Coordination with industry on potential impact of Covid-19 on medicines manufacturing and supplies in Europe

TO:

Commissioner for Health and Food Safety, Ms. Stella KYRIAKIDES
Commissioner Internal Market, Mr. Thierry BRETON
Commissioner Crisis Management, Janez LENARČIČ

C/C:

Commissioner for Home Affairs, Ms. Ylva JOHANSSON
Commissioner for Transport, Ms. Adina VĂLEAN
Commissioner for Economy, Mr. Paolo GENTILONI
Executive Director of the European Medicines Agency, Mr. Guido RASI
Director General for Health and Food Safety, Anne BUCHER
Ambassador Plenipotentiary, Deputy Permanent Representative of Croatia to the EU, H.E. Goran ŠTEFANIĆ

Brussels, 10 March 2020

Dear Commissioner Kyriakides, Commissioner Lenarčič, Commissioner Breton,

Following up on our letter dated 18 February and considering the 6 March 2020 Health Council meeting, we would like to update you on the potential impact of the Corona Virus on medicines manufacturing and supplies in Europe. We reiterate that we do not see any short-term risk to production or supplies in Europe. We have a large manufacturing capacity in Europe that supplies 67% of prescription medicines. We are coping with the challenges and are prioritising the supply of medicines to patients as is the mission of our association.

The uncertainties regarding future developments warrant us to take precautionary measures. We therefore seek a more structured dialogue with the Commission, concerned member states and relevant regulatory authorities to plan for a possible extended duration of the viral outbreak. This could be arranged with the recently established EU Executive Steering Group on Shortages of Medicines caused by Major Events which met for the first time on 4 March 2020. We strongly advise that member states establish parallel dialogues with Medicines

for Europe national associations. The combined exchange of national and EU level information between manufacturers and authorities would be essential to tackle any challenges for medicines supply.

The outbreak began in China which is a major producer of pharmaceutical inputs – notably of active pharmaceutical ingredients and intermediate products. We do not yet have full clarity on the production situation in China because workers are returning in small batches to factories in accordance with the public health rules in the country. According to the WHO, larger production sites will soon be fully operational but smaller production sites (producing intermediates) are facing more difficulties. In addition, logistical issues continue to be a challenge.

We are concerned about the recent decision of India to impose export restrictions on certain active ingredients and medicines. While we believe that the scope of this measure will be limited in impact (affecting a small volume of exports to Europe), we are concerned about measures that clearly disrupt international cooperation. We advise that the EU, US, India and China should cooperate on global supply chain manufacturing issues together with industry to maximise information and efficiency for all patients globally. This could be facilitated by the WHO.

As the outbreak is now occurring in Europe on a large scale in some countries, we should provide clarity for all actors involved in medicines production. We should note that Medicines for Europe has production or laboratory sites in all EU member states except Luxembourg. We advise that member state measures and decrees to limit the movement of people should clearly recognise medicines production and logistics as essential. This will enable manufacturers to continue production and related cross-European logistics for the continued supply of medicines. Where requested, there should be guidance on how to maintain production and logistics while reducing the risk of the spread of the outbreak. For example, our industry's major production centres in Italy are in the outbreak regions in the North of the country. There are impacts on the availability of labour and concerns about logistics and transport in and out of the region. However, our members in Italy have worked to maintain production and transport in the country for the most part. The further spread of the virus to other regions in Europe close to our manufacturing sites would likely cause similar problems. We advise that the Commission provides guidance on transport and logistics issues to avoid unnecessary disruptions.

Our members have been conducting risk assessments at national level in close coordination with national regulators. We strongly advise that the Commission and EMA aggregate this information to assess the potential risks for supply if the outbreak continues. This would enable the Commission and inform manufacturers of potential supply problems and allow them to shift their manufacturing or their excess stocks to address the problem. Legal compliance issues limit the possibility for manufacturer associations to collect and share this kind of information. This information could be used by the authorities to provide information to the whole manufacturing community on production and supply bottlenecks and to find manufacturers who could fill those potential gaps in the system.

