

28 September 2022

Dear colleagues, and friends,

The European Stroke Organisation (ESO) Executive Committee (EC) and Boehringer Ingelheim (BI) had a 2nd meeting on the current shortage of alteplase and tenecteplase on 12.09.2022. We would like to give an update on the current situation.

Feedback from BI:

- The **shortage** of alteplase and tenecteplase is expected to last into 2024
- We had described the **causes** of the shortage in our first letter on 27.07.2022
- **Measures** taken by BI
 - **Immediate** measures
 - Immediate measures taken by BI **until 11.07.2022** (last TC with BI) were described in detail in our first letter. In summary these comprised of
 - **supply prioritization of Actilyse** 10mg, 20mg, and 50mg
 - **Prioritization of Actilyse** production vs Metalyse,
 - **Temporary discontinuation** of the **2 mg** strength of alteplase (Cathflo®)
 - **Communication** with official health authorities, patient and medical associations, and health care professionals on national levels.
 - Establishment of a fair and equitable **allocation process** world-wide and on national levels
 - Establishment of a **Lytics Taskforce**
 - Agreement with EU health authorities on a **shelf-life extension** of tenecteplase on specific batches.
 - Immediate measures taken by BI between **27.07.2022 and 12.09.2022**
 - **Shortening of maintenance downtime** of the manufacturing site leading to additional 4kg of alteplase (according to BI: this corresponds to about 57.000 acute stroke treatments assumed an average consumption of 70 mg alteplase per patient, provided no drug is wasted, and taken into consideration that alteplase is currently also used for patients with STEMI).
 - **Measure to reduce wasted alteplase** by increasing the amount of 10 and 20 mg vials and fewer 50 mg vials, with a total production quantity remaining constant.
 - **Approval of a new manufacturing process** with higher yield of alteplase in agreement with the responsible health authorities.
 - **Intensifying communication** with national BI contacts to further improve knowledge on supply and demand in different **countries**
 - **Medium-term** measures
 - Diversification of production into **new production sites as of 2024**

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Feedback from the ESO:

- As announced in our first letter, ESO has established a **thrombolysis taskforce**. Goals were described in the first letter.
- During the last meeting with BI on 11.7.2022 the impression was that the shortage may not be the same in all European countries.
 - Meanwhile **BI** had therefore **intensified communication** on national levels (see above), to appropriately address the situation
 - ESO performed a small **survey on the current status** in **33** countries between 27.7.2022 and 11.08.2022. Three questions on supply and consumption, communication and existence of a national action plan were asked to 45 representatives from different stroke societies associated to ESO.
 - Results:
 - Feedback received: 25 answers from 22 countries
 - Question 1: **Supply and consumption**: How do you currently estimate the situation of alteplase / tenecteplase supply and consumption?)

Answer	Participants
Unstable	4
Insufficient	3
Stable	18

- Question 2: **Communication**: Do you receive sufficient information on the situation?

Answer	Participants
No	3
Yes	22

- Question 3: Is there a **national action plan** to cope with the situation?

Answer	Countries
No	8
Yes	17

- In **summary**: overall the situation is regarded a stable and action plans have been installed in most participating countries
- Still, there are some countries where there is insufficient communication and supply.
- ESO has informed BI about these results.

Recommendations ESO (modified since 27.7.2022):

- Measures to be taken in your own institution:
 - **Localize storage/s** in your institution / hospital: Keep track of the locations where alteplase is stocked and check if stock is appropriate. Ensure that everyone involved is aware of the stock locations.
 - Set an **inventory target** of alteplase: We recommend a period of 3 to 4 weeks for a regularly dosed thrombolytic therapy as a stock target. To do this, you should use the average alteplase consumption of your clinic (e.g. cumulative amount in mg per month).
 - **Establish communication** with the **pharmacy**: establish a fixed communication structure with the hospital pharmacy and regularly (at least once a month) be informed about the status of stocks.
 - Information to **neighboring disciplines**: Inform other specialist departments site about the shortage, because the need for alteplase can also arise here (e.g. therapy of pulmonary artery embolism). Moreover, use of alteplase for the clearance of occluded catheters should be reserved to particular situations.

- Follow the information regarding extension of the shelf life of thrombolytic agents and be prepared to use the 10 and 20 mg vials instead of the 50 mg vials, when available/introduced in your country, so to avoid waste through leftovers.
- Ensure the right dosages are present in each Stroke bag: ideally, 1 pack 50 mg Actilyse, 2 packs 20 mg, 1 pack 10 mg or alternatively 50/20/10/10 (where available). Replenish only with replacement of the used strengths.
- Local networking: Inform the local emergency services about the current situation, exchange with neighboring SUs in a structured way and document it. There may be existing structures you might want to use like neurovascular networks, tele-stroke networks, stroke registries. The aim is to improve regional availability of thrombolytic therapy by supporting each other. We are aware that the situation in metropolitan areas is different than in rural regions. Thus, this may need to be adapted to the regional needs.
- Definition of **emergency measures**: Discuss with the emergency services and the neighboring SUs possible measures in case of critical stock reduction of alteplase. Again, local conditions need to be taken into account.
- It is of utmost importance to **keep into close contact with BI** to maximize the reliability of the demand which is key

In case you have questions, feedback, or suggestions please contact esoinfo@eso-stroke.org

ESO is on a constant exchange with the company since then.

Best wishes
Thrombolysis taskforce of the ESO Executive Committee

European Stroke Organisation (ESO)



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