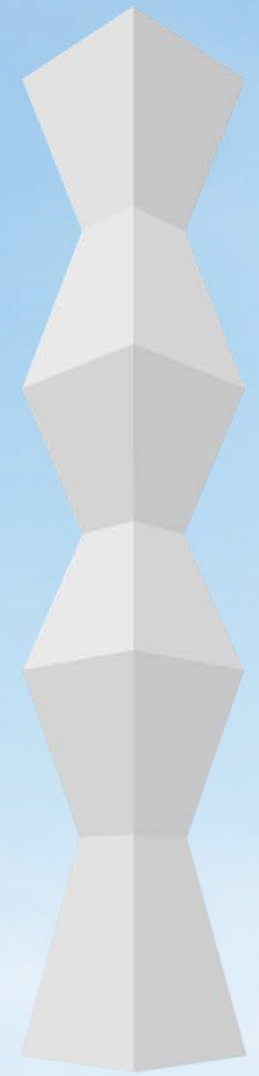
NATIONAL LEGISLATION ON SHORTAGE OF MEDICINES IN ROMANIA



ALIMS SYMPOSIUM
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NATIONAL LEGISLATION ON SHORTAGE OF MEDICINES IN ROMANIA

- The issue of shortages of medicines remains a serious problem with potentially serious consequences for the health of patients.

The obligation of continued supply transposed in Romania as far as MAHs are concerned

- National legislation provides that MAH and wholesalers of medicines actually placed on the Romanian market 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 patients' needs are covered, pursuant to conditions established through an order of the Minister of Health.

- According to this ***ORDER of the Minister of Health No. 269/2017 of 14 March 2017 on mandatory provision of medicinal product adequate and undisrupted stocks*)** →

- **MAH shall ensure adequate supplies equivalent to at least the average monthly turnover of the respective drug over the past three months, representing the minimum necessary to meet public healthcare needs**

- https://www.anm.ro/en/_/ORDINE/Order%20of%20the%20Minister%20of%20Health%20no.%20269_14.03.2017%20and%20Annex.pdf

Responsibilities of wholesale distributors in RO stemming from the transposition of the obligation of continued supply (public service obligation)

- **Each drug included in the health insurance system needs to be distributed by at least 3 different wholesalers**, except for exceptional situations that should be regulated by order of the Minister of Health.
- According to the rules for implementation of the **public service obligation**,

wholesalers shall permanently warrant compliance with the public service obligation by setting up ***buffer stock*** **equalling the average monthly turnover for each *enlisted medicinal product* they distribute**.

- ***Buffer stock*** –quantity of **enlisted medicinal products**, available in the wholesaler's stock between two successive supplies, representing the minimum adequate and continuous stocks able to meet any justified order placed with the respective wholesaler;
- ***Enlisted medicinal products*** *-trade names of medicinal products whose respective INNs are included in the List of International Non-Proprietary Names of on-prescription medicinal products provided to insurants, irrespective of personal contribution within the healthcare insurance system, as well as International Non-Proprietary Names (INNs) of medicinal products provided in the frame of national healthcare programmes, approved by Government Decision No. 720/2008, as amended"*
- **RO doesn't distinguish between full-line distributors and other distributors.**

Limits of of wholesale distributors' responsibilities in Romania

- ***Exceptional circumstances*** - situations notified by the MAH to the NAMMD, in accordance with the law, on matters of quality/safety, failure to supply active substances, withdrawal of the Certificate of compliance with the European Pharmacopoeia or of the Good Manufacturing Practice Certificate, temporary discontinuation of production;

Responsibilities of manufacturing authorisation holders
Responsibilities of the marketing authorisation holders and of the wholesale distributors
Notification of shortages is obligatory

- **OMH 502/2013 on approval of mandatory monthly reporting of placement on the market in Romania and of sales of medicinal products for human use, respectively, by authorised wholesale distributors/importers/manufacturers (https://www.anm.ro/en/_/ORDINE/Order%20of%20the%20Minister%20of%20Health%20no.%20502_11.04.2013%20and%20Annex.pdf)**

