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ORIGINALES

Safe procedure development to manage hazardous drugs in the workplace

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Abstract

Objective: To develop a safety working procedure for the employees in the Intermutual Hospital de Levante (HIL) in those areas of activity that deal with the handling of hazardous drugs (MP).

Methods: The procedure was developed in six phases: 1) hazard definition; 2) definition and identification of processes and development of general correct work practices about hazardous drugs' selection and special handling; 3) detection, selection and set of specific recommendations to handle with hazardous drugs during the processes of preparation and administration included in the hospital GFT; 4) categorization of risk during the preparation/administration and development of an identification system; 5) information and training of professionals; 6) implementation of the identification measures and prevention guidelines.

Results: Six processes were detected handling HD. During those processes, thirty HD were identified included in the hospital GFT and a safer alternative was found for 6 of them. The HD were classified into 4 risk categories based on those measures to be taken during the preparation and administration of each of them.

Conclusions: The development and implementation of specific safety-work processes dealing with medication handling, allows hospital managers to accomplish effectively with their legal obligations about the area of prevention and provides health-care professional staff with the adequate techniques and safety equipment to avoid possible dangers and risks of some drugs.

KEYWORDS: Drugs++ Hazardous++ Use++ Procedure++ Management++ Risk++ Manipulative++ Professional++ Health-workers.

Resumen

Objetivo: Desarrollar un procedimiento de trabajo seguro para los trabajadores del Hospital Intermutual de Levante (HIL) en las distintas áreas de actuación relacionadas con la manipulación de medicamentos peligrosos (MP).

Métodos: El procedimiento se desarrolló en seis fases: 1) definición de medicamento peligroso; 2) definición e identificación de procesos y elaboración de recomendaciones

generales sobre selección y manejo de MP; 3) detección, selección y establecimiento de recomendaciones específicas para el manejo durante la preparación y la administración de los MP incluidos en la GFT del hospital; 4) categorización del riesgo durante la preparación/administración y desarrollo de un sistema de identificación; 5) información y formación a los profesionales; 6) implantación de las medidas de identificación y las pautas de actuación.

Resultados: Se detectaron seis procesos implicados en el manejo de MP. Se identificaron 30 MP incluidos en la GFT del hospital y se encontró una alternativa más segura para seis de ellos. Los MP se clasificaron en cuatro categorías de riesgo en función de las medidas a adoptar durante la preparación y administración de cada uno de ellos.

Conclusiones: El desarrollo e implementación de procedimientos de trabajo específicos para el manejo seguro de medicamentos permite a los responsables de un hospital cumplir de forma efectiva con las obligaciones legales en materia preventiva, así como proporcionar a los trabajadores un medio adecuado para evitar la posible peligrosidad de algunos medicamentos.

PALABRAS CLAVE: Medicamentos, Peligrosos, Procedimiento, Manejo, Seguro, Riesgo, Manipulador, Profesional, Trabajadores sanitarios.

Introduction

In 2004, the National Institute for Occupational Safety and Health (NIOSH) defined the term Hazardous Drug (HD)[1] as those medications presenting one or more of the following risk criteria in humans: carcinogenicity, tetarogenicity or other toxicity for development, reproductive toxicity, organ toxicity at low doses, genotoxicity; and new medications with structure and toxicity profiles similar to existing medications already classified as hazardous according to the previous criteria.

At the same time as the HD definition from 2004[1], the NIOSH published a list of HDs, which was updated in 2010[2], 2012[3], 2014[4] and the draft for the 2016 update was being prepared at the time of writing this document[5], differentiating the risk of those drugs included in three groups (Table 1).

Table 1
Level of risk posed by HDs.

Group 1	Antineoplastic drugs.
Group 2	Non-antineoplastic drugs that meet at least one criterion for hazardous drugs.
Group 3	Drugs that pose a reproductive risk to men and women who are actively trying to conceive and women who are pregnant or breast feeding, but that present no risk for the rest of the staff.

