

TB MEDICINE CRISIS IN ROMANIA

REPORT SUMMARY



Romanian
Health
Observatory

Stop TB Partnership
ROMANIA

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Mapping the need for tuberculosis medicines

REPORT SUMMARY

October 2017, Bucharest

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REPORT SUMMARY

15 medicines essential for the treatment of tuberculosis are reported to have availability or purchasing problems in Romania.

THE PROBLEM

Romanian authorities are unable to provide the full range of essential medicines needed for the treatment of TB, a contagious disease designated as a public health priority in Romania. The majority of the medicines needed for the treatment of drug-resistant tuberculosis (MDR-TB / XDR-TB) are currently not available for patients through the national public health programs run by the Romanian Government.

At this point, international organizations are providing and co-financing the procurement of essential medicines needed for Romanian TB patients. The international funding will end in the first quarter of 2018. The patients will be left without access to the full course of treatment if the Romanian authorities will not be able to take over the procurement. Currently, the Government of Romania - an European Union member state - is not fulfilling its legal obligations towards TB patients.

THE ROOT CAUSE

The existence of absurd and self-contradictory legislation and widespread government red tape blocks Romanian TB patients' access to essential treatment.

THE EFFECT

Curing TB patients in Romania is a serious challenge. The country has the highest number of drug-resistant TB cases in European Union, but one of the lowest rates of successful management of drug-resistant TB in the world. Existing red tape and Romanian government passivity in tackling these problems greatly hampers the therapeutic efforts of the medical doctors and is not helping the spread of tuberculosis among the Romanian population.

“A Romanian TB patient enrolled in a program coordinated and funded by international organisations is luckier than a patient enrolled in the public health program managed by the Romanian government”

- Romanian M.D. specialized in treating TB, September 2017

TB status in Romania

- **21 167 TB patients in Romania in 2016** *
- **The lowest rate of successful TB treatment in the European Union** **
- **1 out of 4 cases of TB** diagnosed in EU in 2015 are from Romania ***
- **1 055 people died in Romania due to TB** in 2015 *
- **12 790 new and recurrent cases** registered in Romania in 2016 **
- People affected by TB come mainly from the young, active population *
- **Bucharest, Dolj, Iași and Bacău:** the counties with the most TB cases in Romania *
- More than **500 new cases of drug-resistant TB are detected annually** **
- According to WHO estimates, 800-1000 new cases of drug-resistant TB should be diagnosed annually in Romania. The lack of equipment and supplies required for a proper diagnosis leads to the detection of only 500-600 cases per year. **

The Romanian Government has decided by Decision 121/2015 that "Tuberculosis in Romania is a priority of public health". Unfortunately, through passivity, the Romanian authorities ignore this major issue and fail to provide TB patients with "complete, continuous and well-administered treatment", an obligation stipulated in the law.

Furthermore, by maintaining contradictory legislation and red tape, Romanian authorities aggravate the situation of TB patients and contribute to the increasing number of patients

* source: Institutul de Pneumoftiziologie "Marius Nasta" UATM-PNPSCT. Endemie TB – iunie 2017.

** source: Institutul Național de Sănătate Publică. Analiza de situație TBC. 2017.

*** source: European Centre for Disease Prevention and Control. Tuberculosis surveillance and monitoring in Europe, 2017.

with drug-resistant tuberculosis (a phenomenon acknowledged by the National Strategy for Tuberculosis Control in Romania).