- **OMH 1345/2016 on daily reporting of wholesale distributors/importers/manufacturers /closed- and open circuit pharmacies on the status of their stocks and trade operations, distribution outside Romania included, conducted with medicinal products for human use in their portfolio**

- **Law 95/2006 Title XVIII –The medicinal product**

❑ ***The MAHs should notify NAMDM if, temporarily or permanently, a drug ceases on the Romanian market;*** *except for in exceptional circumstances, this notification shall be made* ***at least 6 months before*** *the medicinal product is discontinued; when the medicinal product is discontinued on commercial grounds, the notification shall be made* ***at least 12 months in advance*** *of actual discontinuation. In the 6- and 12-month period, respectively, the MAH shall comply with provisions of Art. 804 (2) of the Law 95/2006 Title XVIII –The Medicinal Product, therefore ensuring adequate and continuous stocks of medicines.*

❑ *In relation to wholesalers, MAHs have an obligation to ensure that each drug included in the List of the reimbursed medicinal products by the the health insurance system is distributed by at least* ***3 distributors*** *and buffer stocks are provided at the level of both MAH and first-line distributors.*

Specific definition of product supply disruption or shortage in Romania

According to the **OMH 269/2017 regarding the public service obligation**, in relation to a medicine already placed on the market, **decrease of the national level of stocks for the respective medicine (i.e. the category of drugs with the same INN, pharmaceutical form and strength) under the average monthly turnover for seven consecutive days generates a shortage national alert.**

- **average monthly turnover** -monthly average turnover of the respective medicinal product for the past three months, representing the minimum necessary quantity to meet public healthcare needs;

https://www.anm.ro/en/_/ORDINE/Order%20of%20the%20Minister%20of%20Health%20no.%20269_14.03.2017%20and%20Annex.pdf

Specific legal and other regulatory measures for critical or essential medicines

- Provisions on public service obligation apply to **all medicines placed on the market and included in the national reimbursement system** (as provided by **OMH 269/2017** on mandatory provision of medicinal product adequate and undisrupted stocks)
- The MoH has finalized the development of the **list of medicines of strategic interest** for RO, based on the WHO list of essential medicines, adapted and completed according to therapeutic specific needs.

Other actions the MAH, distributors, or pharmacies are required to take when anticipating or experiencing product supply disruption Legal / regulatory measures are in place

- **Since February 2015**, the NAMMD has been focused, as **additional self-undertaken task**, the management of the dedicated email address, lipsamedicament@anm.ro (engl. shortage@.....), also serving, since **September 2016**, as support to the MoH website http://medicamentelipsa.ms.ro/, e.g. **targeted responses** to patients/patient assoc./HCPS/pharmacies etc. providing **on-request information from wholesalers** on available stocks or on MAH non-marketing notifications.
- **Emergency Ordinance 8/ 02.2018 redefines** :
- ***Public service obligation***: the obligation placed on **MAHs/MAHs representatives** and **wholesalers to warrant the obligation to permanently ensure an appropriate range of medicinal products so as to meet the requirements of a specific geographical area and to deliver the supplies requested over the whole of the area in question within the shortest time possible after order,** as well as the obligation of **pharmacies to purchase medicines if out of stock at the time of the orders**; conditions specific on compliance with the public service obligation are established by order of the Minister of Health
- **New NAMMD and MoH tasks**

❑ **The MoH may establish temporary restrictive measures**, approved by OMH, **regarding their distribution outside Romania.**

❑ **The NAMMD shall notify the MoH and submit monthly reports to the MoH on supply disruptions**, as resulting from:

- - the monthly reports of placements on the Romanian market,
- - MAH notifications of temporary/permanent discontinuation and
- -shortage notifications submitted to the lipsamedicament@anm.ro (engl. shortage@.....) e-mail address

Article 23a of Dir 2001/83/EC obliges the MAHs to notify the authority if a product ceases to be placed on the market even temporarily.
Compulsory reporting of interruption of supply to the NCA
Penalties for non-compliance

- **Since June 2016, notifications are publicly available** on the NAMMD website, in a dedicated section:

https://www.anm.ro/_/DISCONTINUITATE%20MEDICAMENTE/19.01.2018%20Notificari%20Sunset%20pt.postat%20incepand%20cu%20luna%20IUNIE%202016.pdf

- According to OMH 269/ 2017,

„Where wholesalers are unable to meet the justified order, beneficiaries shall notify the NAMMD, in electronic format, to lipsamedicament@anm.ro as well as, for electronic medical prescriptions, respective healthcare insurance houses to which they are allocated."

