QuapoS

Quality Standard for the Oncology Pharmacy Service

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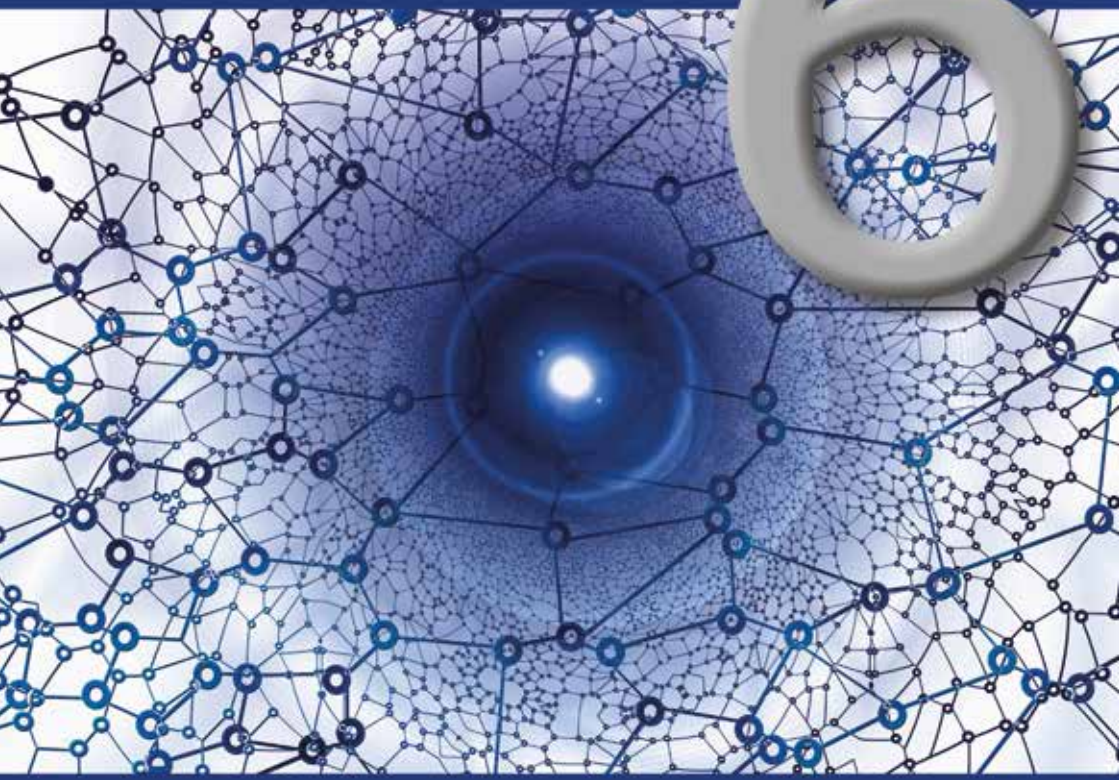

ESOP

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QUAPOS 6

Quality Standard for the Oncology Pharmacy Service

ESOP 2018

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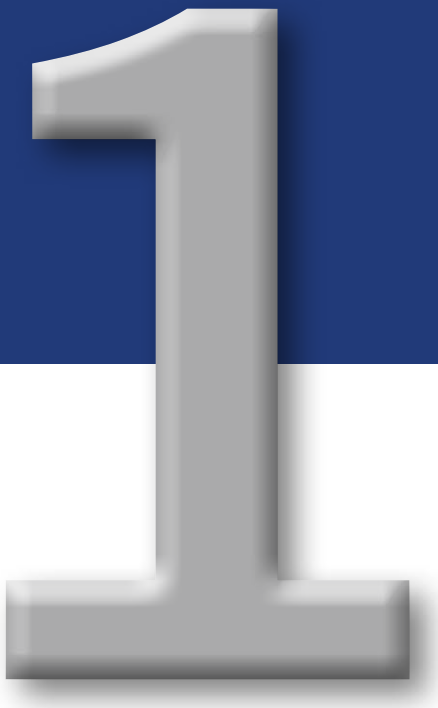

QUALITY ASSURANCE

1.1 QUALITY MANAGEMENT FOR THE ONCOLOGY PHARMACY SERVICE

The certified quality management system (QMS) implemented in the pharmacy department is designed to produce anticancer drugs and/or offer counselling and care for cancer patients or oncology units:

- meet the minimum requirements of DIN EN ISO 9001 for a QM system,
- implement the current quality standards of the pharmacy oncology service and subsequently implementing guidelines for quality assurance,
- achieve systematic quality improvement, through regulated, conceptually coordinated and reproducible operational procedures,
- further develop the quality of patient counselling regarding the drugs used in cancer treatment as well as pharmaceutical care of cancer patients,
- increase drug safety in regard to user and patient protection and maintain the existing QM system.