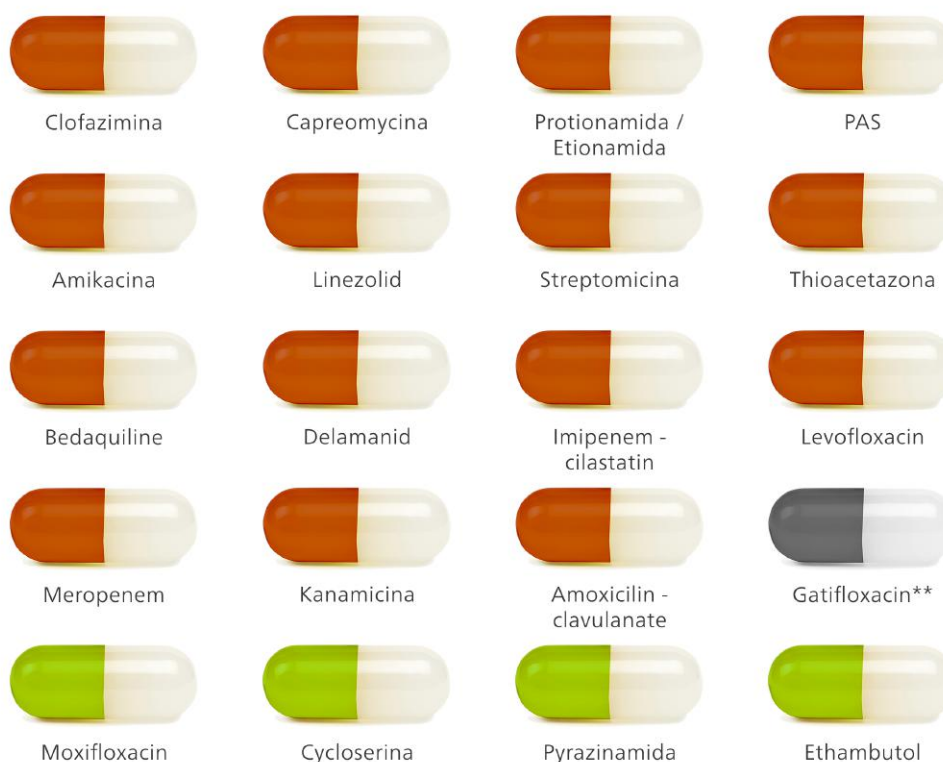
IMPORTANT Anti-TB treatment consists of several drugs that should be administered simultaneously. If the patient takes incomplete anti-TB treatment, then the bacteria will become resistant to the available medicines very quickly.

Out of the 28 investigated TB medicines mentioned as essential or necessary for the treatment of tuberculosis and drug-resistant tuberculosis by the World Health Organization or by the Methodological Guidelines for Implementing the National Program for the Prevention and Control of Tuberculosis in Romania, **15 essential drugs are reported to be unavailable or have disruptions in supply** caused by existing legislative barriers in Romania. Other 3 drugs recommended in international guidelines, but considered to have alternatives, are missing from Romania.

- Of the 20 medicines recommended by the World Health Organization for the treatment of drug-resistant tuberculosis (MDR / XDR-TB), 15 medicines are missing or are reported to have supply difficulties in Romania.
- 8 medicines are not included in the official reimbursement list of the state-funded National Program for TB patients, although they are officially recommended by the World Health Organization guidelines.
- 14 medicines don't have an official price, making impossible their legal purchase by public institutions (they are not included in the MoH Order 1605/875/2014). This represents an important bureaucratic barrier for TB patients access to essential medicines. The Romanian government has a legal obligation to provide this medicines to the patients.
- Centralized tenders were not organized for 14 medicines, either because of insufficient funds or due to bureaucratic barriers. In 5 cases, anti-TB medicines can legally reach patients only if they have a diagnosis of both tuberculosis and HIV.
- 10 essential TB medicines are brought to Romania through special needs authorizations, a grueling and time-consuming procedure which should be used only in isolated and exceptional cases.
- 5 TB medicines do not have an authorization to market in Romania because of lack of commercial interest from the market authorization holder.

It is important to note that some of the medicines mentioned in this report are available in Romania and can be reimbursed to patients for other diseases, but not for tuberculosis. This situation exacerbates already existent inequities: Romanian TB patients are not reimbursed for essential medicines that are instead available to patients with other pathologies.