- **MAH penalties** are provided for not notifying a supply disruption, as per Law 95/2006 Title XVIII The medicinal product

Specific export restrictions in place to mitigate the risk of shortage of medicines: scope and criteria they are based on

- **As per Emergency Ordinance 8/ 02.2018:**

❑ The MoH may establish **temporary restrictive measures**, approved by OMH, **regarding their distribution outside Romania.**

- **As per OMH 269/2017:**

❑ "**10 days before conduct of an intra-Community delivery**, transactions between two or more representative offices of the same company in different countries included, the **MAH, the wholesaler or pharmacies shall notify the NAMMD** by submission of the **filled-in self declaration** in respect of compliance with the public service obligation…"

- "**Temporary list of medicinal products under surveillance** - list of all trade names related to a medicinal product, as defined by INN, pharmaceutical form and strength, under **temporary ban of intra-Community supply and export**"
- "**The Temporary list of medicinal products under surveillance is approved and updated as necessary by order of the Minister of Health** and posted on the website of the MoH and the NAMMD."
- **These export restrictions are considered as part of transposition of the public service obligations under Article 81 !**

Monitoring the shortage situation for a particular medicinal product

- **As per OMH 269/2017**

“The average monthly turnover is calculated based on information submitted to the MoH via the **Electronic System for Inventory Reporting- ESIR,** as regulated by ***OMH no. 1345/2016 on daily reporting of stocks and trade operations carried out with medicinal products for human use included in the National catalogue of prices for medicinal products authorised for marketing in Romania by medicinal product distributors, importers, authorised manufacturers and closed- and open-circuit pharmacies.***

Specific penalties for interruption of supply/shortages

- **Penalties are provided in that respect** (applied to the wholesale distributor, the pharmaceutical unit and MAH in case of non-compliance with the **public service obligations**.
- **If within a period of 3 months it is found that the same contravention has been committed, the distribution or operating authorization shall be withdrawn.**

Actions taken in the case of a MAH is informing NAMMD of its plans to discontinue the marketing of a medicinal product (deregistration), where no other alternative is available

- **Working meetings** are taking place **with the MoH, MAH and NAMMD regarding shortages notifications / deregistration** (some of them, successful ones)

- **The MoH Consultative commissions** evaluate the possibility of resorting to the legal lever offered by ***OMH 85/2013 on approval of the Norms for implementation of provisions of Article 703 (1) and (2) of Law No. 95/2006 on healthcare reform concerning medicinal products for special needs*** if the medicine may not be replaced by a different drug available on the market.

Real life examples on acting on shortage of essential medicinal products

- Issuance of the ***OMH on approval of the List of INNs at high unavailability risk, as provided to insurants in the health insurance system and agreement on a measure to secure their market availability in Romania,*** **in force between 2014 - 2015** → *"Distribution outside Romania of medicinal products included in the List is temporarily suspended"* → according to provisions of Directive 83/2001/EC transposed into the national legislation ("***grounds of public health protection***")

  The List mainly contained **oncologic and diabetes medicines**.

- October 2017 → notification on temporary shortage of the only **asparaginase-containing product** → Issuance of an **Authorisation for special needs** for a different asparaginase-containing medicine
- Between 2016-2017, all MAHs for **immunoglobulins-containing medicines** notified the NAMMD on marketing discontinuation, with immediate patient impact. **No possibility was identified to impose penalties because the respective MAHs did not have legal representatives in Romania** →The MoH has activated the **Mechanism for civil protection** for this issue.
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What has not worked……

- There **are many centrally authorised medicines** which are **not placed on the Romanian market**
- **Legislative limitations on transposition and applicability of Article 81** are the following circumstances:

❖The MAH has not designated a legal representative in RO **and the NAMMD cannot impose penalties on a legal entity outside its borders (as in the case of immunoglobulins MAHs)**

❖**MAHs decide on where to market their centrally authorised medicines**, which is detrimental for other Member States patients (RO included …)

BEMA IV→ NAMMD → 2-4 July 2018 (1)

•STRENGTHS/BEST PRACTICES

- **innovative mechanisms to dealing with shortages of medicines→ The framework includes identification and reporting, assessment and resolution and development of co-operation with external stakeholders.**
- The MoH, the National Agency → are liable for ensuring public health and integration of public health priorities into national policies and strategies.

