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Insights for a Risk-Assessment Tool to Manage Medicines' Shortages

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1. Introduction

Medicine shortages have been spreading in European countries with a substantial impact on the capability of national healthcare systems in ensuring the continuity of care. Shortages sometimes originate from unpredictable and multifactorial causes. They can be due to supply-related factors (e.g., manufacturing issues, regulatory issues, logistics, distribution) and demand-related ones (e.g., fluctuating drug demand, parallel market, tendering, price and reimbursement policies). Moreover, some extraordinary geopolitical events (e.g., Brexit) may also affect the medicines' availability. However, the fragmentation of the National regulatory framework has limited the capability of competent Regulatory Authorities and other subjects involved in the healthcare assistance services in defining suitable problem-solving strategies. Indeed, only in 2019, the EMA and HMA joint task force released the first harmonized "shortage" definition in the European Union and two guidance on shortage notification for manufacturers and on the communication to the public [1]. However, rational and practical shortage risk-assessment metrics are still needed to promote stronger cooperation among European Countries. Although several measures have been proposed by regulators and professional associations [2-4], most of them are designed to face specific shortage's root causes (e.g., manufacturing failures, low price, distribution-problem) and cannot be applied widely.

This work aims to propose a risk-assessment tool for health professionals, regulatory agencies and other stakeholders to triage the shortage impact on public health regardless of its root cause or the affected healthcare setting.

2. Risk assessment tool

A risk assessment procedure has been designed to be fully integrable with other existing and adopted metrics. In particular, the tool permits to define the shortage impact (i.e. high, medium, low) based an overall score that is determined based on three criteria (***Figure 1***): I) type of disease to be treated, II) the availability of therapeutic alternatives and III) the market shares of the product in a specific European Country.

Criterion I

The principles of VEN (Vital-Essential-Nonessential) analysis [5] were adapted to classify the medicinal product for which a shortage is expected/ongoing. Based on the seriousness of the therapeutic indications, a medicinal product can be classified as A) products for life-supporting, life-sustaining or rare diseases, B) products for serious or debilitating diseases (acute or chronic), C) products for other conditions. It is noteworthy that a shortage of a life-supporting medicinal product resulted in a higher impact on patient health than one used to treat a nonserious illness (e.g., cold). If the same medicinal product is indicated for the treatment of more than one disease, the most severe and low prevalent one should be considered.

Criterion II

The seriousness of the shortage impact on public health is also influenced by the existence of therapeutic alternatives that can assure the continuity of the cure. The higher the number of therapeutic options, the lower the threats for patient's access to therapies. Consequently, the scores for Level II

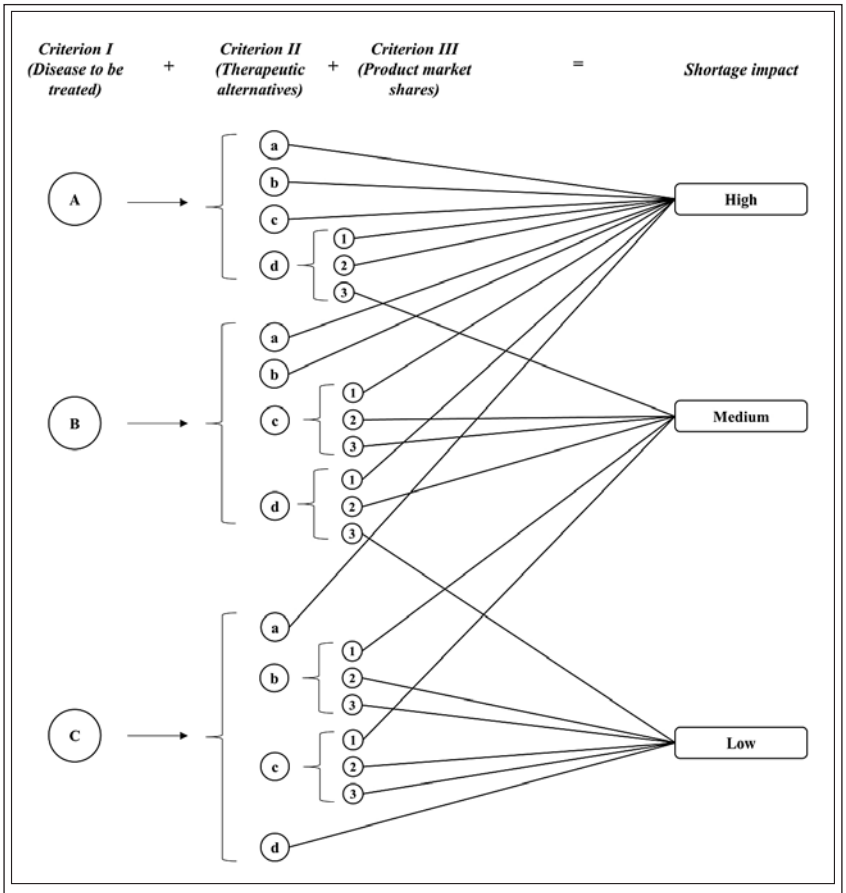

Figure 1 *Risk assessment tool to determine the shortage impact on patient health.*

are: a) not more than two medicinal products containing drug substances in the same ATC level III (same therapeutic/pharmacological subgroup) or IV (same chemical/therapeutic/pharmacological subgroup); b) more than two medicinal products for the same ATC level III, but not for the same ATC level IV; c) more than two medicinal products containing drug substances in the same ATC level IV, but no generic products are available for the same ATC level V (same chemical substance or therapeutic moiety); d) more than two generic products for the same ATC level V.

Criterion III

The more monopolistic is the market of a medicinal product, the higher the risks that competitors are not able to sustain the patient demands during a shortage. Therefore, the higher the market shares of a medicine (expressed as annual volumes), the higher the potential risks for the public health. The Level-III scores were: 1) market shares higher than 50% of the entire national market; 2) market shares between 25-50%; 3) market shares lower than 25%.

3. Conclusions

Due to the economic globalization, the EU Countries cannot face the shortage crisis alone. In this light, harmonized risk-management strategies are needed at EU-level. Although further studies in real-world settings are required to complete the validation of the procedure, the adoption of the proposed algorithm by different stakeholders can be useful to determine in a harmonized way the impact on public health of a medicine shortage, improving the cooperation. Based on the shortage-impact scores (high, medium, low), the most critical medicinal products can be selected in advance, allowing competent National Authorities, healthcare professionals (e.g., pharmacists) and other stakeholders to adopt mitigation strategies in advance.

4. Conflict of Interest

This scientific proceeding does not imply any current or potential conflict of interest with the Administration of affiliation; the view and opinions expressed are those of co-author and should not be attributed to AIFA.

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