The effects of HDs on health, both therapeutic and side effects, are justified in patients because there is a favourable benefit / risk balance; however, exposure in healthcare staff must be reduced as much as possible[6]. The safety and health of the staff is a key matter in any healthcare centre; therefore, it has been necessary to determine some recommendations for handling those HDs that pose a risk for the healthcare staff handling said medications.

Faced with the lack of specific regulations in Spain for handling HDs, and the existence of publications warning about the health risks

associated with certain medications, there has been a social alarm that justifies the fast preparation and dissemination of a working procedure for handling hazardous drugs, in order to minimize risks for the healthcare staff. Following the criteria scientifically established by organizations with acknowledged prestige, we have selected the documents published by the NIOSH in 2014[4], and its 2016 update[5], and by the National Institute of Occupational Safety and Hygiene (INSHT): "Hazardous Drugs: Prevention measures for their preparation and administration", as well as the consensus document "Safety for patient and healthcare staff in the preparation and administration of hazardous drugs"[7], as the basis for the development of a working procedure for handling HDs in our healthcare centre, with the aim to facilitate a method of work that will observe the safety and health of the staff within a safe setting.

Objectives

To develop a safe working procedure for the staff in the Hospital Intermutual de Levante (HIL) in the different areas associated with handling HDs, including any protection equipment required, with the aim to reduce risk and minimize exposure as much as possible.

To disseminate the current information about the risk for workers derived by handling HDs and their waste material in all work areas and positions that might be affected by said handling.

To ensure safety for the staff, the working environment, and the medication.

Material and methods

The working procedure was developed in six stages:

Definition of Hazardous Drug (HD).

Definition and identification of procedures and preparation of general recommendations for the selection and handling of HDs. The procedures involved in HD procedures were defined and identified, and a bibliographic review was conducted about the protection measures for the handler at each one of these procedures, based on the recommendations by the main international associations dealing with HD handling.

Detection, selection and implementation of specific handling recommendations during the preparation and administration of those HDs included in the hospital formulary[8]. The information about the molecules included in the "NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2014"[4] and "Proposed additions to the NIOSH 2016 hazardous drugs list"[5] was compared with the list of medications included in our hospital formulary[8]. In order to determine the specific handling recommendations (infrastructures and individual protection equipment (IPE) for each HD, the following were taken into account: their category within the NIOSH lists (1, 2 or 3),

their formulation, way of administration, and place and conditions of preparation and administration. Besides, therapeutic alternatives with lower handling risks were assessed for each HD.

Classification of risk during preparation / administration and development of a system for identification. In order to facilitate the identification and homogeneity of HD handling, those HDs that shared handling measures during their preparation and administration were grouped into categories.

Information and training for professionals.

Implementation of measures for identification and guidelines for action.

Results

Stage a) Definition of Hazardous Drug (HD)

In terms of occupational exposure, Hazardous Drugs were defined as: those agents that, due to their inherent toxicity, represent a risk for the healthcare staff handling them. The risk posed by these medications is understood in terms of chemical risk, specifically, associated with the carcinogenic, teratogenic, genotoxic, toxic for the reproductive process or for a specific organ at low doses, or by being a new drug similar to those with this type of risks. In this sense, the following rules apply to HDs: protection rules for workers associated with the exposure to chemical agents (RD 374/2001)[9], carcinogenic agents (RD 665/1997)[10] and their subsequent modification (RD 349/2003)[11], and the 2004/37/CE directive[12] about protection against the risks of exposure to carcinogenic or mutagenic agents during work.

Stage b) Definition and identification of procedures and preparation of general recommendations for the selection and handling of HDs

The "potentially hazardous" procedures, activities, operations, equipment or products (article 4.5 of the Law for Prevention of Occupational Risks)[13] will be defined as those that, in the absence of specific preventive measures, will pose risks for the safety and health of the staff developing or using them.

Six procedures involved in HD handling were identified: selection, reception, transportation and distribution, preparation, administration, and waste management.