All aspects defining a consistently high level of quality are integrated in the QM system. These aspects are required for proper patient care.

1.2 RISK MANAGEMENT

Quality management represents the basis for a definitive control of the processes in the preparation of anticancer drugs and counselling and care for cancer patients. It is based on the risk analysis of the department. Controlled handling of the residual risk is connected to the analysis. Processes are continuously analysed, 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 ANTICANCER DRUGS

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

Persons handling anticancer drugs (stocking, production, distribution, or 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.

- Pharmacy auxiliary staff
- Professionals employed by the pharmacy
- Pharmacy sales staff
- Cleaning staff
- Transport staff

2.2 PERSONS IN THE PRODUCTION

In the production and associated quality control laboratory units, only pharmaceutical 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 hazardous substances.
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 and trainee pharmacists
- Pharmacy assistants and residents
- Pharmacy technicians and trainee pharmacy technicians

2.4 RISK EVALUATION, WORKING RULES AND INSTRUCTIONS

Before starting work in an anticancer drug preparation unit, the hazard risks of anticancer drug handling for that unit needs to be evaluated and documented. The employees must be instructed, based upon these findings. In addition to the persons carrying out the production, all employees dealing and working with anticancer drugs must be instructed in respect to relevant EU legal requirements (e.g. hazardous substances regulations) and/or local regulations. The instructions given must be aligned with the different job categories and responsibilities of the staff.
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 (anticancer drugs, latex, etc.)
- Hazards and protective measures
- Aseptic working technique
- Disposal of contaminated materials and devices and of residues of anticancer drugs
- Occupational medicine
- Action in the case of accidents

These instructions must be updated and documented annually. In addition, written working instructions must be prepared specifically to 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 must be inspected at least once a year. If any changes are made, a new documented risk evaluation has to be produced to accord 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 in respect to Advanced Therapy Medicinal Products (ATMPs) as defined by EU regulation 2007-1394.

2.5 RISK OF PERSONNEL WORKING PERMANENTLY WITHIN CENTRALISED ANTICANCER DRUG PRODUCTION

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

2.6 OCCUPATIONAL HEALTH AND SAFETY

Employees working in the areas of anticancer drugs preparation in the pharmacy are dealing with potential carcinogenic, mutagenic and reproductive toxic (CMR) drugs. They must be offered regular (e.g not less than annually) occupational health and safety medical check-ups, taking into account all the relevant factors pertaining to the specific workplace.
These check-ups include:

- Initial medical examination before taking up employment (i.e. full blood counts, chest X-ray).
- Follow-up examinations during the employment at intervals of 1 to 2 years.
- Examinations at the request of the employee 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.
Exposure to anticancer drug must be documented by the employer in a suitable form. This documentation must include the types and amounts of anticancer 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 anticancer drug as well as anticancer drug-related accidents and their management.

2.7 TRAINING, EDUCATION AND PROFESSIONAL SPECIALIZATION OF EMPLOYEES

The goal of training, continuous education, and professional specialisation is to provide personnel with theoretical knowledge and practical skills.

Theoretical knowledge:

- Quality- and Risk-Management System
- National and regional laws, rules, regulations and best practise
- 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 anticancer drugs
- Drug effects and pharmacology
- Clinical pharmacy
- Cancer types and treatment options
- Pathology and impact on dose changes
- Management of Clinical Trials involving anticancer drugs
- Quality control laboratory

Practical training:

- Aseptic working techniques and their validation in simulations of work flow during compounding
- Handling of disposable articles
- 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 anticancer drug prescriptions including parenteral and oral drugs

Clinical pharmacy:

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

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

2.7.1 TRAINING OF NEW PERSONNEL

Training of new personnel in anticancer drug compounding needs to be performed with specific care since handling anticancer drug bears significant risks for humans and product safety.
The training requires planning of time and content requirements and should be performed according to a predefined training program.
Training of persons counselling patients includes the knowledge of the special needs of cancer patients in order to provide individual pharmaceutical care.

