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From:	General Secretariat of the Council
To:	Delegations
Subject:	Shortages of human medicines in the European Union – *Exchange of views*

In view of the meeting of the Working Party on Public Health at Senior level on 15 July 2016, delegations will find attached a note from the Presidency on the above mentioned subject.

ANNEX

SHORTAGES OF HUMAN MEDICINES IN THE EUROPEAN UNION

I. Introduction

Shortages of medicines considered critically important for patients is a growing problem in Europe. They are occurring across the supply chain and for different reasons in different EU Member States. Reports of medicine shortages in the EU are increasing, from both patient organisations and healthcare professionals. For example, professional associations of pharmacists such as the Pharmaceutical Group of the European Union[1] and the European Association of Hospital Pharmacists[2] have raised their voices and called for concrete action from governments, EU institutions and supply chain partners.

As a consequence of such shortages of medicines, patients may not receive the medicines they are prescribed in a timely manner, which could be detrimental to the effectiveness of their treatment and overall health status. This translates into a lower quality and standard of care. To address the problem, EU Member States take different measures to ensure the availability of medicines.

On 17 June The Council (EPSCO) adopted Conclusions on Strengthening the balance in the pharmaceutical systems in the EU and its Member States[3]. The Council invited, among others, the Member States to consider development of exclusively Member States driven voluntary cooperation between relevant authorities and payers from Member States and to explore possible areas in which such voluntary cooperation can contribute to higher affordability and better access to medicinal products[4].

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1 http://www.pgeu.eu/en/policy/20:medicine-shortages.html
The Pharmaceutical Group of the European Union (PGEU) is a European association representing more than 400 000 community pharmacists. PGEU's members are the national associations and professional bodies of pharmacists in 32 European countries, including EU Member States, EEA/EFTA members and EU applicant countries.

2 http://www.eahp.eu/practice-and-policy/medicines-shortages

3 10315/16

4 Point 33 in 10315/16

The Presidency-trio (the Netherlands, Slovakia and Malta) was invited to identify with the Member States a set of mutual experienced concerns and challenges. Therefore the Slovak Presidency aims to initiate a debate on possible ways to tackle the problem of the medicine shortages, which in Presidency's view is faced by many Member States.

The discussion at the WPPHSL will also feed into the debate during the informal meeting of Ministers for Health in Bratislava, planned for 3-4 October 2016.

II. Reasons for medicine shortages

There are a number of reasons why some medicines are becoming more and more unavailable. Those can be related to problems in the medicine supply chain and the performance of individual stakeholders in it, including manufacturers of raw materials (particularly active substances), wholesalers, intermediaries and community pharmacies, or problems related to regulatory issues (e.g. non-compliance with Good Manufacturing Practices (GMP), pricing frameworks), parallel trade, labour disruptions, economic reasons or a changing market situation. The following (non-exhaustive) list gives some examples of different causes:

1. Manufacturing, supply chain and logistical causes:

    - technical issues during the manufacturing process, for example contamination or impurities of products despite adequate quality assurance; some medicines are very complex molecules or sophisticated biotech products that are more exposed to such risks;
    - 80% of antibiotics used in the EU are manufactured outside the EU, often in emerging countries, where GMP requirements differ from those of the EU, which can lead to non-compliance;
    - a limited number of manufacturers of raw materials is risky in view of potential quality defects.

2. Regulatory causes:

- mismatches in volume estimations: the actual prescribed use of a medicine may differ from the company's own estimates (e.g. a paediatric medicine also used in adults); this may cause temporary shortages and require renegotiations;
- non-compliance with GMP for authorised products: increasing reports of issues by GMP inspectors, difficulties in ensuring/controlling GMP throughout the world.
- an essential medicine is authorised but the registration is withdrawn at Member State or EU level by the manufacturer because of safety or HTA concerns.

3. Economic and business related causes:

- in some cases, manufacturers' pricing strategies may have an impact on supply by reducing the sustainability of supply when the price is too high and therefore only a limited number of patients can use the medicine;
- the lack of priority given to smaller markets by the pharmaceutical industry, often related to the use of languages on secondary packaging and the PIL (patient information leaflet) or a shortage of expensive paediatric and oncology medicines;
- a medicine is authorised, but is never marketed in some Member States;
- speculation encourages wholesalers and importers to purchase a medicine in EU countries where the price is lower and sell it in countries where the catalogue price is higher (parallel exports). This then limits the availability in the country from which the medicine is exported;
- decision of the marketing authorisation holder to withdraw the product from the market, for economic reasons or in order to switch demand to a new, patented medicine with the same or a similar active ingredient;

- financial pressure on the pharmaceutical industry: government cost-containment measures may limit their profits, and their shareholders' demands for dividends pressures management into reducing production costs, often to the detriment of quality;
- a medicine is too expensive in relation to its efficacy or represents an unacceptable burden on the budget and is therefore not part of a Member State's reimbursement scheme;
- suspension of delivery or withdrawal from delivery to Member States by the producer for logistic reasons.

4. Causes in relation to the organisation of the pharmaceutical market:

- increase in demand due to the shortage of another product;
- the abolition or absence of public service obligation/minimum national stock-keeping requirements in some countries;
- the imposition of fixed quotas and underestimations of medicines by the pharmaceutical industry, often inaccurately judging the true level of patient needs, as well as removal of the traditional role of the full-line wholesalers as a result of Direct-To-Patient schemes in some markets.

