturing and subsequently their supply chains.

### ***New provisions for Active Pharmaceutical Ingredients (APIs) and production related shortages***

Currently pharmaceutical manufacturers increasingly encounter problems accessing active or key ingredients for the medicines they produce, due to the fact that many sources of active substances for life-saving medicines such as antibiotics are located outside the EU, including in countries with uncertain political and regulatory systems<sup>6</sup>. In addition, fewer medicines production sites, often scattered geographically, lead to supply shortages at a regional or even global level.

The European Union has tried to increase quality assurance through new mandatory regulations for APIs imported from third countries with the adoption of the Falsified Medicines Directive. Under the new Directive, which will fully come into effect on 2<sup>nd</sup> July 2013, APIs imported into the EU must comply with European good manufacturing practice (GMP) with written confirmation of compliance to EU standards. This obviously will take time as many pharmaceutical manufacturers source their products from countries outside the EU. Time will be crucial for these certificates of compliance. Otherwise we could face a new wave of medicine shortages to a much larger extent than it is the case today.

### ***Lack of economic market attractiveness***

Reasons that may drive manufacturers to cease the production of specific medicines include the diminishing demand for products, lower profitability or the intention to move resources elsewhere. The lack of attractiveness of markets from an economic perspective is thus an important motive for unavailability of medicines. If medicines are to be made available on a national market, it is important that all operators, not only pharmaceutical manufacturers, but also full-line wholesalers and pharmacies, can undertake their activities in a sustainable way. Especially in times of austerity and economic hardship it is crucial to consider the economic viability. Measures like international reference pricing lead to a downwards spiral of prices and the marketing of products in countries with the lowest reference prices becomes increasingly unattractive. The spill over effect of low prices therefore undermines the willingness for solidarity with countries, which are facing economic problems.

### ***Disruptions of supplies and unexpected demand of medicines***

Unforeseen medicine shortages may be caused by various interruptions in the normal delivery of medicines through the pharmaceutical supply chain and distribution network. Bad weather conditions, natural disasters or damage to production and storage facilities may result in a shortage of either raw materials or finished medicinal products. Furthermore, sudden outbreaks of viral diseases and a surge in demand for specific

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<sup>5</sup>Ibid

<sup>6</sup>[http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Other/2012/11/WC500135113.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/11/WC500135113.pdf)

products can cause sudden shortages of specific medicines. This was the case with the H1N1 pandemic, where vaccines were reported to be unavailable<sup>7</sup>.

### ***Austerity and economic crisis***

Due to austerity measures and economic difficulties, the medicines supply chain is encountering an unprecedented economic burden. Supply chain partners and specifically pharmaceutical wholesalers are often put in the position of having to pre-finance the healthcare system due to delayed payments. In some countries payment delays escalated to a worrisome level, causing supply chain partners to withdraw credit lines and to ask for pre-payment of medicine deliveries.

The tense economic climate also had a negative impact on wholesale mark-ups, shrinking them to a level at which full-line wholesalers are just about covering their costs. Current cost pressures on wholesalers might also lead to a reduction in the number of deliveries, which on the other hand would force pharmacies to increase their medicines stock levels.

### ***System failures***

Product shortages not caused by the above mentioned reasons should be recognised as a mirror of system failures. System failures are caused by the constant strive of payers for the lowest price possible, often without taking into account the far reaching consequences of the different measures used to bringing prices down. An increasing number of countries have introduced tendering procedures, creating in many cases shortages of products from the successful pharmaceutical manufacturer at least in the short term. Other countries (such as the UK and Germany) encourage or even force the import of pharmaceuticals to benefit from lower prices in other countries.

### ***Supply quotas***

Supply quotas imposed by pharmaceutical manufacturers can have a potential boomerang effect and be the cause of supply shortages instead of avoiding them. Pharmaceutical manufacturers impose supply quotas on pharmaceutical full-line wholesalers in order to try to control and steer the supply of medicines on national markets. In practice, however, quotas when imposed without any flexibility have proved to aggravate the underlying problem rather than addressing it, causing major problems on a daily basis for full-line wholesalers and pharmacies, who struggle to obtain the needed stock of medication for the patients<sup>8</sup>.

The core problem is that in the case of quota restrictions full-line wholesalers are supplied with only certain pre-set quantities of medicines, within defined time periods. The quantities allocated by pharmaceutical manufacturers are often insufficient to meet the demands of full-line wholesalers, especially in case when they try to increase their market share, as usually quotas are based on historic data. If quotas are exhausted, full-line wholesalers are not supplied with additional stocks of the respective products, even in circumstances where there is an obviously higher demand for these products from their usual customers and where pharmaceutical manufacturers clearly have the quantities available to meet the demand. Therefore, full-line wholesalers are obliged to pass on quota restrictions, equally limiting their possibility to meet additional demand from pharmacies and patients.