2.7.2 CONTINUOUS EDUCATION AND PROFESSIONAL SPECIALISATION 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 anticancer drugs compounding unit as well as the staff providing pharmaceutical care and patient counselling should also have the opportunity to participate in internal and external pharmaceutical education programs.
A certificate should document participation.
Opportunities for professional specialisation and continuous education should be taken if offered.

PHARMACY ANTICANCER DRUG UNIT

3.1.1 ROOMS

The following constitutes the required rooms in an anticancer drug preparation department:

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

The design and organisation 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 by microorganisms, particles, and cytotoxic substances to a minimum. Along with the electromechanical control, the rooms should be set up to ensure best practice in preparation, production and documentation.
The entire equipment of the preparation room must be reduced to the necessary minimum and listed on a plan.

3.1.1.1 STOCK RECEIVING AREA

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

3.1.1.2 DOCUMENTATION AREA

The documentation room receives the patients' files and medication orders for review and checking. Patient specific labels for each anti-cancer drug are created.

3.1.1.3 AIR LOCK

Hand sanitisation and the donning 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, 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, which is separated from the remaining areas by one or more air-locks.

3.1.1.6 CHECKING AND RELEASE AREA

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

3.2 ROOM AIR EQUIPMENT, SAFETY WORKBENCH FOR CYTOTOXIC SUBSTANCES AND BIOHAZARD SAFETY CABINETS (BSC-S) AND ISOLATORS

1. A safety workbench for anticancer drugs (SWC) according to DIN 12980 has to be used. Since 2016 Isolators for Cytotoxcis (IFC) are included here. Requirements are described in detail. SWC and IFC are placed and used in an appropriate way.
   The biohazard safety cabinets (BSCs) can be used according to PIC/S guide for preparation in healthcare establishments.
2. The preparation is carried out in a working environment class A (within SWC or BSCs in a class B room). A class C room may be adequate in case the process is validated. An isolator may be used in a class D room.
3. An total exhaust air extraction system is mandatory using a SWC/BSC as an additional safety measure.
4. The ventilation system has to be climatised according to the needs of the personnel (i.e. legal requirements) and the air equalisation of exhaust air. The protective function of the SWC/BSCs has to be maintained.

3.2.1 ROOMS AND EQUIPMENT MONITORING-REQUIREMENTS FOR THE MONITORING OF 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;
- 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 in the EU 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 GHS and the MSDS safety data sheets. Each country must adhere to their national legislation.

ANTICANCER DRUG PRODUCTION

4.1 REQUIREMENTS FOR DRUG MANUFACTURERS

The pharmaceutical company is responsible for its drugs and the information available for the safe use of these products. The finished drug and its various forms of packaging should be designed to enable safe use. Shipment of all cytotoxic drugs should be labelled with a "Yellow hand" warning label and delivered separately.
The information provided regarding the drugs must cover all identifiable needs comprehensively. The information has to be worded to ensure readability and comprehension by patients and health care professionals.
The drug manufacturers must ensure the continuous supply of their products.

4.1.1 HANDLING THE SHIPMENT OF ANTICANCER DRUGS

Only trained pharmacy staff are allowed to accept shipments of anticancer drugs.
Packages or shrink–wrapped anti-cancer drugs need to be opened in a designated location with personnel wearing protective clothing. 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 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 respectively 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 labelled according to the applicable rules and regulations and with the "Yellow hand" warning label.

4.2 PERSONAL PROTECTIVE EQUIPMENT (PPE)

The European Union has issued several Directives to ensure high quality of personal protective equipment (Directive 2016/425). The PPE Guidelines - Version 24 August 2017 aim to facilitate a common interpretation and application of the PPE Directive.
The personal protective equipment must meet the CE (European Conformity) standards and needs to be specified in the hazard evaluation.

Personnel has to wear PPE appropriate for each area identified in the hazard evaluation.

Depending on the working place, PPE consists of:

- protective 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 GOWN

Protective gowns must be sufficiently long (covering the thighs), closed up to the neck, with long sleeves and close-fitting cuffs. They should repel liquids at especially exposed areas and be tested and classified to be used within the hazardous anti-cancer drug. 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

Suitable powder free gloves or glove combinations must be worn and must be changed regularly. They must be changed also in the event of contamination.

