Teva position paper on security of supply

July 2020

Executive Summary

Tackling and preventing shortages is a priority for Teva. To that aim we have deployed tools and processes to minimise supply disruption.

We are continuously looking at our performances to better understand, detect, report, communicate, and act against shortages, notably by looking at the numerous root causes and proposing concrete solutions.

In this context, and considering that we strongly support a pan-European coordinated approach, **Teva proposes a series of concrete recommendations to mitigate and prevent medicines shortages from happening and ensure security of supply** (more details in the position below):

- **Set up a focused, action-oriented High Level Pharmaceutical Forum** led by the European Commission and involving authorities and all concerned stakeholders of the healthcare supply chain, ensuring European coordination and solidarity
- **Ensure sustainable market conditions:** rewarding security of supply is crucial
- **Ensure implementation of tenders MEAT** (Most Economically Advantageous Tender) criteria beyond lowest price through EU Guidance
- **Ensure a modern and digitalized EU regulatory framework** (e.g. multipacks and eLeaflet as the norm)
- **Define a single harmonised pan-European definition** of medicines shortage and critical list of products
- **Secure European investments in manufacturing & supply** through sustainable economic, regulatory and industrial policies and reforms
- **Create a single pan-European harmonised reporting and notification system** on a pan-European critical list of products
- **Avoid unharmonised national definitions** and reporting requirements
- **Avoid national artificial stockpiling or hoarding** which disrupts European patients' equitable and affordable access to the medicines
- **Avoid unproportioned and unnecessary penalties,** creating further unsustainability and increasing the possibility of medicines shortage

Table of Contents

1

General context and lessons learned from Covid-19

As a leading global pharmaceutical company, Teva provides essential medicines to millions of patients around the world every day.

Tackling and preventing shortages is a priority for Teva. To that aim we have deployed tools and processes to minimise supply disruption. We are continuously looking at our performances to better understand, detect, report, communicate, and act against medicines shortage.

Root causes of shortages are numerous.

They cover areas such as:

- manufacturing and quality issues
- economic related issues (e.g., market conditions, unsustainable tender practices and pricing policies)
- supply chain issues (logistics and demand volatility)

They are the results of complex supply dynamics involving the Marketing Authorisation Holders (MAHs) but also every other actor of medicines and APIs (Active Pharmaceuticals Ingredients) supply chain.

The combination of **cost containment measures, lack of market predictability and price pressure, combined with an onerous and rigid regulatory framework** are challenging access to generic and biosimilar medicines, especially for very old inexpensive essential drugs and putting the sustainability of our sector at stake.

As one company alone cannot tackle the complexity of the underlying factors responsible for shortages, **we also welcome pan-European led initiatives which reflect the way the pharmaceutical company supply chain is organised, still preserving the integrity of the single market.** These pan-European initiatives should address, constructively and genuinely, the complexity of the multi-dimensional challenges posed by shortages of medicinal products.

Teva believes that the most sustainable way to address shortages is to set up a **pan-European coordination** with all concerned stakeholders to ensure:

1. harmonisation of definitions and monitoring of shortages
2. addressing their multiple root causes to prevent them
3. increasing the visibility and transparency
4. supporting the industry to mitigate shortages when they occur

We are currently observing the **development of national plans and legislations which will fraction the European market,** and make it more complicated for the industry and other concerned stakeholders of the supply chain to mitigate and prevent shortages.

In some countries, Marketing Authorisation Holders (MAHs) are being asked to face disproportionate, impractical, unrealistic and too broad measures like stockpiling and penalties.

Such requirements only lead to more complexity, increasing risk of supply disruption rather than addressing root causes of shortages and rewarding security of supply.

Stockpiling has been recently mentioned in the context of the Covid-19 crisis by the European Commission Guidance on Optimisation of Supply of Medicines published on April 8th and presented by Mrs. von der Leyen[1].