The way quota systems are imposed on full-line wholesalers significantly differ between pharmaceutical manufacturers and Member States. Some pharmaceutical manufacturers do not communicate the amount of

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<sup>7</sup>[http://www.recombinomics.com/News/01011101/H1N1\\_UK\\_Vaccine.html](http://www.recombinomics.com/News/01011101/H1N1_UK_Vaccine.html)

<sup>8</sup><http://www.appg.org.uk/APPG%20Pharmacy%20-%20Report%20of%20Inquiry%20Into%20NHS%20Medicines%20Shortages.pdf>

products comprised in the quota and only inform pharmaceutical full-line wholesalers once their quota is exhausted. This seriously affects the full-line wholesaler's ability to plan the supply of the product for the national market. Quotas therefore can create tensions in the supply chain and sometimes hinder patients' access to their required medicines rather than facilitating it. Furthermore, the full-line wholesalers are only able to deliver medicines that they have on stock. Even in countries such as Switzerland, where due to economic and legal reasons no medicines exports are allowed, it has been reported that full-line wholesalers do not have sufficient supplies to satisfy the demand of the market due to quotas.

### **Who is affected by medicines shortages?**

Medicines shortages have far-reaching effects throughout the healthcare sector, but above all patients are the ones suffering from the lack of medication.

Due to supply shortages and medicines unavailability, pharmacists need to dedicate more and more time sourcing medicines instead of dedicating this time advising and consulting with patients. Pharmacists are healthcare professionals and their time is too valuable to chase up medicines instead of caring for their patients. In this context it should also be noted that pharmaceutical full-line wholesalers are bound to respect the orders made by the pharmacists and cannot substitute products out of stock with alternative ones (they are legally not allowed to deliver alternative or substitute products). Therefore, in case of shortages full-line wholesalers cannot fulfil their public service function or obligation to provide pharmacies with all products needed by their patients. Medicines shortages have negative effects on full-line wholesalers' ability to distribute medicines whenever and wherever needed.

### **How can supply shortages be overcome?**

The solutions listed hereafter represent the full-line wholesalers' views on how medicines shortages can be combated. Pharmaceutical full-line wholesalers firmly believe that any sustainable solution to resolve the problem of medicines shortages has to take into account all manifold reasons of their cause. Fostering a closer and more transparent discussion and collaboration between political decision makers, health authorities, the pharmaceutical industry, wholesalers, pharmacists, healthcare providers, payers and patients at national and European level are a pre-requisite to ease and diminish shortages of medicines.

#### ***Combating production related shortages***

The European Medicines Agency (EMA) has recently taken a step forward in answering the manufacturing supply interruptions and published a paper on supply shortages caused by manufacturing/Good Manufacturing Practice (GMP) compliance problems<sup>9</sup>. The EMA put together a plan to help the European medicines regulatory network deal with supply shortages of medicines following manufacturing problems. The paper aims at providing a short and medium-term plan to help the European medicines regulatory network prevent, mitigate and manage shortages of important medicines caused by manufacturing/GMP compliance problems.

#### ***Combating shortages due to a lack of economic market attractiveness***

The European Commission is currently tackling the problem of medicines shortages. Under the framework of the Corporate Social Responsibility initiative of DG ENTR, the project group on facilitating supply in small

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<sup>9</sup>[http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Other/2012/11/WC500135113.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/11/WC500135113.pdf)

markets has carried out a survey on shortages of medicines in small countries. The surprising result of this survey shows that there is a significant shortage of products containing old molecules for which there is no economic incentive for bringing these to the markets due to the very limited number of patients. The recommendations put forward included a set of measures improving cross-border collaboration as well as the economies of scale.

Also DG SANCO is currently working on a study analysing how and to what extent existing provisions in the EU pharmaceutical legislation and modalities of application of requirements at EU or national level have served to alleviate identified availability problems.

National competent authorities should consider installing a monitoring system of the consequences of their desire to constantly decrease medicines prices through various mechanisms (international reference pricing, tendering) as well as of specific national requirements to bring products to the market of their country.

### ***Combating disruptions of supplies and unexpected demand of medicines***

In December 2011 the European Commission adopted a legal proposal to better protect European citizens from a wide range of serious cross-border health threats, which is currently under discussion in the European Parliament. Health threats can be biological, chemical or environmental in nature. Existing rules on preparing for and managing health emergencies will be strengthened and the Health Security Committee will be given a stronger mandate to react in a crisis.<sup>10</sup>

Whereas GIRP and its members warmly welcome this proposal, the role of the supply chain and its potential to mitigate availability problems of essential medicines in case of health threats has been underestimated. Practical examples in this respect can be found on national level such as consignment stock held in the premises of pharmaceutical full-line wholesalers. We believe that it is essential that all partners in the supply chain, together with national and European competent authorities, collaborate on crisis preparedness and jointly elaborate emergency plans.

