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## PHARMACY WITH ONCOLOGICAL PROFILE IN ROMANIA. REALITIES AND PERSPECTIVES

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### **Abstract**

*The activity in the pharmacy with oncological profile generates a series of challenges both from the point of view of the staff, of the management and the preparation of the medicines. These challenges are directly related to the legislation regarding the activity with cytostatic drugs, and the connection between the two aspects is the theme of this paper.*

**Keywords:** Pharmacy, oncology, cytostatics)

### INTRODUCTION

In the last 18 years we have witnessed a process of change in the pharmaceutical field, including that specific to hospital pharmacy. One of the fundamental principles on the basis of which the pharmacist carries out his activity is represented according to the Pharmacist's Code of Ethics<sup>1</sup>, art. 4, lit. f), "the provision of pharmaceutical services is done at the highest possible quality standards based on a high level of scientific competence, practical skills and professional performance, in accordance with the progress of pharmaceutical science and practice", the hospital pharmacist becomes concerned with improving the quality of the activities they carry out in support of the patient. Thus, it is necessary to adopt normative acts, consolidate the existing ones, as well as implement European quality standards. (Apan. R.D., Bala C.G., 2021).

The oncology pharmacy represents the pharmaceutical activities of preparation, reconstitution and dilution of cytostatic solutions for the administration of patients. The hospital pharmacist strengthens his active role in the medical team in ensuring the treatment of the cancer patient.

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<sup>1</sup> Published in the Official Gazette, Part I, no. 490 of July 15, 2009.

The advantages of this way of organizing the oncology pharmacy are: the preparation of medicines by specialized personnel, ensuring the quality of the medicine; the possibility of a rigorous control over the risk of contamination, both chemical and microbiological, by organizing a workspace with special facilities; ensuring traceability, patient-drug-final solution "ready to administer"; drug management, pharmacoeconomics.

According to the European Guide to Good Practice in Oncology Pharmacy<sup>2</sup>, the aspects that define the oncological pharmacy are the following: quality management; staff; organization of space and necessary equipment.

### I. QUALITY MANAGEMENT

National Authority for Quality Management in Health and clinical management rules<sup>3</sup>, provide in the standard "*pharmaceutical and medication management ensures continuity of care and patient safety*", as well as compliance with specific requirements on the use of cytostatics. The indicator related to this requirement lists the conditions for the activity of dissolution and dilution of cytostatic drugs, stating that this activity can be performed both in the hospital pharmacy and in the clinic, in compliance with the rules of good manufacturing practice, and the activity must be processed, implemented and must ensure the protection of personnel preparing and administering cytostatic drugs.

The procedure of an activity is regulated by Order no. 600 of April 20, 2018 on the approval of the Code of internal control of public entities, issued by the General Secretariat of the Government<sup>4</sup>. The elaboration of a procedure must take into account "*Reference documents - with a regulatory role related to the procedural activity. The reference documents highlighted in a procedure are, as the case may be, the following: international regulations, primary legislation, secondary legislation, other internal regulations of the public entity*".

The procedure of the cytostatic dissolution activity, as an integral part of the oncological medication management, becomes complex and it must include all the aspects that have a direct involvement with reference to:

- the category of staff participating in this activity;
- space and endowment with technical equipment and protective equipment;
- the actual preparation technique;
- toxic waste management.

### II. ONCOLOGY PHARMACY STAFF

Order no. 444 of March 25, 2019, for the approval of the norms regarding the establishment, organization and operation of pharmaceutical units<sup>5</sup>, issued by the Ministry of Health, mentions:

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<sup>2</sup> See [https://esop.li/wp-content/uploads/2019/12/QuapoS6\\_Roumanian\\_HP.pdf](https://esop.li/wp-content/uploads/2019/12/QuapoS6_Roumanian_HP.pdf), accessed on 27.10.2021.

<sup>3</sup> See <https://anmcs.gov.ro/web/wp-content/uploads/2014/12/11.03-MC.pdf>, accessed on 27.10.2021.

<sup>4</sup> Published in the Official Gazette, Part I, no. 387 of May 7, 2018.

<sup>5</sup> Published in the Official Gazette, Part I, no. 270 of April 9, 2019.

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- art. 45, para. (7) - *"hospitals performing the National Cancer Program - Routine medical treatment of patients with oncological diseases, organized a separate space to meet all conditions necessary to ensure the quality of preparation and personal protection specialist. This space must be located in the vicinity of the oncology department and in it the specialized staff of the closed circuit pharmacy carry out their activity"*.
  - art. 49, para. (1) - *"in the closed circuit pharmacy carry out their activity, in compliance with the legal provisions, specialized personnel composed of chief pharmacist, pharmacists, pharmacy nurses, administrative staff, as well as other personnel necessary to carry out the activities provided in the object of activity of the pharmacy, which will carry out its activity under the coordination and control of the chief pharmacist"*.
  - art. 49, para. (5) - *"the personnel scheme of the closed circuit pharmacy will take into account the volume, the nature of the activity, as well as the number of beds, in accordance with the legal provisions in force"*.