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 is fundamental to safe and aseptic work with anti-cancer drugs. In doing so, 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 ANTI-CANCER DRUGS

In order to ensure minimum safety standards for the production of anti-cancer drugs, it is necessary to employ suitable technical equipment. This must comply with the requirements of relevant EU legislation, such as those regulations applying to medical devices. In addition, the materials used must fulfil the special criteria associated with anti-cancer drug production. All equipment must be sterile, or must 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 ANTI-CANCER DRUGS

Alongside with medical devices regulations, there are additional requirements for the selection of appropriate equipment for the administration of anticancer drug.
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 embraces all coordinated and necessary steps, which lead to a sterile product by using optimal conditions for germ reduction and avoidance of microbial 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 MICROBIAL CONTAMINATION

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

- the room class in respect of cleaning and hygiene
- the safety workbench (LAF - laminar air flow for anti-cancer substance, BSC or Isolator)

- the work materials
- the source materials
- the aseptic production method.

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 in regard to safety, identity, content, quality and purity, and corresponds to the defined quality profile.

4.4.2 VALIDATION

In order to ensure high quality of the production and the final product, it is necessary to validate the whole process according to the workflow. This includes monitoring cytotoxic and microbial 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

Anticancer drug preparation in an anticancer drug hood (SWFC)/isolator/BSC is an aseptic drug preparation process that must be validated.
Compliance with the requirements of the European Pharmacopoeia (Ph. Eur.) 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 microbial contamination, using appropriate microbiological procedures, can be used for validation. A testing plan must be compiled.

4.4.2.2 SURFACE MONITORING

Since most cytotoxic drugs are invisible in solution it is essential to apply a sufficient cleaning procedure not only in case of an accidental contamination but also during every day practice. It is therefore necessary to monitor production and administration areas in defined time intervals for various reasons such as 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 during the classification of rooms.

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

4.5.1 REQUIREMENTS FOR PRESCRIPTION FORM AND PLAUSIBILITY CHECK

Prescribing of the anti-cancer drugs by the physician is submitted in electronic or written form.
The prescription must include at least the following information:

- Patient name, date of birth, gender and identification code
- Body weight, height and/or body surface area
- 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
- A required dose - reduction in the case of 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 regimes for more than one day
- Date and physician‘s signature or in the case of an electronic request, clear identification of the ordering physician by means of secure release

4.5.2 STABILITY OF THE PREPARATIONS

The shelf life of the preparations should be established from the information of 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 reference“.
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. Local governing bodies should be involved in making decisions to adopt stability data.

4.5.3 DOSE ADJUSTMENT

Anticancer 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 decision are discussed below. Because of the organotoxic potential, dose adjustment may be necessary as well.

4.5.3.1 ANTICANCER DRUG DOSAGE IN CASE OF IMPAIRED RENAL FUNCTION

An impaired renal function may increase the toxicity of anticancer drugs and active metabolites through accumulation. A dosage reduction may therefore be necessary for substances which are eliminated renally to a significant extent. Each decision should be made on the broadest possible base of information and the patient‘s individual situation. A condition for a proper recommendation is a measurement of the GFR (glomerular filtration rate) approximation value (generally „creatinine clearance“).

4.5.3.2 ANTICANCER DRUG DOSAGE IN CASE OF IMPAIRED LIVER FUNCTION

Decreased liver function may significantly influence hepatic clearance of anticancer drugs. Some anticancer 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 the therapy. It is associated with febrile neutropenia and associated infections which are main causes of morbidity and mortality of cancer patients.

4.5.3.4 ANTICANCER DRUG DURING PREGNANCY

Cancer treatment during pregnancy is a complex decision and has to be based on individual considerations.

4.5.3.5 THERAPEUTIC DRUG MONITORING, PHARMACOGENOMICS AND PERSONALIZED MEDICATION MANAGEMENT

Therapeutic drug monitoring, pharmacogenomics and personalised medication management are core functions within the pharmacist‘s provision of direct patient care. These activities ensure individualised, 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 the results of the hazard 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 standardised, 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 SWC bench/isolator/BSC and the behaviour 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 form of capsules or tablets. Therefore 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 from

highly toxic substances.
Staff and environmental protection is a key priority and must be ensured through appropriate measures and production conditions.
If drugs are 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

Ready-to-use infusion solutions produced individually for a patient are labelled 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 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 anticancer 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 specifications. A production protocol is maintained.

