QuapoS

Quality Standard for the Oncology Pharmacy Service

ESOP GLOBAL

Member
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QUAPOS 7

Quality Standard for the Oncology Pharmacy Service

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TABLE OF CONTENTS

PREWORD

When the first quality standard with 3 chapters was published in Hamburg in 1996, it was preceded by 4 years of discussion and commentary. This was the beginning of joint efforts to achieve uniform oncological-pharmaceutical services for cancer patients all around the world.

On October 1st 2024 during the ESOP Global General Assembly the 7th version of QuapoS was unanimously approved by ESOP Global delegates. This was preceded by intensive preparation by the quality standard working group, in which contributions from all member countries were incorporated and the correct content and designations were heavily discussed.

The quality standard, now with 6 chapters, not only deals with pharmaceutical issues, but also covers and considers other areas that affect the oncological pharmacy service and patients outside the pharmacy.

We could call it "Essential Requirements for the best practice in the Oncology Pharmacy Services" because the overall goal pursued with this standard is to be a guide for the best approach for every pharmacist, wherever they are dealing with oncology pharmacy services.

The standard works also without commentary, because after almost 30 years of discussion, the progress and findings are very clear. Nevertheless, the members and partners of ESOP Global have set themselves the goal of adding a commentary to this version in the coming months.

So, until then, use the latest edition of QuapoS now to show everyone and the whole world the competence of oncology pharmacy, as it is organized in the ESOP Global.

Kristjan Kongi
Vize President
Quality management and standards

QUALITY ASSURANCE

1.1 QUALITY MANAGEMENT FOR THE ONCOLOGY PHARMACY SERVICE

The certified quality management system (QMS) implemented in the pharmacy or in the pharmaceutical service is designed to produce oncological drugs and/or offer counseling and care for cancer patients or oncology units. It shall:

- meet the minimum requirements of a established QM system;
- implement the current quality standards of the pharmacy oncology service and subsequently implement guidelines for quality assurance;
- achieve systematic quality improvement, through regulated, conceptually coordinated and reproducible operational procedures,
- further develop the quality of patient counseling regarding the drugs used in the treatment of cancer as well as pharmaceutical care of patients and
- increase drug safety for the user, patient and environment, and maintain the existing QM system.
- The QM system integrates all aspects ensuring a consistently high level of quality, which is required for proper patient care.

1.2 RISK MANAGEMENT

Quality management represents the basis for definitive control of the processes in the preparation of oncological drugs and for the counseling and care of oncological patients. It is based on the risk analysis of the department and service. Controlled handling of the residual risk is connected to the analysis. Processes are continuously analyzed, risks are identified and evaluated, and solutions for risk control during drug preparation and/or during the process of pharmaceutical care are found.

PERSONNEL

2.1 PERSONS HANDLING ONCOLOGICAL DRUGS

As a minimum requirement all personnel dealing with oncological drugs must be qualified in understanding the local legal requirements connected to their activities.

Persons handling oncological drugs (stocking, production, distribution, oral dose packaging unit) under the direct responsibility of the pharmacy include:

Pharmaceutical personnel i.e.

- Pharmacists and trainee pharmacists
- Pharmacy technicians and trainee pharmacy technicians
- Pharmacy assistants and residents
- Pharmacy engineers

Non-pharmaceutical personnel i.e.

- Auxiliary staff
- Professionals employed by the pharmacy
- Sales staff
- Cleaning staff
- Transport staff

2.2 PERSONS IN THE PRODUCTION

In the production and associated quality control laboratory units, only qualified personnel may be employed.

Before employees begin their work, they must be adequately educated and trained in aseptic working procedures and in the handling of oncological drugs.

The employees must be familiar with the quality management system of the department and actively involved in its further development.

2.3 PERSONS IN PHARMACEUTICAL CARE

- Pharmacists i.e. clinical Pharmacist
- Trainee pharmacists
- Pharmacy residents
- Pharmacy technicians/assistants and trainee pharmacy technicians/assistants

2.4 RISK EVALUATION, WORKING RULES AND INSTRUCTIONS

Before starting work in an oncological drug preparation unit, the hazard risks of oncological drug handling for that unit needs to be evaluated and documented. All employees, whether they are carrying out the production or dealing and working with oncological drugs, must be instructed based upon these findings, as well being instructed with respect to relevant legal requirements, local regulations and procedures. The instructions must align with the staff‘s job categories and responsibilities.

Depending on the respective requirements, they include the following items:

- Effects of drugs in the case of accidents
- Proper procedures for dealing with hazardous substances (e.g. oncological drugs, latex,)
- Hazards and protective measures
- Aseptic working technique and regulations
- Disposal of contaminated materials and devices and residues of oncological drugs
- Contamination measurement
- Occupational health medicine
- Action in the case of accidents

These instructions must be reviewed and if necessary updated regularly. In addition, written working instructions/SOPs must be prepared specifically for the particular workplace.

Drugs must be classified according to their properties and included in the pharmacy list of hazardous substances.

This list must be amended according to major changes and inspected at least once a year. If any changes are made, a new documented risk analysis has to be produced in accordance with the changes made.

Accidents must be documented. In case of personal injury, the accident must be recorded (minor injuries, incapacity to work for a period of less than three days) and notified to the responsible statutory insurance body and local occupational physician.

Specific hazard evaluation must be conducted with respect to Advanced Therapy Medicinal Products (ATMPs) as defined by EU regulation 2007-1394 or as indicated by local regulation (for non EU countries).

2.5 RISK OF PERSONNEL WORKING PERMANENTLY WITHIN CENTRALIZED ONCOLOGICAL DRUG PRODUCTION

Well-trained permanent employees must be available in adequate numbers for the scope of the production and work load. Permanent workplaces should be avoided in centralized oncological drug production and organized on a rotational basis. The number of persons potentially exposed should be reduced to a minimum.