As we can see, the legislator does not detail the specific category of staff for the cytostatic dissolution activity, but offers the possibility to take into account the nature and volume of the activity. The personnel involved in the cytostatic dissolution activity must be distinct personnel composed of pharmacists, pharmacy nurses, auxiliary cleaning personnel, auxiliary personnel involved in the transport of medicines.

Both the staff involved in the preparation activity, the pharmaceutical staff and the staff involved in the related activities (transport, cleaning, maintenance) must be regularly trained in accordance with the activity they carry out. Newly hired staff should receive a more detailed period of training as well as practical training<sup>6</sup>.

Ordin no. 1,375 of December 6, 2016 for the amendment and completion of the Regulation on working time, organization and performance of guards in public units in the health sector<sup>7</sup>, issued by the Ministry of Health, provides in art. 9, para. (3), point d), a 6-hour program for the activity of dissolution and preparation of cytostatic solutions.

The legislator, although it includes the activity of dissolution and preparation of cytostatic solutions with the reduction of the activity time together with other departments, pathological anatomy, forensic medicine, imaging radiology, in the salary law, Framework Law no. 153 of June 28, 2017 on the remuneration of staff paid from public funds<sup>8</sup>, staff performing this activity do not receive any salary increase related to the toxicity risk to which they are exposed<sup>9</sup>.

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<sup>6</sup> See [https://esop.li/wp-content/uploads/2019/12/QuapoS6\\_Roumanian\\_HP.pdf](https://esop.li/wp-content/uploads/2019/12/QuapoS6_Roumanian_HP.pdf), accessed on 27.10.2021.

<sup>7</sup> Published in the Official Gazette, Part I, no. 988 of December 8, 2016.

<sup>8</sup> Published in the Official Gazette, Part I, no. 492 of June 28, 2017.

<sup>9</sup> See, <https://www.inspectiamuncii.ro/documents/66402/264079/Gid+metodologic+pentru+prevenirea+riscurilor+legate+de+exposere+la+agen%C5%A3i+cancerigeni%2C+mutagens+%C5%9Fi+toxic+for+reproduction/c09a8c32-e5fd-46f7-bf6a-c26bd29ca983>, accessed on 27.10.2021.

The cytostatic drugs in the reconstitution process, being concentrated solutions release vapors, aerosols that can cause an acute and/or chronic toxicity for the people who handle, prepare these drugs. Depending on the chemical structure, they have carcinogenic, mutagenic and teratogenic action (Eitel. A., Scherrer. M., Kummerer. K., 2000). Staff participating in such activities must be staff with a completed family cycle.

### **III. SPACE ORGANIZATION, NECESSARY EQUIPMENT, HEALT AND SAFETY AT WORK**

The only legislative specifications that refer to the space and endowment with necessary equipment in the oncological medicine preparation units are those provided in Order no. 444 of March 25, 2019, for the approval of the norms regarding the establishment, organization and operation of pharmaceutical units, issued by the Ministry of Health, at art. 45, para. (7)<sup>10</sup> which stipulates that "*the space must be organized separately and meet all the conditions necessary to ensure the quality of the preparation, but also the protection of specialized personnel and must be in the vicinity of the oncology department*".

There is a contradiction within these rules, the pharmacy as a department location is always on the ground floor to ensure good supply of drugs, and clinical departments are located upstairs in most situations, so the law provides the possibility, or requires the creation of these spaces within the department clinical features of the pharmaceutical sub-department!

Ensuring the quality of the preparation involves minimizing microbial contamination through the technique of aseptic preparation, the endowment and structure of such spaces are found regulated by Decision no. 10/26.02.2015 adopting the Guide on good manufacturing practice for medicinal products for human use<sup>11</sup>, issued by the Scientific Council of the National Agency for Medicines and Medical Devices of Romania, stating that they refer to the manufacturing process of drugs and not to the reconstitution/dilution of injectable drugs for parenteral administration.

The guide also refers to the provision of special technical equipment in the manufacturing process for "toxic and dangerous substances handled (eg with high pharmacological activity and/or sensitizing properties)", referring to substances in their pure state, not those conditioned - already manufactured. The technical equipment for equipping the space is varied, from ventilation and air filtration installations, niches with laminar air flow provided with filters to absorb the vapors / aerosols formed in the reconstitution process.

Ensuring the protection of personnel involves minimizing contamination with cytostatics during the preparation activity. The protection of personnel is also achieved through personal protective equipment in accordance with Regulation

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<sup>10</sup> Published in the Official Gazette, Part I, no. 270 of April 9, 2019.