The production protocol must contain the following information, i.e.:

- 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 is 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 are approved and signed by a pharmacist.

4.7 DELIVERY OF THE FINIAL PRODUCTS

For "in-house" transport the finished products are delivered in unbreakable, liquid tight, tight closing containers labelled with the inscriptions "Caution Anti-cancer drug" and/or the "Yellow Hand" sign.
If the finished product will be transported out of the institution it needs to comply with local hazardous freight regulations.
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.
Receiving of the final product must be documented.

4.8 PRICING

The costs of a preparation are divided between the following areas:

- material costs:
- drugs
- medicinal devices
- carrier solutions
- consumables
- maintenance costs
- personnel costs
- 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 particularly includes 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 CO-ORDINATION CENTRE

5 PHARMACY AS A CO-ORDINATION CENTRE

The pharmacist has special competences in oncology. He/she implements the quality management of the oncology pharmacy service and takes shared responsibility for patients and staff in all areas of anti-cancer therapy within a multi-professional team.
The pharmacy records and processes all medical and toxicological data relating to the anticancer drugs and supportive therapy. Pharmaceutical interventions are provided.
The available information can be epidemiologically evaluated, documented with regard to clinical, pharmaco-economic 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 in order to ensure that:

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

are not jeopardized.

Hazardous wastes and contaminated objects are collected

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

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

5.2 DECONTAMINATION AFTER LEAKAGE AND/OR ACCIDENTAL SPILL

Appropriate spill kits must be easily available in all designated areas where anti-

cancer drugs are handled.
The removal and disposal of spilled anticancer 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 the annual instruction.

5.3 HANDLING OF ANTICANCER DRUG ON WARDS/UNITS

Nurses and physicians have the main responsibilities in handling anticancer 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-specialized pharmacist should support and advice the ward and unit personnel in establishing operating procedures for safe handling of anticancer drugs and the correct use of personal protective equipment in order to guarantee safe working techniques.

5.4 HANDLING ANTICANCER DRUGS AT HOME

Certain anticancer therapy regimens demand an active substance to be administered over a period of 24 hours or up to several days. This type of therapy is performed both during hospitalisation and / or as outpatient treatment.
Patients, family members and personnel working in the home care setting need to be informed and trained in the handling of anticancer drugs in this environment.

The following points should be specifically stressed during their training:

- Special handling of anticancer 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 co-operation with the responsible pharmacist.

5.5 HANDLING DRUGS WITH SPECIAL ROUTE OF ADMINISTRATION

5.5.1 HANDLING ORAL DRUGS

Oral anticancer drugs are available in capsules or tablets. 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 INTRATHECAL ADMINISTRATION

A dated and annually reviewed procedure for the safe dispensing, release and receipt of intrathecal drugs should be available. A register lists the designated, trained, and authorised personnel to prescribe, dispense, release, check and administer intrathecal chemotherapy. For all aspects of storage, prescription and administration of intrathecal chemotherapy current documented procedures are in place.
The intrathecal prescriptions are screened by a pharmacist and preferably double checked and signed by a clinical pharmacist. Labels have the route of administration printed clearly in the largest font size possible (intrathecal only). For vinca alkaloids, a clear warning of the consequences of administration by other routes has to be added i.e. **„For Intravenous Use Only - fatal if given by other routes“.**

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.

5.5.4 OTHER ROUTES OF ADMINISTRATIONS AND SPECIFIC THERAPIES (I.E. TACE, HIPEC, INTRAVESICAL, RADIOPHARMACEUTICALS, ONCOLYTIC VIRUSES)

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

5.6 EXTRAVASATION (PARAVASATION)

Extravasation presents a serious complication of i.v. drug administration requiring knowledge of the risk factors, preventive measures, immediate detection and treatment.
Guidelines for prevention and an action plan and documentation sheet for the 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.

5.7 MANAGEMENT OF EXCRETIONS

Excretions of patients, who receive anti-cancer 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 regulations need to be followed.