It is a joint responsibility that in cases of sudden disease outbreaks, bioterrorism, other cross-border health crisis, or in case of problems related to the production, storage or distribution of medicines, patients in Europe should be able to have access to the required medicines without delay.

### ***Combating medicines shortages due to austerity measures and economic crisis***

GIRP would like to raise the awareness of European and national decision makers as well as of our European and national supply chain partners about the significant pre-financing function of pharmaceutical full-line wholesalers, which in most cases is largely underestimated. According to a recently published study pharmaceutical full-line wholesalers pre-finance 10.2 billion Euro in the 6 largest European countries alone.

It is easy to imagine that in the current economic climate pre-financing cannot be further extended. Demands by the pharmaceutical industry for earlier or immediate settlement of invoices cannot be met without passing on a part of this demand to pharmacists who are also in a difficult position to request timely payments from governments or social security systems. Delayed payments, the withdrawal of credit lines and the demand for pre-payments of medicine deliveries aggravate the situation of medicines availability in cash-stripped economies.

GIRP therefore appeals to national competent authorities and to payers on national level to take note of the pre-financing function of pharmaceutical full-line wholesalers as well as of the savings they bring to healthcare systems through the bundling of orders from manufacturers to pharmacies. Further pressure on wholesalers'

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<sup>10</sup> [http://ec.europa.eu/health/preparedness\\_response/docs/hsi\\_proposal\\_en.pdf](http://ec.europa.eu/health/preparedness_response/docs/hsi_proposal_en.pdf)

mark-ups would lead to a reduction of service levels and to higher capital demands on pharmacies to increase their stock without bringing any savings to the healthcare sector of a country.

### ***Combating system failures***

Article 81, paragraph 2 of the Directive 2001/83/EC refers to a joint obligation of pharmaceutical manufacturers and wholesalers to “ensure appropriate and continued supplies of medicinal product to pharmacies and other persons authorised to supply medicinal products to the public so that the needs of patients in the Member State in question are covered”. Public service obligations in place in several EU Member states oblige wholesalers to “guarantee an adequate range of medicinal products to meet the requirements of a specific geographical area and to deliver the supplies requested within a very short time over the entire area in question”.

Medicines shortages caused by system failures could be combated by implementation and enforcement of public service obligations on wholesalers and pharmacies. GIRP members already abide in several European countries by public service obligations and in the other EU countries voluntarily fulfil a public service function. In order for public service obligations to work effectively for wholesalers and pharmacies they need to be equally backed-up by the obligation of the pharmaceutical industry to provide adequate and continuous supplies to full-line wholesalers, who - without this obligation of the industry - would not be in a position to fulfil their own obligations. Also, it is essential that these obligations are adequately controlled and enforced.

Furthermore, recent short term emergency measures should translate into long term solutions.

GIRP firmly believes that all actors should strongly collaborate in order to ensure the continuous supply of medicines to patients. Therefore, full-line wholesalers stand ready to closely work together with all supply chain partners, national and European authorities as well as payers and other healthcare providers in order to combat medicines shortages.

### ***Combating negative impacts of supply quotas***

From the full-line wholesalers’ perspective a viable solution for the hurdle imposed by supply quotas on the continuous availability of medicines would be to ask pharmaceutical manufacturers to make the process of the allocation of supply quotas more transparent and less burdensome for wholesalers and pharmacies, taking into account the variations of medicines demand and supply patterns in their country.

In this respect GIRP once again appeals to the stakeholders in the supply chain for an increased collaboration, transparency, responsibility and accountability.

It is evident that the reasons for shortages differ from country to country, and product to product, so solutions should be sought ultimately at national level. However, the cross-border effects of various political and economic measures are not negligible and therefore an in-depth discussion on European level is indispensable to not negatively impact other countries’ healthcare systems and find a sustainable way forward.

*Full-line wholesalers call for and embrace opportunities for increased collaboration and cooperation with the supply chain partners and governments as well as payers in order to find feasible solutions to ensure patients in Europe have continued access to the medicines they require. Our priority as well as our core role and function as pharmaceutical full-line wholesalers is to make sure that pharmacies receive the ordered medicines and patients can access them in a safe and efficient manner.*

## **GIRP**

European Healthcare Distribution Association  
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