<sup>11</sup> See <https://www.anm.ro/medicamente-de-uz-uman/legislatie/hotarari-ale-consiliului-stiintific/>, accessed on 27.10.2021.

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(EU) 2016/425 of the European Parliament<sup>12</sup>. Personal protective equipment consists of: coveralls, gloves, goggles with specific markings, certificates.

According to Law no. 319 of 14 July 2006, on health and safety at work<sup>13</sup>, we can classify the risk of occupational disease caused by exposure to cytostatics, as follows:

- chapter II, art. 5, letter h): occupational disease - the condition that occurs as a result of the exercise of a trade or profession, caused by harmful physical, chemical or biological agents characteristic of the workplace, as well as by overloading various organs or systems of the body, in the process of the work;
- chapter III, Section 4, Art. 12, letter a) - to carry out and be in possession of a risk assessment for occupational safety and health, including for those groups sensitive to specific risks;
- chapter III, Section 4, Art. 12, letter b) - decide on the protective measures to be taken and, where appropriate, on the protective equipment to be used;
- chapter III, Section 1, Art. 7, para. (4) (a) - assess the risks to the safety and health of workers, including the choice of work equipment, chemicals or preparations used and the arrangement of workplaces.

The methodological rules for the application of the law on health and safety at work, Annex 22, the table of occupational diseases with mandatory declaration states "*other malignancies caused by objective occupational exposure and assessed in one of several agents on the IARC list*", certain cytostatics according to of their mechanism of action are part of this list, and certain carcinogens are noted in the occupational noxiousness.

Personnel involved in the preparation of oncological medicines must have regular medical examinations, on employment, during employment and whenever there are suspicions of illness<sup>14</sup>.

#### **IV. PREPARATION OF ONCOLOGICAL MEDICINAL PRODUCTS**

The preparation of oncological drugs is based on a specific form, called the chemotherapy regimen, so a clear distinction must be made between the form used to prescribe drugs in the hospital called "*prescribing conditions*" and the chemotherapy regimen.

The chemotherapy regimen is a personalized medical document for the patient, which contains the following information<sup>15</sup>:

- patient identification, name, sex, date of birth, medical file number;
- diagnosis and type of protocol used;
- treatment cycle number, start date, stop date and next cycle date;
- patient weight, height, body surface;

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<sup>12</sup> Published in the Official Journal of the European Union, L 81, 31 March 2016.

<sup>13</sup> Published in the Official Gazette, Part I, no. 646 of July 26, 2006.

<sup>14</sup> See [https://esop.li/wp-content/uploads/2019/12/QuapoS6\\_Roumanian\\_HP.pdf](https://esop.li/wp-content/uploads/2019/12/QuapoS6_Roumanian_HP.pdf), accessed on 27.10.2021.

<sup>15</sup> *Ibidem*.

- the prescribed medicine, the calculated dose as well as the prescribed dose according to weight or body surface area;
- method of administration of the medicinal product, volume and type of solvent used for reconstitution / preparation;
- date, signature of the prescribing doctor.

If the biological parameters require the reduction of the administered doses, these specifications must be noted in the chemotherapy regimen.

The chemotherapy scheme is elaborated, as it is noted in the doctrine (Bot. A.C., Iancu, D.I., Kubelac, M.P., Todor, N., Achimas-Cadariu, P., Ciuleanu, T.E., 2021), based on some treatment protocols established by the chids. International clinical trials or regulated national protocols. The pharmacist is obliged to know the treatment protocols developed by the specialized commissions, to participate in the meetings of these commissions, to participate in the on-call report, to be part of the pharmacovigilance commission.

The doctrine holds that (Viașu. M., 2015), "*Responsibility pharmacist oncologist begins with evaluating all drugs that are administered before initiation of chemotherapy, how the patient responds to drugs and if they are combined and administered in an optimal regime. This includes the assessment of renal and hepatic function, but also the assessment of aspects of genetic variability or metabolism that could affect the smooth running of treatment.*"<sup>16</sup>

Specialist staff, pharmacists in collaboration with pharmacy assistants must ensure before preparation that the prescription is clear, all ambiguities have been clarified and the drug can be prepared.

The pharmacist has the obligation to contact the doctor in case of discrepancies, ambiguities of the chemotherapy scheme to avoid any risk of error, malpractice, as noted in the doctrine (Apan R.D., Fodor E.M., 2020).

The implementation of the online transmission of the chemotherapy regimen, for manual preparation of cytostatic solutions or for automated preparation involves the use of medical software accredited according to Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83 / EC, of Regulation (EC) no. 178/2002 and Regulation (EC) no. 1223/2009<sup>17</sup>.

The organization of the preparation process must be carefully organized so that there are no undue delays affecting the patient's treatment.