Our members have also expressed concerns about the risk of medicines hoarding in the distribution chain. Although there are no shortages, this disruption has an impact on the industrial market. This could create irrational incentives for stock hoarding. We advise that the Commission and national authorities actively monitor this risk which could unnecessarily create shortages or stock outs for patients. There may also be a need to involve payers in this dialogue to address the economic impact of the outbreak on manufacturing which could have an impact further down the distribution chain. Indeed, a possible decrease in offer of active pharmaceutical

ingredients (API) and intermediates may result in sudden higher costs to produce medicinal products, which may need to be flexibly factored in the dialogue with payers and authorities more generally.

As stated previously, we should act now to prevent potential supply risks if the outbreak continues. We should engage in a structured dialogue to enable regulatory flexibilities to address potential shortages related to active pharmaceutical ingredient production problems – notably the possibility for emergency variation procedures and accelerated regulatory reviews for both active ingredients and for finished products and to move products across different EU markets. This structured dialogue could also be useful to channel information regarding pharmaceutical needs (antivirals and antibiotics) to address the outbreak as we have noted that many of the products proposed to address the virus under the recent IMI proposal are produced by our membership. For some products, we should also consider the possibility of a bulk import exemption into the EU if these products are not widely commercialised in Europe (i.e. hydroxychloroquine) as our members are marketing these products outside the EU where they serve a specific health need.

For these reasons, we call on you to enact the structured dialogue with utmost urgency.

Yours respectfully,

Adrian van den Hoven

Director General

Christoph Stoller

President

Annex: Recap of measures

Reducing time and cost associated with alternative API or ingredient supplier:

- For DCP/MRP/National products: Timelines of variations in the guideline should be respected in all countries for validation time, the start of the variation procedure and for national finalisation.
- For CP products: Timelines of EMA for variations are mostly in accordance with legislation. Shorter timelines should be considered in case of urgency to supply the market.
- Registering an alternative source of API can take up to 12 months. Any alternative source of APIs should be preferably registered before the Marketing Authorisation of the medicines. However, maintaining several API suppliers in the dossier without actual purchasing APIs for production creates challenges for MAHs in view of the workload, API production oversight, audits and regulatory maintenance effort. Some policy measures should be put in place to encourage companies to look for alternative suppliers:
    - Incentives to reward manufacturers sourcing a second API supply as this is considerably more expensive than a single supply. For example, tender criteria should reward multiple API sources as part of security of supply (which is currently not recognised by any payers in the EU in any material way).
    - Information that is GMP related should be kept out of the Regulatory dossier and should be secured in a centralised GMP system to reduce the regulatory maintenance burden.
    - In urgent cases of adding a new API supplier, the procedure should be simplified and quicker.

Temporary imports: To balance the difficulties and costs of temporary Imports due to a shortage, Health Authorities should provide:

- Clear timelines and guarantees that committed import quantities are purchased, even if a competitor returns to the market. Otherwise alternative manufacturers face a financial risk for supplying a shortage.
- Flexibility in accepting products from another market without repacking with a translated patient information leaflet. The Commission should accelerate work on electronic patient information to permanently solve this issue.
- Flexibility for import licenses: In emergencies, we should allow medicines approved outside the EU (in highly regulated markets).

Repackaging:

- Allow secondary repackaging on a case by case approval by the NCA without adding the repackaging site to the regulatory dossier.
- Non-serialised products should be allowed on an exceptional basis (e.g. small volume, critical hospital products).
- Acceptance and implementation of an e-leaflet instead of a paper base leaflet, for example in hospitals where they do not use paper leaflets in any case. Alternative Dossier/ alternative medicinal product:
- If a product is already approved in another European market, a zero day repeat use procedure (RUP) should be the basis to register the dossier in the MS where the shortage occurs.
- An extended use of article 126a should be considered in cases when the MAH is not able to use the standard MA procedure.