



## COUNTRY PROFILE: CANCER MEDICINES SHORTAGES

# ROMANIA

### Introduction

EU indicators	2018 ratings
Political environment rating (10=high)	5.4
Effectiveness of system in policy implementation (5=high)	2.6
Infrastructure rating (10=good)	5.6
Level of corruption (5=low)	2.0

The cancer medicines shortage crisis in Romania is just as problematic as it was five years ago; in 2013, The Economist reported more than 20 types of cancer medicines missing.<sup>1</sup> This report aims to provide an insight into the reasons why shortages continue to impact the lives of Romanian cancer patients.

Romania has the lowest share of GDP dedicated to healthcare in EU at 4.9%, which is significantly below the EU average of 9.9%.<sup>2</sup> Struggling with a health system that is underfunded, an unstable political situation and lack of adequate healthcare infrastructure and administration, the country faces a barrage of serious issues.

Romania is among the top ten countries in Europe for the highest cancer mortality rates.<sup>3</sup> With this in mind, a comprehensive and updated cancer control plan was developed in 2016 (the Romanian National Integrated Multi-Annual Cancer Control Plan 2016-2020). Although the plan was never approved or implemented, the process for rolling out population-based screening programmes for breast, cervical and colorectal cancer was initiated. Romania does not currently have a high quality cancer surveillance programme, leading to a subsequent lack of knowledge around the exact number of cancer cases in the country.

With fundamental steps in cancer surveillance lacking, unsurprisingly, the issue of cancer medicine shortages does not always remain high on the list of priorities for policymakers. According to the definition of the European Medicines Agency (EMA), a medicine shortage “occurs when supply cannot meet demand at a national level.”<sup>4</sup> Based on new analyses conducted by the Romanian Health Observatory, during 2015-2017, more than 2600 complaints about lack of medicines have been filed with the National Agency for Medicines and Medical Devices (NAMMD).<sup>5</sup> Most of these medicines are used to treat cancer. During the period of analyses, 24 medicines from the list included in the National Oncology Program faced shortages or were permanently withdrawn in Romania, and a further 13 were identified as being at significant risk of discontinuation.

*“Shortages are happening every day, every week, every month. There is no change from five years ago.”*

– Patient, Pharmacist and Physician Representatives

#### Box 1. National Oncology Program, Romania

The National Oncology Program covers a list of 113 medicines for people diagnosed with cancer. All included medicines are fully reimbursed by the National Health Insurance House (CNAS) in Romania. Access to these medicines is theoretically guaranteed by the Romanian Constitution. However, there is no reliable system to proactively prevent and solve shortages when they occur.

*“A box of cisplatin (vials of 50mg/ml) costs €6. Six Euro is not an amount a patient should lose their life for.”*

– Monica Althamer,  
Patient Representative

**What is happening on the ground?**

Shortages are a serious issue in Romania, affecting a large number of patients and making their lives incredibly challenging. Facing a cancer diagnosis is scary, impacting patients both emotionally and physically. Coping with cancer is already difficult but imagine if the hope of recovery or symptomatic relief was taken away because the medicine you needed had gone missing, not just for a few days, but for months on end. The 2018 medicines shortages survey conducted by the European Association of Hospital Pharmacists (EAHP) reported that the mean duration of shortages in Romania is six and a half months. Furthermore, the report highlights the example of bleomycin, a medicine used to treat different types of cancers, which was not available in the country for two years.

As a result of medicines shortages, a large number of patients are forced to turn to the unofficial community of ‘underground’ volunteers in Romania to purchase generic inexpensive cancer medicines from other countries such as Austria, Bulgaria, Germany and Hungary. This is also only an option for those patients who can afford to purchase the medicines, whereas many less affluent patients are forced to wait until the shortage crisis is over. Moreover, while this might be a solution for oral medicines, intravenous medicines procured by patients cannot be administered in hospitals as the safety and Good Pharmacy Practice cannot be guaranteed.