5.8 RESEARCH AND DEVELOPMENT

In oncology research and development should preferably be conducted in a multi-professional way. Pharmacists may contribute to these important research activities in designing and conducting the trials. Results from research and development improve efficacy, suitability and quality of patient care.
In research, scientific and ethic rules as well as specific guidelines for the field of research must be complied with.

5.8.1 MANAGEMENT OF CLINICAL TRIALS

Through his/her involvement in clinical trials in oncology, the pharmacist provides an important contribution to ensure the quality of the investigational drug and to the data collected in the clinical trial.
The pharmacist is responsible for the proper receipt, storage, inventory, reconstitution or production, delivery and destruction of the investigational drug (which he/she performs based on national and international regulations i.e. Guideline for Good Clinical Practice (GCP)) and the correct documentation.

PHARMA-CEUTICAL CARE

6 PHARMACEUTICAL CARE

The pharmacy team works in a patient-orientated way in providing pharmaceutical consultations and care.
Part of the oncology clinical pharmacy service is the direct contact with patients who receive anticancer drugs.
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. It is these activities that form a component of patient-oriented oncology pharmacy service for cancer patients.
The implementation of consultation and care services requires a structured approach.

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

6.1 DEVELOPING A PHARMACEUTICAL CARE PLAN

The care plan is an important tool within the scope of patient-related care. This procedure focuses on the patient‘s questions and problems and allows for results-oriented implementation.
The content of the care is recorded in writing, thus allowing the success of the process using defined monitoring parameters.
The care plan that 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 appropriate 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 optimizing care and multidisciplinary collaboration as a part of team discussions and continuing education/further education.

6.2 CHRONO-ONCOLOGY

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

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

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 anticancer therapy. Thus, it is pertinent to provide efficient antiemetic supportive therapy from the start.
The choice of an appropriate therapeutic intervention should be guided by the following aspects:

- Emetogenic potential of the cytotoxic therapy
- Individual risk factors of the patient
- Different phases of nausea and emesis
- Therapeutic guidelines of professional organisations based on evidence-based medicine (EBM)
- Pharmaco-economic 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 aetiology, 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 cytotoxics. Although alopecia treatment options are still very limited, aspects and concerns about alopecia should be addressed during patient counselling.

6.4.4 MUCOSITIS

Inflammation of the mucosa -mucositis- can be found in several body locations and organs (i.e. stomatitis, oesophagitis or cystitis). Many oncological patients experience mucositis which is a very common side effect of cancer chemo- and radiation therapy. Mucosal lesions can be very painful and significantly impair the cancer patients' quality of life.
It is one of the pharmacist's responsibilities to give specific recommendations for individual patients regarding mucositis prophylaxis and treatment. As part of quality assurance, the pharmacist should also develop general prophylaxis and treatment guidelines, in collaboration with other oncology healthcare professionals.

6.4.5 MANAGEMENT OF DIARRHOEA

Diarrhoea is a serious complication of anticancer therapy. Specific cytotoxics as well as radiation therapy can cause diarrhoea as an adverse effect. Immunological, infectious or cancerous processes can also cause diarrhoea that needs to be included in the diagnostic evaluation.
Untreated diarrhoea may lead to weakness, electrolyte imbalance and exsiccosis, and may rapidly escalate. It is one of the pharmacist's responsibilities to ensure implementation of early and adequate treatment of diarrhoea.

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 counselling should include discussing changes in taste sensation that may occur during cancer chemotherapy 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 recognising adverse drug reactions (ADR) on the skin and offering suggestions for treatment. An important consultation task involves prophylaxis from drug reactions on the skin.

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, diarrhoea, 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 the 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 thrombosis VTE significantly reduces the survival rate, adequate primary prophylaxis and therapy and a secondary prophylaxis are necessary. 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 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.

6.5 ADHERENCE TO ORAL ANTICANCER THERAPY

Oral anticancer therapy will increase significantly over time. Many patients receive it long term. This requires a significant degree of adherence to and understanding of the therapy by the patient in order to achieve the desired therapeutic outcome. 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 and optimizing the medication treatment plan.

6.6 UNCONVENTIONAL METHODS IN CANCER THERAPY

The oncology specialized pharmacist should have knowledge about complementary and alternative medicine (CAM) regarding cancer treatment. If requested he/she 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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