2.6 OCCUPATIONAL HEALTH AND SAFETY

Employees working in areas of oncological drug preparation in the pharmacy are dealing with potential carcinogenic, mutagenic and reproductive toxic (CMR) drugs. All necessary precautionary measures must be in place and they must be offered regular (according to national regulations) occupational health and safety medical check-ups, taking into account all the relevant factors pertaining to the specific workplace.

These check-ups should include:

- Initial medical examination before taking up employment
- Follow-up examinations during employment at intervals of 1 to 2 years.
- Examinations at the employee‘s request if there is a suspicion of work-related health problems

It is recommended that the examinations include biological monitoring of occupational exposure, although it is of limited relevance.

The employer must document exposure to oncological drugs in a suitable form. This documentation must include the types and amounts of oncological drugs used and the frequency of their preparation for each employee handling these drugs. Furthermore, a continuous use of technical and personal protective measures has to be ensured by implementing standard operating procedures regarding compounding, disposal, and clean-up of oncological drugs as well as oncological drug-related accidents and their management.

2.7 TRAINING, EDUCATION AND PROFESSIONAL SPECIALIZATION OF EMPLOYEES

The goal of training, continuous education, and professional specialization is to provide personnel with theoretical knowledge and practical skills. All carried out training must be documented.

Theoretical knowledge:

- Quality- and Risk-Management System
- National and regional laws, rules, regulations and best practice
- Safe handling of hazardous substances within the facility
- Hazards and protective measures, equipment and disposal of contaminated material
- Accident prevention and management
- Hazardous waste handling
- Drugs and dosage forms
- Stability and incompatibility
- Production management
- Working in an aseptic area
- Technical equipment for the production and administration of oncological drugs
- Drug effects and pharmacology
- Clinical pharmacy
- Cancer types and treatment options
- Pathology and impact on dose changes
- Management of Clinical Trials
- Quality control laboratory

Practical training:

- Aseptic working techniques and their validation in simulations of work flow during compounding
- Handling of disposable articles and medicinal products
- Simulation of accidents and their management
- Handling different documentation systems
- Packaging, quality management system for distribution and disposal of contaminated material
- Methods for practical training evaluation

- Handling a spill-kit
- Checking oncological drug prescriptions including parenteral and oral drugs

Clinical pharmacy:

- training by simulation for medication reconciliation, therapeutic education, medication adherence evaluation

Team members coming into contact with patients and their relatives need to be trained to meet patient's needs in order to provide proper patient care. This includes knowledge about disease stages and factors influencing the patients' quality of life, including psychosocial circumstances and communication skills.

2.7.1 TRAINING OF NEW PERSONNEL

Training of new personnel in oncological drug compounding needs to be performed with specific care since handling oncological drug bears significant risks for humans, environment and product safety.

The training requires planning of time and content requirements and should be performed according to a predefined training program and documented.

Training of persons counseling patients includes knowledge of the special needs of cancer patients in order to provide individual pharmaceutical care.

2.7.2 CONTINUOUS EDUCATION AND PROFESSIONAL SPECIALIZATION OF PERSONNEL

The goal of continuous education and professional specialization programs is to keep personnel informed about the latest developments and innovations.

Personnel working in the oncological drugs compounding unit as well as the staff providing pharmaceutical care and patient counseling, should also have the opportunity to participate in internal and external pharmaceutical education programs.

A certificate should document participation.

Opportunities for professional specialization and continuous education are highly recommended and should be taken, if offered.

PHARMACY ASEPTIC PREPARATION UNIT

The aim of the centralized aseptic preparation unit is to assure high quality in every step of the handling process of oncological drugs including protection of the final product against microbiological and particle contamination. At the same time it has to protect pharmacy personnel, other healthcare professionals, patients, and visitors against exposure to anti-cancer medications. Engineering controls must also safeguard the environment.

In addition to standardizing practice, centralizing oncological drug preparation also provides economic benefits in respect to staffing, equipment and drug usage.

All preparation of oncological drugs should be performed in a centralized area designed to maintain aseptic working and safe handling of anti-cancer preparations.

The preparation of CMR drugs must be centralized under pharmacists' responsibility according to local law.

3.1 ROOMS AND EQUIPMENT

3.1.1 ROOMS

The required rooms in an oncological drug preparation department are:

- Stock receiving area
- Documentation area
- Air-lock (multiple, if necessary)
- Preparation/storage area
- Production room
- Checking and release area

The design and organization of the unit should allow personnel to implement clean and safe working standards.

The design, configuration, and layout of the rooms must be designed to reduce the contamination with microorganisms, particles, and cytotoxic substances to a minimum. Along with electromechanical control, the rooms should be set up to ensure best practice in preparation, production and documentation.

The entire equipment in the preparation room must be reduced to the necessary minimum and listed in a plan.

3.1.1.1 STOCK RECEIVING AREA

A clearly marked area for receiving and checking shipments equipped with necessary storage space and a working area for disposing of primary packages.

3.1.1.2 WORKFLOW MANAGEMENT AREA

A documentation room can be useful for organising work flow in the unit and review, checking patient records and medication orders in preparation.

It should be equally accessible to the production/clean room area and the regular pharmacy areas. There should be a separate flow for incoming and outgoing prepared materials.

3.1.1.3 AIR LOCK(S)

Hand sanitisation and the donning and doffing of personal protective equipment takes place within this buffer area. Separate air locks should be used for personnel and material.

3.1.1.4 PREPARATION/STORAGE AREA

In this area the medication, personal protective equipment, devices and infusion solutions are stored according to good storage practice and prepared for use in the production room.

3.1.1.5 PRODUCTION ROOM

Preparation takes place in a separate, clearly designated cleanroom work area, separated from the remaining areas by one or more air-locks and equipped with all the necessary equipment.