The Guidelines clearly stipulate that "Stockpiling practices in anticipation of possible shortages can further contribute to the actual appearance of such shortages" and are calling to avoid national stockpiling.

Alternatively, we believe – as currently proven by the Covid-19 situation – in **joining forces and showing solidarity**: a fundamental value of the European Union and the way forward to deliver on the shortages issue.

Following the Covid-19 health crisis, **Europe will have to face an economic crisis** which will challenge even further access to medicines.

Therefore, in order to ensure access and sustainability of healthcare systems in the long term, **it is crucial to maintain a concrete action-oriented dialogue with the industry,** also looking at the lessons learned from the Covid-19 crisis.

In this context, and as an overarching recommendation, Teva is convinced that maintaining a pan-European coordination is needed.

The role of the European Commission is central in ensuring this coordination with all concerned stakeholders, capitalizing on all pragmatic efforts made in the direction of tackling shortages by adapting the current EU Framework to give adequate and reasonable flexibility for the industry to supply the market in the context of the Covid-19 situation.

Additionally, Teva would like to propose a series of concrete recommendations to mitigate and prevent medicines shortage from happening.

[1] https://ec.europa.eu/info/sites/info/files/communication-commission-guidelines-optimal-rational-supply-medicines-avoid.pdf

THE KEY OBJECTIVE would be to share the learnings from the Covid-19 situation and draw the conclusions to establish a pan-European and effective policy framework to prevent shortages in the long term and ensuring a well-functioning, sustainable and competitive industry that continues to act as a catalyst to enable sustainable access to medicines for patients.

Teva is therefore calling for all concerned stakeholders to join a **focused, action-oriented High Level Pharmaceutical Forum led by the European Commission** and involving Ministers of Health and policy makers, regulators, payers, industry and other concerned stakeholders of the healthcare supply chain.

In summary, there are some **key learnings** from the Covid-19 crisis to be learnt and considered moving forward:

- Manufacturers had **contingency plans** in place avoiding any major disruption for critical products
- **National hoarding and stockpiling** undermine the industry's ability to deliver equitable supply in all markets
- **EU and national coordination** to ensure equitable supply of medicines is important
- Avoiding shortages requires **bilateral dialogue,** demand visibility and close cooperation between governments/ regulators and actors

2

A single pan-European system for detection and notification of medicines shortage

In order to be able to notify any interruption of supply to competent authorities, actors of the pharmaceutical supply chain must continuously monitor the supply and demand situation of their medicinal products and should notify the competent authorities as stated in the EMA/HMA guidance of July 2019[1].

A shortage can occur at different levels of the supply chain:

- at the manufacturer's level
- at the wholesaler's level
- at the distributor's level, etc.

A notification should therefore be sent in case of a potential shortage by the actor facing or foreseeing a shortage. A notification does not automatically translate into a real shortage.

Additionally, in case of multisource products (generics/biosimilars), a shortage does not necessarily lead to public health issues, due to the fact that other identical or similar products may exist and can be used. However, it can lead to a surge of demand for the alternative products, creating a brutal increase of demand for such products.

Therefore, actors of the supply chain should be informed of potential bottle necks to best assess how they can prevent and/or mitigate any potential shortages. Additionally, studies[2] have shown that old and very inexpensive molecules or certain galenic forms (e.g., injectable) are more subject to shortages than others.

[1] https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guidance-detection-notification-shortages-medicinal-products-marketing-authorisation-holders-mahs_en.pdf

[2] https://www.fda.gov/media/131130/download (FDA report, as one example)

To enable market predictability, Teva would like to make the following **recommendations**:

We encourage **a single Pan-European definition for the List of Critical Medicines,** avoiding the development of different national lists.

The development of a multitude of national Lists of Critical Medicines will be extremely complex and costly to manage for pharmaceutical companies, and fragment the single market, especially if it is associated with high level of stockpiling requirements and penalties.