**Table 1. Examples of cancer medicines affected by shortages in 2017 - 2018**

Name of cancer medicine	Indication
Asparaginase	Acute lymphoblastic leukaemia
BCG (Calgevax)	Early stage bladder cancer
Calcium Folate	Administered to diminish the harmful effects of certain medicines and chemotherapeutic agents
Carmustine	Lymphoma; myeloma; brain cancer; Hodgkin’s disease; non-Hodgkin’s lymphoma
Chlorambucil	Chronic lymphocytic leukaemia; low grade non-Hodgkin’s; Hodgkin’s lymphoma; waldenstrom’s macroglobulinaemia
Cisplatin	Testicular; ovarian; bladder; head and neck; lung cancer; cervical cancer; breast cancer
Melphalan	Myeloma; melanoma; ovarian cancer; sarcoma polycythemia rubra vera; advanced breast cancer
Vincristine	Leukaemia; lymphoma; myeloma; breast cancer; head and neck cancer; other cancers; paediatric solid tumours
Methotrexate	Acute lymphoblastic leukaemia; breast cancer; head and neck cancer; lung cancer; non-Hodgkin’s lymphoma; osteosarcoma; other cancers

Physicians and pharmacists are also impacted. In some cases when a prescribed medicine is missing in Romania, pharmacists and physicians turn to their network of connections – it is worth highlighting that some health professionals such as pharmacists are able to source medicines in Romania, if they have the right connections, when many others are unable to.\*

**Why do inexpensive cancer medicines go missing?**

The causes for cancer medicines shortages are multifaceted. Contrary to popular belief, in Romania, the problem is not about funding as most of the cancer medicines missing are generic and inexpensive. Many are essential cancer medicines listed in the WHO Model List of Essential Medicines and referenced in the ESMO Clinical Practice Guidelines.

Source: Romanian Health Observatory (RHO), expert interviews

\*Expert interviews

### Main reasons for cancer medicines shortages in Romania

- **Low prices** - Romania has some of the lowest prices for medicines in Europe – a result of the Romanian State Price Policy which places a price ceiling on medicines. Some of the following causes for shortages in Romania stem from this low price ceiling.
- **Parallel exports** – The EU trade laws allow free movement of goods across borders. Due to the low price ceiling of medicines in Romania, parallel traders are able to purchase medicines for low prices and sell them in higher-price countries. This leads to a depletion of stocks in Romania.<sup>6</sup>
- **Lack of commercial incentive for manufacturers** – Low price ceilings in Romania make the market less attractive for manufacturers to continue to supply medicines to the country. This results in manufacturers withdrawing medicines from the Romanian market.
- **Inability to forecast demand for medicines** – Without knowledge of how many cancer cases there are in the country, it is difficult to forecast the amount of cancer medicines needed for patients. Current legislation states that manufacturers must be able to supply adequate stocks of medicines for the internal Romanian market but the actual demand for medicines is not clear.
- **Administrative capacity** – In addition to the causes listed above, other aggravating factors include administration issues such as lack of expertise, procedural and legal deficiencies, budget constraints, and the political situation in Romania. With the frequent changes in government, it can be difficult to mobilise political will and find the administrative capacity to address the issue of medicines shortages.

### Case study. Tamoxifen shortage, 2016

Tamoxifen is an oral form of hormone therapy used in the prevention and treatment of breast cancer. It is an inexpensive medicine which has been on the market for decades. It is used in women who are oestrogen receptor positive (ER+). Tamoxifen is on the WHO Model List of Essential Medicines and also on the National Oncology Program in Romania. Two years ago, tamoxifen disappeared from the Romanian market for six months.

The impact on women with breast cancer was high as breast cancer is one of the most common cancers in Romania. In 2016, there were approximately 7,000-9,000 new cases of breast cancer. About 40,000 women were living with the disease in the country. Of these women, more than half are ER+.

A shortage of tamoxifen presents a challenging situation because, although there are alternatives to tamoxifen, these are generally more expensive. Tamoxifen is mainly used to maintain remission from cancer and is used to prevent recurrence in the adjuvant and curative setting. Disruption in treatment could result in cancer recurrence. Tamoxifen is also used in the metastatic and non-curative setting to prolong and improve the quality of survival.

To ensure the supply of tamoxifen to women with breast cancer, alongside several other medicines, tamoxifen is currently being procured by the Romanian health authorities using an "Authorisation for Special Need." This is a temporary measure in place as there is no regular uninterrupted supply of the medicine.