3.1.1.6 CHECKING AND RELEASE AREA

The final, labeled product is received, checked, and released.

3.2 ANTICANCER DRUGS CONTAINMENT UNITS AND HEATING, VENTILATION AND AIR CONDITIONING SYSTEM (HVAC)

For the preparation of anticancer drugs a containment unit has to be used according to regional regulations that is suitable for the protection of the staff and the products.

1. The preparation has to be carried out in a cleanroom environment that is equipped with a Heating, Ventilation, and Air Conditioning ventilation system (HVAC) in coordination with the containment unit's air volume requirements and the needs for the personnel (i.e. legal requirements).

2. The required classification according to the ISO 14644-1 Cleanroom Standards depends on the type of containment unit used.

3.2.1 ROOMS AND EQUIPMENT MONITORING REQUIREMENTS FOR MONITORING ENVIRONMENTAL CONTAMINATION

The clean room and equipment control require an ongoing monitoring program with appropriate intervals.

For a controlled workplace and equipment, the parameters to be checked include:

- microbiological contamination and active air samples;
- particulate counts;
- HEPA/ULPA filtration and integrity;
- room air quality and air changes per hour and
- velocity and pressure differentials.

Specifications to be maintained depend on the grade of the room and type of equipment.

3.3 CLASSIFICATION OF ONCOLOGICAL PREPARATION ACCORDING TO CMR RISK

The Classification of CMRs is based on the strength of evidence showing that they present one of the CMR types of hazards to human health. Other references are also available such as the Globally Harmonized System (GHS) and the material safety data sheets (MSDS). Each country must adhere to their national legislation.

ONCOLOGICAL DRUG PRODUCTION

4.1 REQUIREMENTS FOR DRUG MANUFACTURERS

The pharmaceutical company is responsible for its drugs, labels and the information available for the safe use of its products. The finished drug and its various forms of packaging should be designed to enable safe use. Shipment of all anticancer drugs should be labeled with a “Yellow hand” warning label and delivered separately.

The information provided regarding the drugs must cover all identifiable needs comprehensively. The information must be clear to ensure readability and comprehension by patients, caregivers and health care professionals.

The drug manufacturers must ensure a continuous supply of their products.

4.1.1 HANDLING A SHIPMENT OF ONCOLOGICAL DRUGS

Only trained pharmacy staff are allowed to accept shipments of oncological drugs.

Packages or shrink–wrapped anti-cancer drugs need to be opened in a designated location with personnel wearing protective clothing/gloves. Product damages or contaminations need to be documented and reported to the manufacturer and the occupational safety department. The cause of the defect needs to be evaluated and eliminated as soon as possible.

4.1.2 RETURN OF SHIPMENTS TO THE PHARMACEUTICAL COMPANY/WHOLESALER

Return of shipments of anti-cancer drugs to the pharmaceutical company and wholesaler have to be coordinated with the recipient.

The packaging container must allow for safe transfer and safe removal of the anti-cancer drug.

The shipment has to be arranged and labeled according to the applicable rules and regulations and with the “Yellow hand” warning label.

4.2 PERSONAL PROTECTIVE EQUIPMENT (PPE)

The personal protective equipment must meet the well known international standards and needs to be specified in the hazard evaluation.

Personnel have to wear certified PPE appropriate for each area identified in the hazard and risk evaluation.

Depending on the working place, PPE consists of:

- protective overall/gown (possibly in combination with cuffs)
- protective gloves
- respiratory protective equipment
- protective hair and beard covers
- protective eyewear
- protective footwear

The choice of personal protective equipment depends on the hazard evaluation of the work environment.

4.2.1 PROTECTIVE OVERALL AND GOWN

Protective gowns must be sufficiently long (covering the thighs), closed up to the neck, with long sleeves and close-fitting cuffs. The protective overall must be the correct size. They should repel liquids especially in exposed areas, and be tested and classified to be used with hazardous anti-cancer drugs. For reasons of product protection they should be sterile or at least low germ count and give off as few particles as possible.

4.2.2 DISPOSABLE GLOVES FOR PROTECTION

Gloves must be tested, classified and suitable for use with hazardous and oncological drugs. Suitable powder-free gloves or glove combinations must be worn and must be changed regularly. In the event of contamination or damage, they must be changed immediately.

4.2.3 BREATHING PROTECTION, PROTECTIVE EYEWEAR, HAIR/BEARD COVERS, PROTECTIVE FOOTWEAR

Personnel in the production area must wear an appropriate protection of the head, covering all head and facial hair, appropriate breathing protection, protective eyewear and footwear according to the needs of the individual working place and task. PPE must be changed regularly and each time after contamination.

4.2.4 DONNING AND DOFFING OF PPE

The correct donning and doffing of PPE has to be trained and is fundamental to safe and aseptic work with anti-cancer drugs. In so doing, the quality of the product is ensured and the greatest possible degree of safety is provided for all persons involved.

4.3 EQUIPMENT FOR PRODUCTION

4.3.1 TECHNICAL EQUIPMENT FOR THE PRODUCTION OF ONCOLOGICAL DRUGS

In order to ensure minimum safety standards for the production of anti-cancer drugs, it is necessary to use suitable technical equipment. This must comply with the requirements of relevant legislation as applied to medical devices. In addition, the materials used must fulfill the special criteria associated with anti-cancer drug production. All equipment must be sterile, or be suitable for disinfection before use. The condition of the devices must be inspected at regular intervals and maintained. Technical equipment is also part of hazard evaluation.

4.3.2 TECHNICAL EQUIPMENT FOR THE ADMINISTRATION OF ONCOLOGICAL DRUGS

Alongside medical device regulations, there are additional requirements for the selection of appropriate equipment for the administration of oncological drugs.