The following HD handling recommendations were reviewed: by the NIOSH[4], INSHT[6], Oncology Nursing Society (ONS)[14], American Society of Health-System Pharmacists (ASHP)[15], National School of Occupational Medicine in the Instituto de Salud Carlos III (ISC)[16], U.S. Pharmacopoeia (USP)[17] and International Society of Oncology Pharmacy Practitioners (ISOPP)[18]; and based on these, general

recommendations for HD handling were prepared for each of the procedures detected (Appendix 1)[19,20].

Stage c) Detection, selection and implementation of specific handling recommendations for those HDs included in the hospital formulary

Twenty-nine (29) medications included in the hospital formulary[8] were identified as molecules classified as hazardous by the "NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2014"[4] and "Proposed additions to the NIOSH 2016 hazardous drugs list"[5]. Besides, even though acenocoumarol was not included in the NIOSH lists, it was considered a HD given its similarity with warfarin (NIOSH List 3). Therefore, 30 medications included in the hospital formulary were finally identified as HDs. According to their level of risk, none was included in List 1 (antineoplastic drugs), 12 were from List 2 (non-antineoplastic drugs that meet at least one criterion for hazardous drugs), and 18 were from List 3 (drugs that pose a reproductive risk to men and women who are actively trying to conceive and women who are pregnant or breast feeding, but that present no risk for the rest of the staff).

A pharmaceutical alternative with lower risk in handling was found for six of the 30 HDs included in the hospital formulary. Five of these six HD were oral solid formulations that could be split or crushed for their administration to patients with swallowing problems; therefore, instead of splitting or crushing, it was decided to prepare oral liquid formulations as magistral formula in a biological safety cabinet (BSC), to simplify preparation and administration and reduce handler exposure to the drug. The remaining HD was marketed in vials, so it was decided to purchase it as magistral formula in vials in order to minimize exposure. Thus, the final list included 36 HDs.

Finally, based on the classification of each HD in the NIOSH lists[4,5], their formulation, and the Technical Document by the INSHT: "Hazardous Drugs: Prevention measures for their preparation and administration"[6], a list was prepared with all HDs and the specific handling recommendations for each one of them (Appendix 2).

Stage d) Classification of risk during preparation / administration, and development of a system for identification

According to the specific measures for handling each HD included in the list of specific recommendations (Appendix 2), these were classified into four categories from lower to higher risk at handling during preparation and administration. In order to simplify HD handling, common measures were established for each category. In the case of those medications with different protection measures according to the reproductive risk for the staff, it was decided to implement the protection measures for the group of professionals with the highest level of protection. In order to differentiate each category, an identification

system was implemented, based on a colour code from lower to higher level of protection during preparation and administration (green, yellow, blue and red) (Table 2). The number of HDs included in each category was: 16 in Green, 10 in Yellow, 8 in Blue and 2 in Red (Appendix 3).

Table 2
Color code based on the specific management recommendations during the preparation and administration of the MP

COLOUR	RECOMMENDATIONS (Meeting the safety rule)
GREEN	Preparation[1]: No preparation required. Administration: Single gloves. No splitting or crushing. If it is necessary to split or crush the dose: - It would be of choice to use liquid oral formulations (consult with the Pharmacy Unit). - If no liquid oral formulation available, splitting will be done at the Pharmacy Unit, in a Class II B2 BSC with double gloves, lab coat / overalls and mask.
YELLOW	As a general rule, they should not be manipulated by personnel under reproductive risk[2,3]. Preparation: single gloves. Administration: Double gloves and lab coat; in case of risk of splashing, accidental disconnection of the system, administration through catheter, or patient who does not collaborate, use eye protection (goggles) and respiratory protection (mask). **In the exceptional case in which these must be PREPARED by staff at reproductive risk, they must be protected with double gloves, lab coat, goggles and mask.**
BLUE	Preparation: In the Pharmacy Unit, in Class II B2 BSC with double gloves, lab coat and mask. **In the exceptional case in which it is not possible to prepare in Class II B2 BSC, use double gloves, lab coat, eye protection (goggles) and respiratory protection (mask).** Administration: Double gloves and lab coat; in case of risk of splashing, accidental disconnection of the system, administration through catheter, or patient who does not collaborate, use eye protection (goggles) and respiratory protection (mask).
RED	Preparation: At the Pharmacy Unit in Class II B2 BSC with closed systems for preparation and administration. Double gloves, protective lab coat (preferable overalls) and masks. If not possible to prepare in Class II B2 BSC, use eye protection (goggles) and respiratory protection (mask). Administration: Closed systems of administration, double gloves, lab coat / overalls, and eye protection (if risk of splashing) and mask (if risk of inhalation).