**Table 2. Who is involved in tackling shortages in Romania and what are the current initiatives?**

Competent Authority	Responsibilities and current initiatives
Ministry of Health (MoH)	<ul style="list-style-type: none"> <li>● The Ministry of Health manages a website showing stocks of medicines (<a href="http://ser.ms.ro/access/user">ser.ms.ro/access/user</a>).<sup>7</sup> Manufacturers, pharmacies and distributors are legally obliged to update the website with their medicine inventories. However, compliance is unknown.</li> <li>● The NAMMD, on behalf of the MoH, manages a public website (<a href="http://medicamentelipsa.ms.ro">medicamentelipsa.ms.ro</a>) where healthcare professionals and patients can submit information about a shortage in their area.<sup>8</sup> The Agency tries to find temporary solutions to ensure medicine supply or seeks to provide information about alternatives.</li> <li>● In extreme cases where the numbers of medicines drop below a defined fixed level of stock, the Ministry is able to put a temporary ban on parallel exports.</li> <li>● In 2016, a joint procurement agreement was signed between Romania and Bulgaria. One of the aims of the agreement was to facilitate exchange of medicines in short supply between the two countries. Although the agreement was not implemented, on 23rd of October 2018, it was announced that discussions with Bulgaria had taken place to resume negotiations.</li> <li>● On 22nd of October 2018, the Romanian MoH also reported intentions to collaborate with the Republic of Moldova for the procurement of medicines. Further to this, on 5th of November 2018, plans for a cooperation agreement with a focus on medicines supply issues between Romania and the Sultanate of Oman were announced.</li> </ul>
National Agency for Medicines and Medical Devices (NAMMD)	<ul style="list-style-type: none"> <li>● The NAMMD receives and manages notifications for shortages or permanent discontinuation of medicines from the marketing authorisation holder (MAH).</li> <li>● In the case of a medicine shortage where no alternative treatment is possible, the NAMMD is able to request an 'Authorisation for Special Needs' on a wholesaler request to bring medicines into the country. Medicines brought in on special needs authorisation are exempt from the Romanian price policy regime established by the law. The special needs authorisation is valid for 12 months but is currently issued on a case-by-case basis. CN Unifarm SA is the only medicine distributor owned by the Romanian State and is responsible for the procurement of cancer medicines using the special needs authorisation.</li> </ul>

## Looking to the future

It is evident that this ongoing situation of cancer medicines shortages in Romania cannot continue. Representatives of patients, pharmacists and physicians had several considerations and potential solutions to help mitigate shortages in Romania, described below:

- Currently, the number of cancer cases in Romania is unknown due to inadequate surveillance and monitoring. Without this, it is impossible to know the volume of medicines needed. Lack of data is not a cause of shortages but it can become an issue when trying to mitigate shortages.
- It is important that the health authorities and policymakers recognise that medicines shortages pose a significant public health issue and more needs to be done. It needs to remain high on the list of priorities.
- The current initiatives in place to mitigate cancer medicines shortages are short-term answers to a long-term problem. The system needs to be proactive with regards to knowing when a shortage might occur, currently it is reactive.
- In some cases, the information on the website showing stocks of medicines is somewhat misleading as it is not always clear whether the medicines are actually available or not. Accuracy of the information on the website is unknown. The information should be able to inform patients and physicians whether there is a genuine shortage situation.
- Distributors and pharmacists are currently required by law to update their medicine inventories onto the medicine stocks website, however there is no consequence if it is not done. This process should be monitored and managed more closely.

## Potential solutions

### Solution 1

#### Improve cancer surveillance in the country

- Improve the quality of the existing regional population-based cancer registries so that they document cancer incidence and cancer stage within the country.

### Solution 2

#### Establish strategic plan for medicines shortages

- Trigger further investigation during a medicine shortage and, if necessary, use the temporary parallel export ban or special needs authorisation when a large amount of medicines are missing and a large number of patients are affected.
- Furthermore, Romania could look into implementing legislation similar to the 2016 Health Law in France: place restrictions during a shortage to prevent wholesalers from selling medicines outside of the country for export.
- Consider shortening the supply chain where manufacturers and wholesalers supply directly to hospital pharmacies during a medicine shortage.
- Provide more detail on medicamentelipsa.ms.ro website in response to shortage notifications: specifically, if there are stocks, the name and location of distributors, name of hospitals receiving the medicine, date of availability in hospitals and duration of availability.

### Solution 3

#### Develop a reporting system for medicines shortages

- Closely monitor and mandate the national medicine stocks website ([ser.ms.ro/access/user](http://ser.ms.ro/access/user)) to ensure all distributors and pharmacies in Romania update their medicine inventories regularly in a timely manner.

### Solution 4

#### Establish procurement models designed to prevent medicines shortages

- If possible, consider re-evaluating the Romanian Price Policy and the prices for inexpensive, essential cancer medicines including those on the WHO Model List of Essential Medicines in order to prevent parallel exports or withdrawals of essential medicines from the market.

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