For example, protection from contamination and light, reduction in the risk of extravasation, avoidance of incompatibilities, mix-ups and the timely administration during parenteral or local application must also be taken into account. This has to be coordinated with the administrating unit.

4.4 ASEPTIC WORKING TECHNIQUES

Aseptic working techniques include all coordinated and necessary steps, which lead to a sterile product by using optimal conditions for particle reduction and avoidance of microbiological contamination.

The detailed planning, preparation and post-processing of the entire aseptic production process have a crucial impact on the quality of the product.

4.4.1 MEASURES FOR AVOIDING PARTICLE AND MICROBIOLOGICAL CONTAMINATION

Validation includes evaluation of the entire work process and all aspects of aseptic techniques, i.e.

- Room class in respect of cleaning and hygiene
- Safety workbench (LAF - laminar air flow for anti-cancer substance, BSC or Isolator)
- Work materials
- Source materials
- Aseptic production method
- Personnel working in oncological drugs preparation unit

During production and monitoring procedures, the validation of the entire process includes all carefully planned and defined methods which ensure that the medication produced within the unit meets all requirements with regards to safety, identity, content, quality and purity.

4.4.2 VALIDATION

In order to ensure high quality production and final product, it is necessary to validate the whole process in the workflow. This includes monitoring cytotoxic and microbiological contamination as well as particles. Appropriate alert and action limits should be set for the results of particulate and microbiological monitoring.

4.4.2.1 ASEPTIC TECHNIQUE VALIDATION

Oncological drug preparation in an oncological drug hood (SWFC)/isolator/BSC is an aseptic drug preparation process that must be validated.

Compliance with the requirements of the relevant pharmacopoeia for parenteral drugs is fundamental. Local guidelines and legislation should be followed.

A product prepared in a simulated production procedure instead of an anti-cancer drug, which is then tested for the absence of microbiological contamination using appropriate microbiological procedures, can be used for validation. A testing plan must be compiled and actions documented.

4.4.2.2 SURFACE MONITORING AND CROSS CONTAMINATION

Since most anticancer drugs are invisible in solution it is essential to apply a sufficient cleaning procedure in case of an accidental contamination and also during every day practice. It is therefore necessary to monitor production and administration areas in defined time intervals for evaluation of potential dermal exposure and health risks. Wipe sampling for surface residue of anticancer and other hazardous drugs in healthcare settings is currently the method of choice to determine surface contamination.

4.4.2.3 PARTICLE MONITORING

A validated process must be in place for monitoring particles in the production area. Clean rooms should be routinely monitored based on a formal risk analysis and the results obtained should be used for the classification.

4.5 REQUIREMENTS FOR THE PRODUCTION OF READY-TO-ADMINISTER ANTI-CANCER DRUGS

4.5.1 REQUIREMENTS FOR PRESCRIPTION OR DRUG ORDER FORM AND PLAUSIBILITY CHECK

The prescription of anticancer drugs by the physician is submitted in electronic or written form and must include at least the following information:

- Patient name, date of birth, gender and/or identification code/national ID
- Body weight, height, body surface area and laboratory values for the calculation of the dose
- Requesting ward, outpatient unit or medical office
- Drug prescribed (International Non-Proprietary Name - INN name)
- Dose i.e. calculation according to body surface area, body weight or absolute dose
- Required dose – a reduction for impaired organ function or other parameters must be indicated
- Route and duration of administration
- Type and volume of carrier solution
- Diagnosis

- Dates and/or days and times to administer if required by treatment regimens for more than one day
- Date, name and physician's signature or in the case of an electronic request, valid electronic identification of the ordering physician

It is a pharmacist responsibility to conduct the plausibility check and validate the prescription and document the action.

4.5.2 STABILITY OF THE PREPARATIONS

The shelf life of the preparations should be established from the information provided by the manufacturer and/or international pharmaceutical publications or by employing stability studies.

Stability studies should be carried out according to the „Guidelines for the practical stability studies of anticancer drugs: A European consensus conference".

The results of the stability studies published in the international publications should be carefully compared with the conditions of the local production in terms of solvent, container, temperature, humidity, light, concentrations and transport conditions, if applicable. The extrapolation of the results should be justified. The involvement of local governing bodies depends on national practice.

4.5.3 DOSE ADJUSTMENT

Oncological drugs have a narrow therapeutic range, which are, to a large extent, eliminated as unchanged or toxic metabolites. Impaired organ function may lead to dose adjustments. The criteria and principles which can influence such decisions are discussed below. Because of the toxic potential, dose adjustment may be necessary as well.

4.5.3.1 ONCOLOGICAL DRUG DOSAGE IN CASE OF IMPAIRED RENAL FUNCTION

An impaired renal function may increase the toxicity of oncological drugs and active metabolites through accumulation. A dosage reduction may therefore be necessary for substances which are renally eliminated to a significant extent. Each decision should be made on the broadest possible base of information and the patient's individual situation. A recommendation for dose adjustment should only be based after measurement of GFR (glomerular filtration rate) or by calculation of the „creatinine clearance".

4.5.3.2 ONCOLOGICAL DRUG DOSAGE IN CASE OF IMPAIRED LIVER FUNCTION

Decreased liver function may significantly influence hepatic clearance of oncological drugs. Some oncological drugs with biliary elimination accumulate with decreased hepatic clearance. Therefore, pharmaceutical services are very valuable in providing dosage modifications after evaluating patient specific clinical laboratory data.

4.5.3.3 THERAPEUTIC SCHEME MODIFICATION IN CASE OF BLOOD COUNT CHANGES

The myelosuppressive effect of the therapy with anti-cancer drugs is a limiting factor in the treatment of a patient resulting in a delay or discontinuation of therapy. It may lead to febrile neutropenia and associated infections which are main causes of morbidity and mortality in cancer patients.