AVAILABILITY OF MULTIDRUG-RESISTANT TUBERCULOSIS MEDICINES* IN ROMANIA



* RECOMMENDED BY THE WORLD HEALTH ORGANIZATION ** GATIFLOXACIN (MISSING) IS INCLUDED IN THE WHO GUIDELINES, BUT IT IS NOT CONSIDERED ESSENTIAL BY THE ROMANIAN MEDICAL COMMUNITY

**15 MEDICINES MISSING
OR WITH PURCHASE PROBLEMS**

**4 MEDICINES AVAILABLE
ON THE MARKET**

TB MEDICINES WITH SUBSTANTIAL RISK OF DISCONTINUITY

Very High Risk Group (medicines with registration problems in Romania)

- Clofazimine
- Para-Aminosalicylic Acid (PAS)
- Capreomycin
- Protionamide

High Risk Group (TB medicines not included in the official reimbursement list at the specific section of the TB national program or non-priced medicines)

- Levofloxacin
- Linezolid
- Meropenem
- Amoxicillin & clavulanic acid
- Imipenem & cilastatin

Medium Risk Group

- Kanamycin
- Rifabutin
- Delamanid

“I don’t know if the TB medicine crisis is caused by bad intentions or indifference.”

- Romanian MD working in a TB specialized healthcare facility, September 2017

CAUSES OF THE TB MEDICINE CRISIS

All of the following drugs are recommended for the treatment of tuberculosis in international guidelines developed by the World Health Organization.

1. A significant number of essential TB medicines are not included in the official national reimbursement list (Government Decision 720/2008) under the section dedicated to the TB treatment national program.

Harmful effects: None of these essential medicines can be centrally purchased by the Romanian Government using funds earmarked for the National Program for the Prevention and Control of Tuberculosis. This situation is a serious barrier to access to treatment for the Romanian TB patients.

Bureaucratic absurdity: The same medicines not included in the official reimbursement list for the National Program for the Prevention and Control of Tuberculosis are included in the National Program for HIV. Practically, patients diagnosed with HIV and TB are more fortunate than patients who have only a diagnosis of tuberculosis, as access to essential treatment is restricted for the latter.

Failing to accurately update the official reimbursement list for the National Program for the Prevention and Control of Tuberculosis led to a situation where medicines that are no longer recommended for the treatment of TB by WHO guidelines, such as Ciprofloxacin, are still included in the official reimbursement list, while essential medicines such Clofazimin are absent.

Paradoxes: There are serious inadequacies in the very way in which these legal acts are formulated. Different articles of the Health Law 95/2006 or from the secondary legislation are not correlated and contradict each other.

It should be noted that the Ministry of Health has proposed changes that solve some of these legislative contradictions. Until the publication of this report, these changes were not approved by the Romanian Government.

- 2. Nearly half of the TB essential medicines recommended by the World Health Organization were not granted an official purchase price by the Romanian authorities. Therefore, they cannot be legally purchased by the Ministry of Health.**

Harmful effects: In order to be procured by the authorities with funds earmarked for the National Program for the Prevention and Control of Tuberculosis, these medicines should receive an official purchase price (according to the MoH order 1605/875/2014). Without this price, essential TB medicines cannot be bought and cannot reach patients.

Bureaucratic absurdity: Four drugs are in an illogical situation. They are included in the official reimbursement list allowing their reimbursement (Government Decision 720/2008), but not in the list setting their purchase prices (Ministerial Order 1605/875/2014). Without being included in both lists, the authorities cannot procure these medicines from funds earmarked for TB patients. Example of essential medicines included on the reimbursement list but without a purchase price: *Kanamycin*, *Para-aminosalicylic acid*, *Rifabutin*, *Capreomycin*.

Paradoxes: One essential medicine for the MDR/XDR TB patients, Protionamide, was excluded from the list of purchase prices in April 2017. However, Protionamide is maintained in the official reimbursement list being, at least in theory, allowed to be reimbursed to patients with drug-resistant tuberculosis. But in the absence of an official purchase price, the medicine cannot reach patients. In Romania, there is no alternative to this treatment.

