EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – quality, safety and efficacy

PHARMACEUTICAL COMMITTEE
22 October 2012

PHARM 610

Subject: Shortages of medicinal products due to quality or manufacturing issues

Agenda point: 2. a)

Background

In recent months, there have been a number of serious shortages of medicinal products in the European Union. The causes of these shortages include manufacturing problems, poor product quality (e.g. contamination of sterile products) and lack of production capacity. The problem is exacerbated when the manufacturer has no other manufacturing site and when no proper alternative treatment is available in the short term.

In such situations, some national competent authorities may not have received all relevant information on time to take appropriate action. Moreover, the decision on alternative treatment is often left to health care professionals. This may expose patients to adverse reactions associated with the use of alternative medicinal products.

With a view to helping the Member States, the European Commission has therefore investigated this concern and summarised all best practices and legal tools available to national competent authorities. These tools are summarised in the Annex.

In parallel, the European Medicines Agency, in cooperation with the European Commission and the Member States, is currently finalising a reflection paper on medicinal product supply shortages caused by manufacturing/GMP compliance problems. This paper will put forward a set of short-term and medium-term actions to tackle this problem.

Lastly, the CMDh is currently drafting Best Practice Guidance (BPG) on collaboration between Member States in relation to GMP non-compliance issues to facilitate collaboration between Member States on GMP issues notified to the group.

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Point for discussion

The Commission is proposing that the Member States exchange information on any possible new developments in shortages caused by manufacturing problems.

The Commission is proposing to discuss the Annex summarising best practices available to national competent authorities to tackle shortages of medicinal products.

Annex

Best practices available to national competent authorities to tackle shortages of medicinal products

	Legal tools
1	Article 126a of Directive 2001/83/EC on the use of medicinal products authorised in another Member States: "*In the absence of a marketing authorisation or of a pending application for a medicinal product authorised in another Member State in accordance with this Directive, a Member State may for justified public health reasons authorise the placing on the market of the said medicinal product".*
2	Article 81 of Directive 2001/83/EC on the obligation of continuous Supply: "*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".*
3	Article 5.1 of Directive 2001/83/EC on the use of unauthorised medicinal products: "*A Member State may, in accordance with legislation in force and to fulfil special needs, exclude from the provisions of this Directive medicinal products supplied in response to a bona fide unsolicited order, formulated in accordance with the specifications of an authorised health-care professional and for use by an individual patient under his direct personal responsibility".*
4	Article 23a of Directive 2001/83/EC on the notification of cessation of marketing: "*After a marketing authorisation has been granted, the holder of the authorisation shall inform the competent authority of the authorising Member State of the date of actual marketing of the medicinal product for human use in that Member State, taking into account the various presentations authorised.* *The holder shall also notify the competent authority if the product ceases to be placed on the market of the Member State, either temporarily or permanently. Such notification shall, otherwise than in exceptional circumstances, be made no less than 2 months before the interruption in the placing on the market of the product. Upon request by the competent authority, particularly in the context of pharmacovigilance, the marketing authorisation holder shall provide the competent authority with all data relating to the volume of sales of the medicinal product, and any data in his possession relating to the volume of prescriptions.*
5	Article 63.3 of Directive 2001/83/EC on labelling exceptions: " *When the medicinal product is not intended to be delivered directly to the patient, or where there are severe problems in respect of the availability of the medicinal product, the competent authorities may, subject to measures they consider necessary to safeguard human health, grant an exemption to the obligation that certain particulars should appear on the labeling and in the package leaflet. They may also grant a full or partial exemption to the obligation that the labeling and the package leaflet must be in the official language or languages of the Member State in which the medicinal product is placed on the market.*"
6	Article 5(3) of Regulation (EC) No726/2004 on CHMP opinion: *At the request of the Executive Director of the Agency or the Commission representative, the Committee for Medicinal Products for Human Use shall also draw up an opinion on any scientific matter concerning the evaluation of medicinal products for human use.[..].*

7	Article 20 of Regulation (EC) No 726/2004 on referral for medicinal products that have been authorised via the centralised procedure: 1. *Where the supervisory authorities or the competent authorities of any other Member State are of the opinion that the manufacturer or importer established within the Community territory is no longer fulfilling the obligations laid down in Title IV of Directive 2001/83/EC, they shall forthwith inform the Committee for Medicinal Products for Human Use and the Commission […].* *2. The Commission shall request the opinion of the Agency […]* *3. Following an opinion by the Agency, the Commission shall adopt the necessary provisional measures, which shall be applied immediately. […]"*
8	Article 31 of Directive 2001/83/EC on EU interest referral for medicinal products that have been authorised via the decentralised procedure or mutual recognition procedure: "1. *The Member States, the Commission, the applicant or the marketing authorisation holder shall, in specific cases where the interests of the Union are involved, refer the matter to the Committee for application of the procedure laid down in Articles 32, 33 and 34 before any decision is reached on an application for a marketing authorisation or on the suspension or revocation of a marketing authorisation, or on any other variation of the marketing authorisation which appears necessary. […]".*
Possible remedies	
9	Request to MAH when notifying the competent authority the interruption, either temporary or definitive, of a medicine on the territory: – the volume of sales of the concerned medicinal product and data in his possession relating to the volume of prescriptions; – when possible an indication of the expected dates of the shortage and possible alternatives;
10	Identify alternative medicinal products/treatments in the EU or in third countries: – meet other MAHs of "equivalent" medicinal products asking to increase their production in order to cover the shortage; – import from third countries (variations) – or authorisation to place on the market.
11	Identify alternative manufacturers: – speed up variations of marketing authorisations; – import from third countries and invite MAH to apply for a marketing authorisation.
12	Contact with MAH: – increase shelf-life and re-label shelf-life for existing batches (speed up variation to the existing marketing authorisation); – re-allocate and repackage from another MS ;

13	Contact with Health Care Professionals – Advice on the use of alternative treatments; – Switch to other available pharmaceutical forms; – Introduction of temporary dose reduction; – Restrict the use of the product to specific categories of patients who have no adequate alternative – Rationalisation of prescriptions – and accounting of the distribution;
Communication	
14	Establish the complete picture of the situation in particular whether the shortage will affect the entire European Union. In such case, activate the EU regulatory network Incident Management Plan of the European Medicines Agency and/or discuss the topic further within The Co-ordination Group for Mutual Recognition and Decentralised Procedures (CMDh);
15	Use the existing Rapid Alert Notification system for recalls due to quality defects described in the Compilation of Community Procedures or equivalent system for exchange of information on shortages of "essential medicines" due to manufacturing or quality problems;
16	When available, communicate a realistic timeframe for resumption of supply
17	Inform without delay the other competent authorities results of the GMP inspection in the manufacturing plant;
18	Update the websites to give accurate information for the Health care professionals on known or expected issues with respect to shortages on their territory;
19	Assess the need to communicate to public versus preventing alarmist and counterproductive behaviour (e.g. communication might trigger stock piling);
20	Ensure complementarily between ’core’ communication at EU level and more detailed communication at national level Communication at EU level should coexist with national communication strategies: - when status and impact of the shortage differ from country to country; - when clinical practices vary between member states.
21	Proactive, early communication to help managing impact; keep information updated ;
22	Communicate with international partners that may be affected by the issues leading to shortage e.g. US, Canada.