4.5.3.4 ONCOLOGICAL DRUGS DURING PREGNANCY

Cancer treatment during pregnancy is a complex decision and has to be based on individual considerations and discussed in a multi-professional team.

4.5.3.5 THERAPEUTIC DRUG MONITORING, PHARMACOGENOMICS AND PERSONALIZED MEDICATION MANAGEMENT

Therapeutic drug monitoring, pharmacogenomics and personalized medication management are core functions within the pharmacist‘s provision of direct patient care. These activities ensure individualized, safe and effective management of the patients’ outcome.

4.6 PRODUCTION

Production is based on working rules for hazardous substances and the production specifications, including results of the risk evaluation.

The work techniques defined in the local regulations and production specifications are mandatory. Compliance must be regularly inspected.

4.6.1 PRODUCTION INSTRUCTIONS

Production instructions are created and available before the start of any production process. Internal quality management assures standardized, general, active-substance-based or medicinal-product-based production. They should undergo regular review and updating within the scope of the QMS.

4.6.2 WORKFLOW IN AN ASEPTIC PRODUCTION SETTING

Workflow includes all steps within the production. Special attention is paid to the safe handling of drugs and medical devices. The organization of all items in the containment and the behavior pattern of the personnel in the production area has to be planned.

4.6.3 PRODUCTION OF ORAL FORMULATIONS

In most cases anti-cancer drugs are available in the form of capsules or tablets however, other dosages or pharmaceutical forms like suspensions or solutions are required i.e. in pediatric oncology or tube feeding, because they are easy to administer and flexible in dosing. To produce such formulations, special precautions must be taken since the process may result in contamination with highly toxic substances.

Staff and environmental protection is a key priority and must be ensured through appropriate measures and production conditions.

If a drug is turned into a new pharmaceutical form, it should additionally be ensured that the therapeutic effect is not impaired either through a lack of stability or incompatibility.

4.6.4 LABELLING OF THE READY TO ADMINISTER DRUGS (RTAS)

RTA infusion solutions produced individually for a patient are labeled in accordance with national regulations. Labels should be applied directly to the primary container after completing the preparation in order to avoid mix-ups. Unambiguity with regard to the patient identification and production number should be ensured, as should good legibility and long-term adhesion. Along with information on the active substance used, dosage, carrier, volume, expiry date and storage conditions, additional information is relevant like infusion time and rate, ward designation, units providing oncological therapy, amount, and name of anti-cancer drug contained.

Supplemental information on the outer packaging regarding storage and application may be of use. A warning label ("Yellow hand") must be on all oncological drugs.

4.6.5 DOCUMENTATION AND APPROVAL OF THE FINAL PREPARATION

Specifications on the documentation in the case of aseptic production of infusion solutions is in accordance with national requirements. A production protocol must be maintained.

The production protocol must contain the following information:

- Date and time of production
- Name and quantity of the commercial drugs used and their batch numbers and expiry date
- Name and batch number of medical devices
- Special precautions of the production process
- Type and result of any in-process controls
- Name of the person who produced the drug

However, additional information on the preparation may be useful. In-process controls can be performed using weighing-based software and/or the "four-eye principle".

Prior to release, the production protocol and the final product is checked, approved and confirmed by a pharmacist or by a competent and trained pharmacy staff member.

4.7 DELIVERY OF RTA PRODUCTS AND TRANSPORT CONDITIONS

For "in-house" transport the finished products are delivered in unbreakable, liquid tight, tight closing containers labeled with the "Yellow Hand" sign.

If the finished product will be transported out of the institution it needs to comply with its specific storage conditions, local hazardous freight regulations and labelled accordingly.

Cytotoxic compounds partially belong to the group of hazardous freights. They have the UN number 1851 and need to be arranged under drug, liquid, toxic.

Receipt of the final product must be documented.

4.8 PRICING

The costs of a preparation include:

- 1 material costs
- drug costs
- medicinal devices
- carrier solutions
- consumables
- maintenance costs
- 2 personnel costs
- 3 service fees

The applicable contracts must be taken into account when billing the health insurance provider.

4.9 SOURCE OF INFORMATION

Essential information sources consist of a pharmacy library with relevant print and digital media and relevant software. This should include internet access allowing for retrieval of scientific database information, use of search engines, available links, electronic mail, and other services.

Audio and video material for educational purposes should also be available.

PHARMACY AS A COORDINATION CENTER

Oncology pharmacists are involved in the care of cancer patients during all phases of their treatment; this requires special competencies in the oncology field. The pharmacist implements quality management in the oncology pharmacy service and takes shared responsibility for patients and staff in all areas of anticancer therapy, within a multi-professional team.

The pharmacy records and processes all medical and toxicological data relating to the oncological drugs and supportive therapy. Pharmaceutical interventions are provided and should be equally recorded.

The available information can be epidemiologically evaluated, documented with regard to clinical, pharmacoeconomic and ecological aspects, integrated in advisory procedures, and used for the training of personnel.

5.1 WASTE DISPOSAL

The principles of waste disposal are:

- waste avoidance
- waste recycling
- waste disposal

Waste disposal is done to ensure:

- the health and well-being of persons;
- the environment (air, water, ground, animals, plants and landscape); and
- public safety

are not jeopardized.

Hazardous waste and contaminated objects are collected:

- as separate waste
- at the place of their origin
- in appropriate, labeled collecting containers

In general, cytotoxic waste is considered hazardous waste. It should be collected in specific containers, which have to be hermetically sealed and labeled. Cytotoxic waste disposal needs to comply with local hazardous waste regulations.

5.2 DECONTAMINATION AFTER LEAKAGE AND/OR ACCIDENTAL SPILL

Appropriate spill kits must be easily available in all designated areas where oncological drugs are handled.

