LIFE SCIENCES

COVID-19: Guidance for Marketing Authorisation Holders on Flexibility and Regulatory Expectations

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Guidance for Marketing Authorisation Holders (MAHs) on regulatory expectations and flexibility during the COVID-19 pandemic has been published by the European Medicines Agency, the European Commission and the European medicines regulatory network.

The aim of the regulatory authorities in publishing the Guidance is to implement appropriate measures to minimise the risk of medicinal shortages, while at the same time ensuring that highest standards of quality, safety and efficacy of medicines in the EU are maintained.

The guidance, entitled ***"Questions and Answers on Regulatory Expectations for Medicinal Products for Human Use During the COVID-19 Pandemic"***, may offer some comfort to MAHs as they face unprecedented challenges in striving to ensure continuity of supply of medicines.

The Guidance, which will be updated as the pandemic evolves, currently focuses on the following four areas:

1. Marketing Authorisations

The Guidance sets out how marketing authorisation procedures for medicines for use in COVID-19 patients can be expedited, how zero-day mutual recognition procedures can be used, and how medicines currently unauthorised in a particular member state may be made available there. It also sets out advice for MAHs struggling to meet deadlines for filing renewal applications or facing having "sunset clauses" in their authorisation triggered.

2. Ensuring continuity of supply of COVID-19 medicines

MAHs may experience supply chain disruptions due to the manufacturing, distribution and trade restrictions arising from the pandemic (Read our previous briefing on supply chain disruption here). The Guidance recognises these difficulties, and acknowledges that steps should be taken by the regulatory agencies to ensure MAHs can easily source materials from alternative suppliers, or that they can add new manufacturing sites, as easily as possible.

An exceptional change management process (ECMP) has been made available to MAHs for vital COVID-19 medicines, which allows the rapid implementation of changes to suppliers and/or manufacturing/supply sites where necessary to reduce the risks of shortages.

This will allow, for example, MAHs to source materials (e.g. reagents, active substances) from suppliers that are not specifically mentioned in the authorisation, if this is necessary to prevent or mitigate shortages, by making an application to the relevant authority under the ECMP. MAHs that wish to rely on the ECMP must notify the relevant national competent authority that granted the marketing authorisation or the European Medicines Agency (in the case of centrally authorised products). The relevant authority will assess the notification and specifically whether the application concerns crucial medicines for use in COVID-19 patients, and must decide, within two working days, whether it agrees to the application of the ECMP. Although deferred, the corresponding variation application is still required no later than 6 months following the implementation of the change under the ECMP. During that time, certain conditions will still need to be complied with to ensure the quality of the medicine.

While welcome, the ECMP has very limited scope, and only applies to medicines for use by patients with COVID-19, and for changes required to address supply chain/manufacturing challenges resulting from the current pandemic. The process will not apply to other vital medicines.

3. Quality Requirements

Without prejudice to the flexibility of the ECMP, the Guidance states that quality requirements should continue to be complied with, including for medicines administered to COVID-19 patients.

If MAHs are finding it particularly difficult to perform quality controls

as a result of the pandemic, they are invited to present an adapted control scheme on a risk-based approach to the relevant authority, which can be submitted as a variation in accordance with EU requirements. The Guidance states that COVID-19 related variation applications will be promptly dealt with, although there does not appear to be a dedicated procedure for variations linked to the pandemic. It remains to be seen if additional measures will be implemented as the crisis evolves, or if a further relaxation of quality controls in respect of the most vital COVID-19 medicines will follow. While such flexibility would relieve pressure on the supply of the most critical medicines during the pandemic, MAHs should always be alert to the potential risk of product liability, which will continue to lie with the MAH in the event of a subsequent product liability issue.

4. Labelling and Packaging

The Guidance stresses that the regulatory flexibilities in Directive 2001/83/EC should be fully utilised. Directive 2001/83/EC allows member states to grant exemptions to certain labelling and packaging requirements to address severe problems with availability of products. This measure should be used to facilitate the movement of medicinal products within the EU so that they can be made available in those member states where they are most needed.

Member states are asked to accept that, where there are severe shortages of a particular medicinal product in their state, the labelling may not be translated into the relevant official language, national specific information may not appear, and that the presentation may differ from the presentations authorised and which usually appear on the product in that member state.

The Guidance addresses key areas in which MAHs may face difficulties with COVID-19, and demonstrates the focus of the regulators in seeking to minimise risks of shortages. Separately, the European medicines regulatory network has established the EU Executive Steering Group on Shortages of Medicines Caused by Major Events to provide strategic leadership for urgent and coordinated action to prevent and mitigate supply disruptions within the EU. MAHs should review the Guidance, and should seek to avail of the ECMP, where appropriate, to mitigate supply chain risks.

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