III. Possible action by the EU Member States

To address the shortages of medicines the Member States have taken initiatives at national level. However, shortages could be better prevented if the Member States join efforts and the Presidency believes that there is a need for better cooperation among the Member States

Exchange of information on medicine shortages

The EU legislation on medicines imposes a legal obligation for the marketing authorisation holder to ensure, within the limits of their responsibilities, a continuous supply (Article 81 of Directive 2001/83/EC)[5], and to notify any interruption of the supply two months in advance (Article 23a of Directive 2001/83/EC). National competent authorities in most of the EU Member States have started monitoring the situation and publish the list of medicines (usually via their websites) which currently are not available. However, there is still very little reliable EU-wide data available and therefore no clear understanding of the scope and extent of the problem.

At EU level, the European Medicines Agency (EMA) may be involved in certain situations within its mandate, for example when a medicine shortage is linked to a safety concern or affects several Member States. In 2013, the EMA decided to establish a public catalogue[6] of potential, ongoing and resolved shortages of medicines that are authorised at EU level or that are being evaluated as part of a community procedure[7] (irrespective of whether the shortage is secondary to a manufacturing capacity issue or the discontinuation of a medicine). However, this catalogue by no means gives a complete overview of all medicine shortages occurring in the EU, as most shortages are dealt with at a national level.

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5 Directive on the Community code relating to medicinal products for human use (OJ L 311, 28.11.2001, p.87).

6 EMA Shortages catalogue

7 I.e. medicines that have been assessed by the EMA's Committee for Medicinal Products for Human Use (CHMP) and/or the Pharmacovigilance Risk Assessment Committee (PRAC). See:http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/01/WC500159389.pdf

Regulatory action at Member State level

The Slovak Republic is just one of the EU Member States where a shortage of medicines has recently negatively impacted patients' access to medicines. In order to address this problem the Slovak Republic decided on and implemented legislative measures: the monitoring of supply, the regular publication and updating of information on medicines suspended from delivery by marketing authorisation holders for patients in the Slovak Republic, as well as preventive measures to regulate re-export (medicines imported to Slovakia for patients, but re-exported for economic reasons). These measures have one common objective – to ensure patients' access to medicines. However, such measures and those of other Member States have raised concerns at EU level in connection with the free movements of goods (pharmaceuticals are considered goods).

Recently, in accordance with Article 81 of Directive 2001/83/EC, the French authorities are making marketing authorisation holders and operators responsible for developing management plans to anticipate any shortages that the French market might face in respect of medicines of major therapeutic significance.

Other possibilities for cooperation at EU level

The Presidency believes that the EU Member States could strengthen the exchange of information as well as regulatory cooperation between responsible national authorities. Any cooperation in those and other areas leading to action at EU level would be beneficial to the Member States. **To this end and in order to have a structured and fruitful debate at the SLWPPH, the Presidency would like to address the following questions to the delegations:**

1. If Member States support the exchange of experience and the sharing of best practices on national regulatory measures on medicines shortages, which would be the most appropriate work fora?

2. An overview and exchange of information on medicines shortages could be established. The database could be linked to national databases/registers and would provide a consolidated overview of shortages in the European Union and the measures taken by Member States. Which structure at EU level could in your view most competently fulfil such a task?

3. Could regional/cross-border cooperation in purchasing (joint procurement) be an option that would contribute to solving the shortages problem?

4. Do you think that a mechanism for the exchange of medicines that are lacking in some Member States but available in larger quantities in others is feasible?

5. Do you think that the involvement of interested stakeholders could be helpful in order to create awareness and find solutions? If yes, how and in what areas do you think this involvement should take place?

6. Could changes to the existing regulatory framework at EU level help reduce shortages?

7. What are the feasible measures at EU level? Can manufacturers be obliged to at least offer essential medicines to all MS; reduce strategic market entry/delays?

Sources:

1. EAHP's 2014 survey of the medicine shortage problem: http://www.eahp.eu/practice-and-policy/medicines-shortages

2. EMA web site: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000588.jsp&mid=WC0b01ac05807477a5

3. The Pharmaceutical Group of the European Union (PGEU): http://www.pgeu.eu/en/policy/20:medicine-shortages.html

4. European Association of Pharmaceutical Full-Line Wholesalers (GIRP) position paper: http://www.girp.eu/sites/default/files/documents/Medicines%20shortages%20reflection%20paper%20including%20exec.%20summary%20FINAL.pdf

5. COST Action "European Medicines Shortages Research Network - addressing supply problems to patients (Medicines Shortages)": http://www.cost.eu/COST_Actions/ca/CA15105

6. Bulletin of the World Health Organisation 2012: http://www.who.int/bulletin/volumes/90/3/11-101303/en/

7. EFPIA POLICY PROPOSALS TO MINIMISE MEDICINE SUPPLY SHORTAGES IN EUROPE: http://www.efpia.eu/uploads/Modules/Documents/pac-280214-ai6-a2-shortages-position-paper-final.pdf

8. Common position between organisations for patients, consumers, and healthcare professionals involved in the activities of the European Medicines Agency: http://download.eurordis.org.s3.amazonaws.com/documents/pdf/common-position-supply-shortages-final-10-2013.pdf

9. Commission reply to EP question E-00535/2001 on parallel exports: http://www.europarl.europa.eu/sides/getAllAnswers.do?reference=E-2011-000535&language=EN

10. Commission reply to EP question E-009450/2014 on shortages of medicines in hospitals: http://www.europarl.europa.eu/sides/getAllAnswers.do?reference=E-2014-009450&language=EN

11. Study on the Availability of Medicinal Products for Human Use: http://ehtpa.eu/pdf/Matrix_report.pdf