The list should focus on molecules and/or galenic forms which need specific attention, such as old and very inexpensive molecules or some specific galenic forms (e.g., injectables).

We call for **a single Pan-European harmonised reporting and notification system,** focusing on the Pan-European critical list of products.

An harmonisation of definitions and reporting conditions across EU markets is key, hence **a single Pan-European notification system** (covering both centralised and national marketing authorisations) **should be created for all concerned stakeholders of the supply chain:**

We encourage **an harmonised pan-European requirement regarding notification timelines and definition, aligned with the European guideline EMA/674304/2018**, and avoiding divergence at national level, which plays against against efforts to mitigate and prevent shortages (e.g., Italy with a requirement for a 4-month notification prior to a shortage).

We also call for **a pan-European common portal with standardised information, accessible to MAHs and other appropriate stakeholders** (e.g., Wholesalers), and which includes the following information: presentation of concerned medicine, market share in volume and expected date of market supply.

More transparency and more interaction with competent authorities about potential disruption or interruption of supply is key to ensure a proactive management system that can respond to market signals.

3

Mitigate shortages by introducing some regulatory flexibility

In the context of the Covid-19 crisis, the European Commission is advising to implement regulatory flexibility[1] covering for example procedures for changes in suppliers of APIs, the designation of new manufacturing sites.

With the same spirit, Teva would like to make the following **recommendations**:

ON IMPORTATION

The costs to import products are considerably high (e.g., repackaging, translation, logistics…). However, the main limitation in the use of this action is the lack of a predictable timeline from the competent authorities to approve such a product and the quantity needed especially due to market dynamic fluctuations.

In this context, Teva calls for:

- **Flexibility to grant import licence:** In emergencies, we should allow medicines approved outside the EU (from highly regulated markets, where standards are at the same level) as fast as possible.
- **Clear regulatory timelines to approve imported products and flexibility in accepting the product from another market** without repacking with a translated patient information leaflet. The Commission should prioritise and accelerate work on electronic patient information to permanently solve this issue.
- **Clear engagement on volumes requested** to mitigate critical shortages and coordination of the offers so to avoid work when not needed, encouraging joint collaboration to find solutions in a trusted environment

[1] https://ec.europa.eu/info/sites/info/files/communication-commission-guidelines-optimal-rational-supply-medicines-avoid.pdf
[2] A secondary packaging component means a packaging component that is not and will not be in direct contact with the dosage form (e.g. Outerbox / Leaflet)

ON SECONDARY PACKAGING[2]

While repackaging operations are to be done in full compliance with EU Good Manufacturing Practice (GMP) requirements, the requirement to register a repackaging site for an exceptional repackaging is delaying available products.

In this context, Teva calls to:

- **Allow secondary repackaging** based on a case-by-case approval by the National Competent Authorities without the need to add the repackaging site to the dossier.
- **Allow non serialised products on exceptional basis** (e.g., small volume, critical hospital products).
- **Accept and implement as soon as possible e-Leaflet** instead of paper base leaflet.

  Remark: This would also reduce the complexity of the industry supply chain, bottle necks responsible for manufacturing constraints, while facilitating a much more harmonised single market and aligned with the EU Green Agenda (less CO2 emissions and papers used).

ON ALTERNATIVE DOSSIER REGISTRATION

We are witnessing a reduction in alternative dossiers available due to the cost and workload related to their maintenance, sunset clauses, etc., which motivate companies to cancel their unused, non-marketed back up dossier.

In this context, Teva calls for:

- A so-called "zero day repeat use procedure" equivalent of registering a copy of dossier of an already approved product in another European market. This could be automatically granted in another member state and become the basis to register swiftly the dossier in the country where the shortage occurs.
- An extended use of the article 126a procedure to be considered in cases when the MAH is not able to use the standard MA procedure.
- The Regulatory Authorities could offer the possibility for a MA copy fast track registration from another Company already active in the Market with the same products, notably if no alternative dossier is available.

