Potential impact of coronavirus infection on availability of human and veterinary medicinal products – Status report

EU Executive Steering Group on shortages of medicines caused by major events
Agenda item 3
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An agency of the European Union

Background

- Chinese authorities have identified a cluster of novel coronavirus 2019-nCoV infections in Wuhan, Hubei, China. Cases have now been detected in several countries in Asia, but also in Australia, Europe, North and South America. Further global spread is likely
- Many active pharmaceutical ingredients are produced in China and the virus outbreak may affect the manufacturing capacity and stability of the supply of these ingredients (due to shutdowns of factories and transportation networks). This could lead to shortages of medicines worldwide

Preliminary actions taken (1/2)

1. Letter to EU Industry Associations (human and veterinary):
   - Reminding of obligations for reporting of disruptions/ cessations
   - Requesting perspective on preparedness
   - Requesting advance alerts for issues that may affect the pharmaceutical sector
2. Information request to the SPOC Network:
   - Information on any confirmed supply disruption due to the outbreak
   - Information or signals on potential disruptions
   - Information on particular medicinal products at risk
3. Information exchange with international partners

Preliminary actions taken (2/2)

4. Review of available data sources to determine potential impact of supply disruptions from China:

- Supply chains for Centrally Authorised Products (CAPs)
- Active substances directly imported into the EEA from China
- Finished product manufacturers located in China that have been inspected by an EEA authority

5. Review of ongoing inspection requests to establish if any impact due to postponement of inspections as a result of travel restrictions

Feedback from EU Industry Associations

- No specific disruptions yet, and only limited short term impact expected at this moment due to inventory already in place due to the Chinese New Year break, but major challenges are anticipated if lockdowns continue
- In addition, not just disruption of manufacturing but also logistics that will be impacted
- Economic impact on the broader economy – resumption of manufacturing with controls may take place short term

Feedback received from the SPOC Network

- Request for information sent to all NCA SPOCs on 6 February 2020 (48 in total):

✓ **Objective**: to understand the potential impact of COVID-19 infections on the supply of human and veterinary use MPs for the EU market

✓ **Response rate:** 29 Member States – and 35 NCAs in total - provided feedback

- Authorities continue monitoring the situation and are liaising with MAHs/relevant stakeholders to identify products at risk of supply and critical in their territories
- No confirmed signals or supply disruptions related to the coronavirus outbreak have been reported yet

Information received from international partners

- All authorities are monitoring the situation:
  - No supply disruptions due to COVID-19 reported by international partners so far
  - A number have contacted individual manufacturers or importers

Potential impact on the availability of CAPs (1/2)

- Identification of registered manufacturers located in China based on information in EMA database (SIAMED)
- 155 sites in China are registered manufacturers of CAPs
  - 104 manufacturers of intermediates
  - 63 manufacturers of active substances
  - 10 manufacturers of finished products
- Around 20 inspections coordinated by EMA of manufacturers located in south-east Asia may need to be postponed; no immediate impact on the authorisation of medicinal products is anticipated

Potential impact on the availability of CAPs (2/2)

- **195 CAPs** have at least one manufacturing site (active substance, intermediate or finished product) located in China
- There are also 25 ongoing MAAs with at least one manufacturing site located in China (15 H and 10 V)
- Only **5 CAPs** (4 H and 1 V) have both active substance and intermediate manufacturing site located only in China
- 26 CAPs have active substance manufacturing site in China only and 2 CAPs with finished product manufacturing site only in China
- There are around 68 MAHs concerned

Medicines at risk of supply: Methodology

- Is based on the methodology already used in the context of the Brexit preparedness, adapted to the COVID-19 scenario
- Consists of
  - A risk assessment
  - A criticality assessment
- Can be applied for both CAPs and NAPs

Medicines at risk of supply: Risk assessment

- MAHs of **CAPs** which have at least **one manufacturing site** (active substance, intermediate or finished product) located in **China** will be contacted by EMA
- EMA will request information on **preparedness** and any possible **supply disruptions** due to the outbreak
- Based on the information received from MAHs, EMA will develop a **risk matrix** taking into account e.g. number of manufacturing sites located in China in the supply chain, single source of active substance/intermediates in China and single source of finished product in China