TB MEDICINES	Market Authorization in Romania	On the TB Reimbursement List	Official purchase Price	Purchased from TB funds
CLOFAZIMINE	No	No	No	No
CAPREOMYCIN	No	Yes	No	No
p-AMINOSALICYLIC ACID	No	Yes	No	No
PROTHIONAMIDE	No	Yes	No	No
LEVOFLOXACIN	Yes	No	No	No
LINEZOLID	Yes	No	No	No
MEROPENEM	Yes	No	No	No
KANAMYCIN	Yes	Yes	No	No
AMOXICILIN-CLAVULANATE	Yes	No	No	No
IMIPENEM-CILASTATIN	Yes	No	No	No
RIFABUTIN	No	Yes	No	No
DELAMANID	Yes	Yes	Yes	No
BEDAQUILINE	Yes	Yes	Yes	No
AMIKACIN	Yes	Yes	Yes	No
STREPTOMYCIN	Yes	Yes	Yes	No

* Yellow: the drug is not registered by a MAH, but procured by the state wholesaler

Table: status of TB medicines with availability problems in Romania

3. A very useful legislative provision for TB patients is unused due to the passivity of the Romanian authorities.

Harmful effects: At the beginning of 2017, the approval of a legislative amendment allowed all TB medicines recommended by the World Health Organization's guidelines to automatically receive full reimbursement in Romania (Ministerial Order 487/2017) and, consecutively, to be included on the official reimbursement list in the specific section dedicated to the TB National Program. However, a single drug, Delamanid, has benefited from this provision for the time being (Decision 159/2017) and has been placed on this list.

Bureaucratic absurdity: These medicines can benefit from the provision only if the Marketing Authorization Holder (MAH) submit a health technology assessment (HTA) application to the National Agency for Medicines and Medical Devices (NAMMD). According to the legislation, even in the absence of this request, NAMMD may initiate ex officio the evaluation of the respective medicine if it meets one of the criteria provided by the law.

However, the legislation does not explicitly provide for the obligation of the Romanian authorities to carry out this assessment in the absence of an interested MAH and in the presence of a major public health concern.

Paradoxes: The fact that some of these drugs don't have a registered indication in Romania for TB treatment (so-called off-label medicines), even if they are recommended by WHO guidelines, is sometimes used as a bureaucratic argument against the need to change legislation. In fact, there are medicines with no registered indication in Romania for TB, which are included in the official reimbursement national list under the specific section dedicated to the TB National Program - for example Moxifloxacin. At the same time, other off-label TB medicines are not included in the official national lists required for reimbursement. There is no explanation for these different approaches.

4. Essential medicines for the treatment of drug-resistant TB (MDR / XDR-TB) are not registered on the Romanian market.

Harmful effects: Essential medicines for patients with drug-resistant tuberculosis have no marketing authorization in Romania and therefore cannot be purchased by the Ministry of Health. Clofazimine and Capreomycin are the most worrying examples. This is caused by a lack of commercial interest from the market authorization holders. The pharmaceutical pricing policies of the Romanian government combined with a number of patients who do not guarantee profit have turned Romania into an unattractive market for the companies that produce essential TB medicines.

Bureaucratic absurdity: Medicines without a market authorization can be brought to Romania only by issuing a *special needs authorization*. This solution is "temporary", as explicitly stated in the legislation. Today, 10 essential TB medicines are brought in Romania by special needs authorizations, which has turned from a "temporary" solution into a permanent one. Such special needs authorizations are issued both for registered medicines and unregistered medicines in Romania, both for medicines with indication for tuberculosis, and without (off-label).

In the absence of coherent and consistent legislative solutions, this provision tailored only for exceptional cases became the rule. This makes TB medicines purchasing rules unpredictable, subject to the good-will of different decision-makers and exposed to supply disruptions.

Paradoxes: The procedures for obtaining a special needs authorization are laborious and time-consuming. The submission file must contain a large number of documents, including five different certificates, which may expire prior to approval of the special needs authorization, requiring their re-filing. The time for obtaining a special needs authorization for TB medicines recommended by the WHO guidelines is between 6 and 8 months.

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