The removal and disposal of spilled oncological drugs may be performed only by properly trained personnel.

The procedure to be followed after leakage and/or accidental spillage is part of the working rules and annual instruction.

5.3 HANDLING OF ONCOLOGICAL DRUG ON WARDS/UNITS

Nurses and physicians have the main responsibilities in handling oncological drugs on the wards and units. These include accepting, storing, preparing for administration, administering anti-cancer drugs as well as handling patient's excretions (patient's family members may also be involved) and managing accidental spillage of anti-cancer drugs.

The oncology pharmacist should support and advise the ward and unit personnel in establishing operating procedures for safe handling of oncological drugs and the correct use of PPE in order to guarantee safe working techniques.

5.4 HANDLING ONCOLOGICAL DRUGS AT HOME

Certain anticancer therapy regimens demand an active substance be administered over a period of 24 hours or up to several days. This type of therapy is performed both during hospitalization and / or as an outpatient treatment.

Patients, family members and personnel working in the home care setting need to be informed and trained in the handling of oncological drugs in this environment.

The following points should be specifically stressed during their training:

- Special requirements for handling oncological drugs
- Handling of application devices
- Management of spillage or other incidents
- Management of extravasation
- Handling patient's excretions
- Cytotoxic waste disposal.

An individual care plan should be established in cooperation with the responsible pharmacist.

5.5 HANDLING DRUGS WITH A SPECIAL ROUTE AND MODE OF ADMINISTRATION

5.5.1 HANDLING OF ORAL DRUGS

Oral oncological drugs are available in capsules/tablets or in liquid formulation. In handling and administering of oral drug forms a person has to use appropriate PPE, and if necessary single use tools i.e. spoon.

5.5.2 OTHER ROUTES OF ADMINISTRATION AND SPECIFIC THERAPIES (I.E. TACE, HIPEC, INTRATHECAL, INTRAVESICAL, ONCOLYTIC VIRUSES).

Specific administrations of oncological drugs require extra attention from all staff involved in conducting the procedure. Pharmacists should give advice to make sure that a proper way of handling oncological drugs and waste is carried out and that all the necessary PPEs and devices are used.

5.5.3 INFUSION PUMP

Infusion pumps may be set up, operated and used only for their intended purpose pursuant to the “law on medical devices” and associated statutory orders, and in accordance with generally recognized technical requirements and occupational safety and accident prevention legislation.

5.6 RADIOPHARMACY

A radiopharmacist is a respected expert in radiopharmacy, a guarantor of quality and safety of radiopharmaceuticals, a partner for nuclear medicine staff and an important person for the everyday running of a nuclear medicine department.

5.7 EXTRAVASATION (PARAVASATION)

Extravasation is a serious complication of i.v. drug administration which requires knowledge of the risk factors, preventive measures, immediate detection and treatment.

Guidelines for prevention and an action plan and documentation sheet for the management and treatment of extravasation must be at hand in all wards and units providing oncological therapy.

An extravasation kit for immediate treatment of extravasation must be easily accessible in the ward or unit.

5.8 MANAGEMENT OF EXCRETIONS

Excretions of patients, who receive anticancer therapy, may contain significant amounts of cytotoxic substances.

Health protection measures should be provided to all persons handling these excretions. In addition, applicable disposal rules and institutional or national regulations need to be followed. Training and education must be provided to all persons (i.e. patients and family members).

5.9 RESEARCH AND DEVELOPMENT

Oncology research and development should preferably be conducted in a multi-professional way. Pharmacists may contribute to this important activity by designing, conducting, evaluating research and publishing its results and findings. Results from research and development improve efficacy, suitability and quality of patient care.

In research, scientific and ethical rules, as well as specific guidelines for the field of research, must be complied with.

5.10 MANAGEMENT OF CLINICAL TRIALS

Through his/her involvement in clinical trials in oncology, the pharmacist's role is to provide important contributions to ensure the quality of the investigational drug and the data collected in the clinical trial.

The pharmacist's role in clinical trials is to be responsible for the proper receipt, storage, inventory, blinding, reconstitution or production, delivery and destruction of the investigational drug (performed based on national and international regulations i.e. Guideline for Good Clinical Practice (GCP) and the correct documentation.

5.11 PHARMACIST AS A COORDINATOR IN THE DRUG COMMITTEE AND MEMBER OF TUMOR/TUMOR MOLECULAR BOARD

The pharmacist is a member of a multi professional team and must bring in his/her special knowledge in the drug committee, tumor/tumor molecular board and any other relevant hospital committee.

PHARMA-CEUTICAL CARE

The pharmacy team works in a patient-orientated way providing pharmaceutical care and pharmaceutical consultations.

The direct contact with oncological patients is one part of oncology clinical pharmacy.

Patient-orientated service is developed whilst considering the special features of the inpatient and outpatient area. In addition, the pharmacy conducts consultations with the attending physicians and responsible nursing staff. These activities form a component of patient-oriented oncology pharmacy services.

Consultation and care-service require a structured approach.

The communication of information is possible either directly through patient dialogue or indirectly by creating and handing out patient information materials.

6.1 PHARMACEUTICAL COUNSELING

The care plan is an important tool within the scope of patient-related care. This procedure focuses on the patient‘s education, questions and problems and allows for results-oriented implementation. The care plan should also include education about drug administration and oral drugs adherence evaluation.

The content of the care is recorded in writing, thus allowing the success of the process using defined monitoring parameters.

The care plan is created and agreed upon includes the systematic analysis of all drug-related questions concerning therapy and follows the widely used SOAP formula that has received multi-professional recognition:

S = subjective: the patient‘s subjective complaints and problems are described or inquired about and then documented.

O = objective: identifiable and measurable, objective parameters and symptoms are determined and documented.

A = Assessment: the objective and subjective content is systematically analyzed according to information, actions are demonstrated and discussed.