Order no. 75/2010 for the approval of the Rules of good pharmaceutical practice, issued by the Ministry of Health<sup>18</sup>, provides only for the preparation of main medicinal products and makes no reference to the reconstitution of medicinal products.

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<sup>16</sup> See <https://www.politicidesanatate.ro/farmacistul-oncolog-parte-importanta-a-echipei-terapeutice/>, accessed on 27.10.2021.

<sup>17</sup> Published in the Official Journal of the European Union, L 117, 05 May 2017.

<sup>18</sup> Published in the Official Gazette, Part I, no. 91 of February 10, 2010.

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Although centralized reconstitution also aims at pharmaco-economic aspects, currently the reporting of drug use only allows the reporting of therapeutic units, vials, so the difference between the dose required by the patient and the dose per therapeutic unit considered residual, can no longer be used and it becomes waste. In this way, there are large losses of drugs, and if we take into account that oncological drugs have high prices, there are sometimes substantial economic losses.

## V. WASTE MANAGEMENT

According to the classification of waste resulting from medical activity, cytotoxic drugs are registered as hazardous waste.

Order no. 1,226 of December 3, 2012 for the approval of the Technical Norms on the management of waste resulting from medical activities and of the Methodology for collecting data for the national database on waste resulting from medical activities, issued by the Ministry of Health<sup>19</sup> chapter II, art. 7, letter g) states that: *“chemical and pharmaceutical wastes are solid, liquid or gaseous chemicals that can be toxic, corrosive or flammable; expired drugs and residues of chemotherapeutic substances, which may be cytotoxic, genotoxic, mutagenic, teratogenic or carcinogenic; these wastes are included in the category of hazardous waste”*, we can use the phrase - *cytostatics become hazardous only after they are waste*.

Waste resulting from cytostatic dissolution activity, empty vials or vials containing drug residues, shall be collected in packaging containing yellow polyethylene bags, placed in special places and in impermeable, airtight packaging with a temporary and permanent closure system. Packaging must be marked with the waste code, for cytostatic drugs 180108 and the 'biohazard' icon.

In the event of accidental breakage and / or leakage in each area where cytostatics are handled, decontamination kits should be provided to remove and dispose of the drug as soon as possible.<sup>20</sup>

## CONCLUSIONS

A Following the analysis of the above chapters, we can conclude that, in 2021, the oncology pharmacy in Romania is still in its infancy, it is necessary to adopt some normative acts, consolidate the existing ones as well as implement the European quality standards.

The conduct of such an activity involves legislation in various fields and obliges the hospital pharmacist to a continuous challenge and analysis. As noted, there is a legislative vacuum that can block the development of procedures, although practical work requires in these situations to use the recommendations of European guidelines.

The oncologist pharmacist becomes an active member of the medical team, fights with the doctor in treating this condition that holds the 2nd place, after cardiovascular diseases, as a cause of death in the EU.

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<sup>19</sup> Published in the Official Gazette, Part I, no. 855 of December 18, 2012.

<sup>20</sup> See [https://esop.li/wp-content/uploads/2019/12/QuapoS6\\_Roumanian\\_HP.pdf](https://esop.li/wp-content/uploads/2019/12/QuapoS6_Roumanian_HP.pdf), accessed on 27.10.2021.

The conclusion of the 18 years of activity in the hospital pharmacy with oncological profile is the following: the pharmacist is "master" of drugs. The synonyms of the verb "to master" are varied: to possess, to possess, to have, to know, to retain, to dominate, to calm, to temper, to calm, to calm, to govern, to lead and they become needs in clinical practice. In order to master a medicine, you must know everything about it, whether it is notions that we know from the literature or notions that we learn from clinical practice and that use us to ensure quality treatment of our patients. , because: we have common patients with doctors, we need to make sure of this and we can do it by providing accurate data about the drug or drug combinations and improving the work we do. The development of a modern concept of pharmacy in the conditions of an outdated legislation is very difficult, it must be adapted to the concrete situation we have in order to ensure in the future a master pharmacist on the drug.

If in the past, the pharmacist was defined by the activity of prescription, now he defines something else, which essentially has the same principle, of drug preparation and knowledge. The concrete situation we have, we understand it only by looking around us how things have evolved over time; if in 2002 at the beginning of my career, we took some drugs from a shelf and sent them to the hospital ward, now in 2021 we have come to prepare the drugs, ready to administer to patients and even talk about "oncology pharmacy" or implement systems automatic preparation. I strongly believe that the need for reality tells us what we have to do, where to go provided we say the present. "If we look around our colleagues, everyone is a specialist in something, research, management, legislation, prescription, clinical (gastroenterology, psychiatry, infectious, cardiology, oncology, etc.) and I think this is the future, the acquisition of specialties and skills.

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