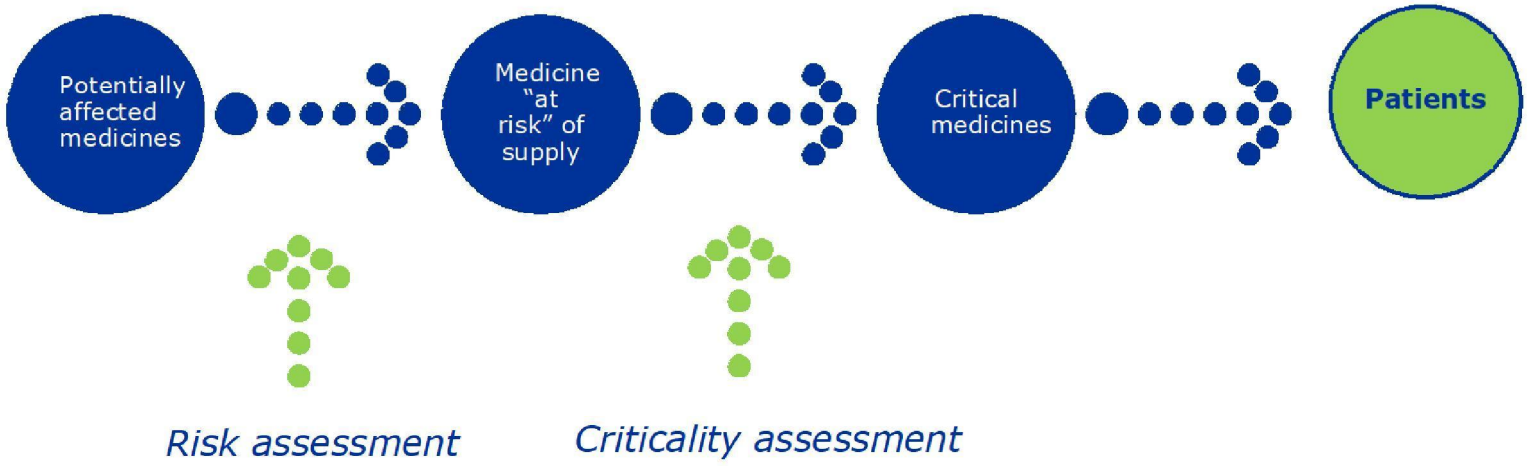
Medicines at risk of supply: Criticality assessment

- All products considered "at risk of supply" based on the information received from MAHs, will be subject to a **criticality assessment**
- The methodology is based on the Criteria for classification of critical medicinal products for human and veterinary use, and foresees two parts:

  PART A: CHMP/CVMP with the support of EMA will look at **therapeutic use,** i.e. the medicinal product is an integral part of the treatment for or prevention of a disease, which is life-threatening or irreversibly progressive, or without which the public and animal health could be severely harmed

  PART B: EMA will liaise with MSs with respect to the **availability of therapeutic alternatives** for each medicinal product, e.g. other products in the same class or even other classes, and generics

Medicines at risk of supply: Flowchart



Analysis of data from EUDRAGMDP for CAPs and NAPs (1/2)

- First phase concluded:
  - **486** registered importers in the EEA importing active substance from China
    (may yet include a small number of duplicates)
  - **~2267** active substances imported directly from China
    (duplicates as far as identifiable were manually removed, some may yet be included, for example Vitamin B1 - Thiamine mononitrate, difficult to capture completely manually; different qualities of the same AS were kept, for example Naproxen EP, Naproxen USP would be 2 different AS)
  - **767** active substance manufacturing sites located in China
    (best figure following clean-up of data; 778 sites previously reported)

Analysis of data from EUDRAGMDP for CAPs and NAPs (2/2)

- Second phase ongoing:
  - China APIs by therapeutic class – (selected);
    - Antibiotics, diabetes products, hypertension products, anti-virals, anti-malarial products (WHO request), anti-epileptics, anti-coagulants
  - Extension to Indian sites: APIs imported into EEA and FP manufacturers of interest
  - APIs manufactured in EEA

Inspections in the context of the Centralised Procedure

- For all the ongoing inspections, as discussed at the February 2020 CHMP meeting:
  - To monitor the situation/safety restrictions in the countries to be inspected
  - To ask the inspectors appointed to inform as soon as possible in case they foreseen any difficulty in travelling to the areas where the sites to be inspected are located
  - If needed, to liaise with Rapporteurs, inspectors and CHMP and take actions as appropriate (postponing the inspection, amending the sites etc.)
  - It may be that an inspection may be required for an application and that an opinion may be delayed should restrictions continue