P = Plan: A care plan with defined therapeutic objectives is created after a preliminary assessment and the necessary measures are precisely defined.

At appropriate intervals, achievement of the objectives is verified using the defined parameters and symptoms and the results are recorded in writing.

The documentation and evaluation of the care plan according to SOAP is also suitable for presenting and discussing patient cases for the purpose of therapy optimization and multidisciplinary collaboration, as a part of team discussions and continuing education/further education programs.

6.2 CHRONO-ONCOLOGY

Chrono-oncology is a method of treatment in which the times of administering anti-cancer drugs are chosen according to the existing biological rhythms of the patient. The therapeutic aim is to improve the bioavailability and efficacy of the anti-cancer drugs while simultaneously achieving a reduction in the extent of their adverse effects. So far as clinical results are available, the knowledge gained in the area of chrono-oncology is intended to be used to optimize the relationship between dosage, therapeutic effect and adverse effects.

6.3 DRUG-DRUG, DRUG-FOOD INTERACTIONS

During the patient care process drug-drug and drug-food interactions have to be evaluated and discussed with the physician and the patient by the oncology pharmacist.

6.4 SUPPORTIVE THERAPY

It is one of the pharmacist's main responsibilities to give specific recommendations regarding prophylaxis and treatment of different side effects and supportive therapy. A pharmacist must be capable of recognizing adverse drug reactions (ADRs) and as part of quality assurance, the pharmacist should also develop general prophylaxis and treatment guidelines, in collaboration with other oncology healthcare professionals.

6.4.1 MANAGEMENT OF NAUSEA AND VOMITING

Nausea and vomiting are perceived by patients as frightening and particularly unpleasant adverse effects of anticancer therapy. Their severity may even lead to premature termination of treatment. Thus, it is crucial to provide efficient antiemetic supportive therapy from the beginning.

The choice of an appropriate therapeutic intervention should be guided by the following aspects:

- Emetogenic potential of the treatment cycle
- Individual risk factors of the patient
- Different phases of nausea and emesis
- Therapeutic guidelines of professional organizations based on evidence-based medicine (EBM)
- Pharmacoeconomic aspects

The implementation of the chosen therapeutic intervention should be supported by:

- Cooperation between patient, physician, pharmacist and other involved professionals
- Compliance-supporting measures
- Additional prophylactic measures

6.4.2 PAIN MANAGEMENT

Most cancer patients experience pain which is different in etiology, type and intensity. Signs of pain should be identified early and therapy should be consistent and appropriate, including all pharmacological and non-pharmacological options. Proper pain management strategies should focus on effective collaboration within a multi-professional team.

6.4.3 ALOPECIA

For patients under chemotherapy treatment, alopecia can be perceived as a burdensome adverse effect of many anticancer drugs. Although alopecia treatment options are still very limited, aspects and concerns about alopecia should be addressed during patient counseling.

6.4.4 MANAGEMENT OF MUCOSITIS

Inflammation of the mucosa – mucositis – can be found in several body locations and organs (i.e. stomatitis, esophagitis or cystitis). Many oncological patients experience mucositis which is a very common side effect of chemo- and radiation therapy. Mucosal lesions can be very painful and significantly impair the cancer patients' quality of life.

6.4.5 MANAGEMENT OF DIARRHEA

Diarrhea is a serious complication of anticancer therapy. Specific anticancer drugs and new immunotherapy treatments as well as radiation therapy can cause diarrhea as an adverse effect. Immunological, infectious or cancerous processes can also cause diarrhea which needs to be included in the diagnostic evaluation.

Untreated diarrhea may lead to weakness, electrolyte imbalance and exsiccosis, and may rapidly escalate.

6.4.6 NUTRITIONAL ADVICE AND THERAPY

Almost all oncology patients suffer from extreme weight loss. This not only leads to worsening of the patient's general condition, but cachexia also causes further therapy intolerance and an increased risk of developing adverse effects.

Nutritional treatment needs to be focused on the patient's well-being.

Part of nutritional counseling should include discussing changes in taste sensation that may occur during oncology treatment and should deal with the increased energy requirements. The pharmacist as a member of a multi-professional team should provide guidance on how the patient might benefit from dietary changes.

Provision of related written information material and instructions is beneficial to the patient.

6.4.7 MANAGEMENT OF UNDESIRABLE DRUG EFFECTS ON THE SKIN

The pharmacist must be capable of recognizing adverse drug reactions (ADRs) on the skin and offering suggestions for prophylaxis or treatment.

6.4.8 FATIGUE

Fatigue is the most common and limiting side effect in cancer patients. Fatigue refers to both physical and psychosocial deterioration and greatly influences and affects the quality of life of the patient. It can often be overwhelming for the patient's daily life, negatively influencing adherence to cancer treatment. Fatigue is worsened by comorbidities and influenced by the occurrence and severity of other symptoms such as pain, insomnia, depression, anxiety, diarrhea,

and risk factors including gender and age. The underlying pathophysiological mechanism of fatigue is still largely unknown. There are no general treatment recommendations for alleviating the symptoms of cancer related fatigue symptoms, although co-treatment of symptoms and moderate physical activity can contribute to improvement.

6.4.9 TUMOR-RELATED OSTEOPOROSIS

Cancer patients are at a higher risk of developing osteoporosis. Since they are treated with significant success and have longer survival times, osteoporosis is an increasingly significant long-term complication. The pharmacist should counsel the patient on matters such as lifestyle with a healthy diet, physical activity and supplementation of calcium and vitamin D.

6.4.10 THROMBOSIS PROPHYLAXIS AND TREATMENT IN TUMOR DISEASES

Cancer patients are at increased risk for thromboembolic complications. Since a venous thromboembolism (VTE) significantly reduces the survival rate, adequate primary prophylaxis, therapy and a secondary prophylaxis may be required. Recommendations on primary prophylaxis can be made by the clinical pharmacist for patient groups with special risk factors.