4

Prevent shortages by tackling their root causes

A

Optimize the EU Regulatory Framework via digital tools

The EU has high regulatory standards in place which need to be complied with before or while a medicine is placed on the market.

This Regulatory framework is onerous and the cost to maintain a medicine on the market has increased over the years[1]. These costs had to be absorbed by the generic and biosimilar industry while facing at the same time cost containment policies at national level.

While Teva encourages these high standards to be maintained, we also consider that enhancing regulatory cost efficiency and fit-for-purpose regulatory measures, can be achieved by **making the most of the telematics tools at pan-European level.**

These tools, while providing the same high regulatory standards, **can reduce the administrative cost to perform basic regulatory administrative work** for the industry but also for the regulators. It will foster greater economic resilience and therefore, provide accessibility to affordable medicines.

More specifically on variations, Teva calls for the targeted amendment of:

- the EC Variations Regulations 1234/2008 and
- Variations Classification Guideline

to be considered as soon as possible to modernise the current variations system and to reflect the evolution in technology and regulatory needs.

This will ensure smoother and faster processes which will help to mitigate and prevent medicines shortages.

[1] Due to the introduction of the falsified medicines directive, the change of the variations legislation, Brexit, etc.

B

Support Market Conditions that reward security of supply

For Teva and the off-patent industry overall, the combination of:

- cost containment measures
- lack of market predictability, combined with
- an onerous and rigid regulatory framework

are challenging access to generic and biosimilar medicines, especially for very old inexpensive essential drugs.

Tendering systems are pushing the industry to consolidate and rationalise its supply chain **playing against a healthy multisource and competitive market.**

Tenders are being allocated on cost base and not on value base. A company investing in securing its supply chain will bear significant costs (e.g., sourcing a second active pharmaceutical ingredient made in Europe) and will unfairly compete with a company which has not made any efforts to secure its supply chain, as tenders currently focus only on cost as the only criteria. **It does not reward any company efforts in securing its supply chain.**

It also pushes the industry to rationalise their supply chain and to consolidate where they can, to minimise cost, reducing the number of actors, and exposing furthermore the supply chain to potential risks. **It also has an impact on market competition.**

This has to change.
Indeed, the larger the number of API suppliers and manufacturers guaranteeing supply is, the less likely patients are exposed to medicines shortages. The European Union and member states definitely need to **put the right economic, regulatory and industry framework in place which rewards investments in medicines quality and security of supply.**

Teva would like to make the following **recommendations**:

AT A NATIONAL LEVEL

We encourage authorities to design new pricing models, setting up "stability" pacts with the generic and biosimilar industry, allowing to find common ground on the need to sustain the healthcare system and providing incentives to sustain essential medicines, also by promoting measures to increase the uptake of generic and biosimilar medicines.

AT THE EU LEVEL

In the context of the existing EU Procurement Directive, **we call on the Commission to specifically look at developing guidance to best implement the MEAT** (Most Economic Advantageous Tender) **criteria for pharmaceutical products for the market where tender practices are used.**

In this context, it is important to:

- adjust the number of tender winners according to the market, product and country characteristics
- use lead times that guarantee a steady supply of medicines and
- reward investments increasing the supply chain robustness and therefore security of supply (for example, multiple API sources - currently, registering an alternative source of API can take up to 12 months as part of security of supply)

All these points are crucial if we are not only to address the economic root causes of shortages but it is also part of the solution for the reflection on the EU industrial policy, and notably how to introduce the right incentives to secure manufacturing in Europe.

5

Specifically, on stockpiling and penalties measures taken by some member states

Teva strongly encourages member states to revisit any plan to introduce or implement mandatory stockpiling and unproportioned penalties associated to a national critical medicines list.