The Agency facilitates early access to medicines pursuant to an order of the MoH on approval of conditions for authorisation of human medicinal products for compassionate use.

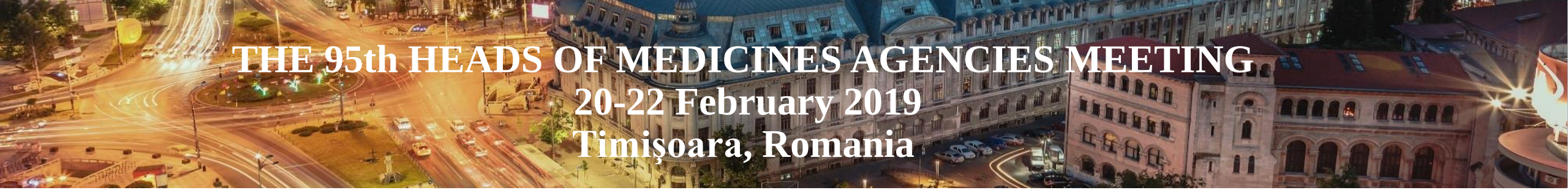
- **facilitates access to medicines considering switches from Rx to OTC (**decision of the Agency's Scientific Council).
- **monitors the market for availability and reports to the MoH→The MoH Advisory Specialised Commissions decide on appropriateness of authorisation of special needs medicines.**
- **posts on the Agency's website Notifications relevant for supply disruption and Intra-Community deliveries.**

BEMA IV→ NAMMD → 2-4 July 2018 (2)

- **works with the MoH** for draft of national legislation on measures for optimal avoidance of public health impact of shortage such as:
- **Order of the MoH on mandatory provision of medicinal product adequate and undisrupted stocks** (There are certain additional technical aspects to be improved, such as the algorithm triggering the national shortage alert, for which several formulas have been established, currently under testing);
- **Order of the MoH on daily reporting of stocks and trade operations** carried out with medicinal products for human use included in the National Catalogue of Prices for medicinal products authorised for marketing in our country by medicinal product wholesalers, importers, authorised manufacturers, closed- and open- circuit pharmacies;
- **has formulated answers to the Commission's questionnaire on implementation of Article 81** provisions in the various MSs, discussed in the Pharmaceutical Committee and the HMA –EMA Task force on availability.

The Minister of Health:

- has had the **initiative to discuss the issue of parallel trade with other EU ministers,** which has been identified as one of the causes of the European drug deficit.
- **has finally launched the EU Civil Protection Mechanism**



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- Regulatory provisions are instated in Romania, aimed to as much as possible avoid shortage impact on public health.
- IE highlights that, as seen from meetings with various MAHs, the latter are reticent to the legislative approach to shortages.
- IT advises on shortage avoidance-related legislative measures initiated in Italy, difficulties encountered such as late notifications or lack of notification, which has now led to submission of a new legislative proposal to the Italian Parliament to revise related legislation by extension of the mandatory period for notification and provision of penalties for non-compliance.
- HMA members are informed on the Task Force on Availability initiative to build up a system for regulators in the EudraVigilance consisting of a system of contact points for availability issues, to start in March.
- FI mentions the need to limit the number of exceptions in relation to obligatory notification, whereas Brexit-triggered shortages seem to need a special approach.
- AT emphasises that, in spite of the relative difficulty to notify shortages in advance, it is also planning to request notification.
- Representatives of LV, FI, NL, EE, CZ have also expressed appreciation regarding the Romania's legislative approach on shortages.

Thank you!