6.4.11 PROPHYLAXIS AND THERAPY OF TUMOR LYSIS SYNDROME (TLS)

TLS is a potentially life-threatening complication of tumor therapy due to acute renal failure or cardiac arrhythmias. Treatment of TLS should be done through a multi-professional team including a pharmacist.

6.4.12 STRESS MANAGEMENT IN CANCER PATIENTS

Cancer patients often feel stressed. There are many different ways to manage stress, every person feels and handles stress differently. Some techniques are learning to relax, meditation, distraction, massage, exercise, talking with a psychologist and a spiritual counselor.

6.4.13 PREVENTION AND TREATMENT OF CANCER RELATED INFECTIONS

Infectious diseases are important causes of morbidity and mortality in patients with cancer. It is important to characterize the major pathogens to which patients with cancer are susceptible, with a focus on the prevention, diagnosis, and treatment of major common and opportunistic infections.

By ensuring the optimal use of granulocyte colony-stimulating factors, antimicrobials, antifungals and antivirals the pharmacist plays a fundamental role in providing informed advice to the multidisciplinary team dealing with the patient.

6.4.14 TREATMENT OF CYTOKINE RELEASE SYNDROME

Cytokine release syndrome (CRS) is an acute systemic inflammatory syndrome characterized by fever, cytokine production, capillary leak, and multiple organ dysfunction. The goal of CRS management is to prevent life-threatening toxicity while sustaining the antitumor effects of the immunotherapy, which require coordination by a diverse multidisciplinary team (hematologists, intensivists, neurologists and pharmacists). One of the most important pharmacist interventions is patient follow-up to monitor toxicities, adverse events, and concomitant and contraindicated drugs. Cytokine release syndrome is an extremely serious event that must be monitored by a multidisciplinary team in which the pharmacist is the reference figure for the management of rescue drugs and pharmacovigilance studies.

6.5 PALLIATIVE CARE

In the absence of curative treatment approaches, palliative care should be integrated into the care of the patient at an early stage. In order to provide patients with the best possible symptom-oriented treatment, multi professional cooperation between the various specialties is essential.

Pharmacists have an important role to play: They prepare medicines, e.g. preparing palliative chemotherapies, mixed infusions and individualized formulations if there are no suitable ready-to-use medicines available. Pharmacists also give advice on the correct use of medicines and provide information on the availability of medicines, their tolerability, side effects and interactions, as well as their possible applications and help in choosing appropriate medicines

6.6 TREATMENT MANAGEMENT FOR PARTICULAR CATEGORIES OF PATIENTS

6.6.1 CHEMOTHERAPY FOR PATIENTS WITH RENAL OR HEPATIC IMPAIRMENT AND ON DIALYSIS

Hepatic and/or renal function plays a key role in the elimination of some conventional chemotherapeutic agents and kinase inhibitors. Changes in dosing may be necessary to prevent increased toxicity caused by drug accumulation. Monoclonal antibodies are less likely to be affected.

Dialysis eliminates smaller molecules, including a number of cytostatics, from the body. In such cases, careful timing of dosing is essential to achieve the desired effect and maintain safety.

Respective measures are described in summaries of product characteristics or specialised guidelines. Pharmacists can evaluate the case and make individualized recommendations for the treatment plan.

6.6.2 CHEMOTHERAPY IN THE VARIOUS STAGES OF LIFE

Due to differences in the nature of diagnoses and the physiology of the young organism, treatment of children and young adults demands a different approach to the treatment of adults. Clinical evidence is often limited and off-label use is frequent.

The older adults and the elderly comprise the main bulk of cancer patients. While age itself does not contraindicate treatment a more careful approach is essential in frail, senior patients who may be burdened by incl. organ malfunctions, malnutrition, cognitive disorders.

6.7 CANCER SURVIVORSHIP

Cancer survivorship care focuses on the health and well-being of a person with cancer from initial diagnosis, through treatment until the end of life. This includes physical, emotional, mental, social and financial effects of cancer on the patient.

A pharmacist is a member of a multi-professional cancer survivorship team whose main goal is to optimize the care of cancer survivors and ensure that each survivor‘s diverse and complex needs are addressed. This includes involvement in the delivery of supportive care services in the crucial post-treatment period and in the development of cancer survivorship care plans.

Survivorship care plans should include:

- general patient information
- cancer treatment history (diagnosis, treatments completed and ongoing)
- systematic follow-up treatment (possible late- and long-term effects)
- cancer surveillance (cancer screening tests)

Pharmacists have a role to play in:

- providing general support in the management of ongoing problems and side effects, and with late toxicities resulting from cancer treatment
- educating and promoting healthy living after cancer treatment ceases, by incorporating lifestyle changes to reduce the risk of developing a recurring or secondary cancer.

6.8 ADHERENCE TO ORAL ANTICANCER THERAPY

Oral anticancer therapy has been rapidly developing for some years now and will continue to develop. Many patients receive it long term. In order to achieve the desired therapeutic outcome it is necessary for the patient to have a significant degree of therapy adherence, which is only possible if the patient knows the prescribed treatment. Adherence is affected by various factors and is improved by having support from a multi-professional team. The pharmacist should play a key role in supporting the patient by consultations, comprehensive information, monitoring and optimizing the medication treatment plan.

6.9 UNCONVENTIONAL METHODS IN CANCER THERAPY

The oncology specialized pharmacist should have knowledge about complementary and alternative medicine (CAM) regarding cancer treatment and, if requested, should be able to give advice about unconventional treatment methods which are not approved or accepted by the school of medicine. However, some scientific evidence of those unconventional treatment methods is mandatory.

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