Indeed, extra stockpiling raises several questions and concerns among which:

The lack of proportionality of the stockpiling requirement (e.g., French and Dutch current requirements) and penalties (e.g., French new provisions) which are not adapted to the multi causal context and the root causes of shortages

The scope is too broad and not adapted to the criticality of products concerned (e.g., French and Dutch current requirements), making the stockpiling requirement impracticable (as regards to already limited stock capacities and/or specific storage conditions) or leading to waste (e.g., products with short shelf life and/or difficult storage conditions)

Unrealistic implementation timelines and requirements (e.g., industry has limited manufacturing capacity which cannot be changed overnight)

Extreme stockpiling requirement (e.g., France / The Netherlands) could also **impact availability of the concerned medicines in other European markets,** moving stocks from one market to the other to comply with the requirements, hence potentially paving the way for additional shortages

As a result, companies will assess the complexity, risk and the cost of supplying the market and may decide to withdraw the products from certain markets in case of economic risks, which may ultimately worsen the out-of-stock situation.

For the above mentioned reasons, **Teva strongly opposes those types of short term and quick fix measures,** and calls on the policy makers, regulators, industry and relevant stakeholders of the pharmaceutical supply chain to tackle the root causes and consider the recommendations of this paper, moving from mitigating to preventing shortages from happening.

6

How is Teva getting organised to ensure better security of supply

Tackling and preventing shortages by ensuring security of supply is a priority for Teva.

As such, Teva is committed to investigate, identify and address the root causes identified above in this document, which impact our ability to supply medicines to the best extent we can. **To that aim we have deployed tools and processes to minimise supply disruption.**

We are continuously looking at our performances to better understand, detect, report, communicate, and act against shortages. **We are also collaborating with authorities to best address external barriers** which impact our ability to best mitigate or prevent the root causes of shortages.

INTERNAL ORGANISATION

Teva has already a robust organisation to monitor and address supply issues. **Teva has notably set up a multi-functional shortages Task Force aiming at:**

- Ensuring full compliance with EU guidelines for detection, notification, and communication of drug shortages
- Providing agreed advice to improve internal processes to avoid drug shortages such as an SOP describing Drug Shortage Management

FOR THE DETECTION

At Teva we have increasingly established **robust practices covering:**

- **Market forecasting methods** to identify potential out-of-stocks as long as we can access timely information on competitor behaviour and anticipate market dynamics
- **Inventory management techniques:** We have a proactive management system that manages our inventories, enabling our local markets to perform on time adjustment of their forecast, and performing a rapid adjustment of replenishment and manufacturing planning in order to mitigate potential market constraints whenever possible

FOR THE NOTIFICATION

At Teva, **we strive to be compliant with European and national legislation and notify authorities accordingly.** We follow up these notifications in monthly metrics. However, as a global company, the national variability in the notification systems and requirements complicates the setup of a centralised process to ensure efficient notification, hence the importance of a pan-European harmonised system as highlighted in the recommendations of this paper.

IN RELATION TO THE LIST OF CRITICAL MEDICINES

Teva has defined a list of critical products where interruption of supply will result in a potential risk to public health and to Teva's sustainability. A prioritisation, which integrates products characteristics such as the critical list of WHO Essential list of medicines and/or the chronicity of treatment, is performed to put a special attention on these products by the entire Teva Organisation. If products are in high ranking segmentation, then several actions take place to grant delivery service level.

FROM A REGULATORY PERSPECTIVE

Teva is already engaged in reducing drug shortages by a variety of regulatory mitigating actions. The interactions with authorities can be a deciding factor and the response time and requirements can have an impact on the availability of alternative products (e.g., importation, repackaging, alternative dossier registration), hence the need for permanent regulatory flexibilities and optimisation.

FROM A MANUFACTURING PERSPECTIVE

Teva performs risk assessment and manufacturing optimisation initiatives for critical medicines (e.g., site transfers).

FROM A SUPPLY CHAIN PERSPECTIVE

Teva monitors market dynamics (e.g., use of artificial intelligence), assesses and adapts demand forecast in relation to priority medicines (e.g. prioritisation of shipping).