The number between brackets corresponds to the number of the NIOSH list in which this medication is included. Acenocoumarol by similarity with warfarin (not included in NIOSH). List 1: Antineoplastic or cytostatic agents. List 2: Non-antineoplastic medications that meet one or more NIOSH criteria to be considered of risk. List 3: Non-antineoplastic medications with effects on reproduction, and that can affect men and women who are trying actively to conceive, and pregnant or breastfeeding women, but that don't represent a risk for the rest of the staff. 1 Whenever possible, the original blister will be kept at re-packaging. 2 Staff at reproductive risk: men and women who are actively trying to conceive, and pregnant or breastfeeding women. 3 For treatments prescribed continuously and that need to be prepared, this will be done at the Pharmacy Unit (PU) in CSBIIB2. Exceptional treatmetns will be prepared according to the protection measures already mentioned and, in case of persistence, their preparation will be similarly assumed by the PU. MG: Magistral Formula; Class II B2 BSC: Class II Type B2 Biological Safety Cabinet; CLDT: Closed System for Drug Transfer.

Stage e) Information and training for professionals

With general application, and according to Articles 18 and 19 of the Law for Prevention of Occupational Risks[13], workers must receive adequate information and training about the risks derived of the presence of any hazardous chemical agent present in their working place, as well as about the prevention and protection measures to be adopted. In particular, the training of the staff working with hazardous drugs is a key aspect to prevent occupational risks.

Therefore, all professionals involved in handling medications were informed through a Conference for the Safe Use of Medications that was publicized externally and given by the Pharmacy Unit and the Occupational Risk Prevention Unit, with the participation of the

Occupational Risk Prevention Unit from the Conselleria de Sanitat Universal y Salut Pública of the Community of Valencia.

Moreover, fortnightly internal sessions were given to the entire healthcare staff, in order to present the code of identification by colours; all the required materials for fast reference were provided, and there was training on the Procedure for "Safe Drug Handling".

In the same manner, the PPEs required were provided in all grounds and departments in which MPs could be handled.

Stage f) Implementation of measures for identification and guidelines for action

Reception and storage: HD labelling by colours based on their category in the classification, both in their packaging (for those HDs distributed in their original package) and in their primary preparation.

Distribution: HDs in the Green and Yellow categories will be normally distributed with the label assigned at reception. The drugs in red and blue categories will be prepared at the Pharmacy Unit and will be identified in the secondary conditioning with red and blue labels, respectively.

Preparation and Administration: Based on the colour code recommendations (Table 2).

Discussion

The potential exposure to HDs in each procedure where these are present will depend on various factors[19]:

Intrinsic risk posed by the medication due to its carcinogenic, teratogenic, or genotoxic potential, as well as reproductive toxicity and organ toxicity at low doses.

Sensitivity of the handler: allergies, pregnancy, breastfeeding, reproductive age.

Level of exposure: Penetration or absorption ability of the medication, concentration, amount, handling duration and frequency, type of activity, place, and associated risk of exposure (formulation).

Structure: human resources (education and training, number of handlers), premises (design and technical specifications, availability and type of BSC), use of closed system drug transfer devices (CSTDs) for preparation and administration, and availability of automatic systems.

Use of prevention measures: technical measures (BSC), CSTDs, automatic systems, organization measures (cleaning procedures, actions for spillage and maintenance, waste management and handling techniques) and secondary prevention measures (SPMs), that should feature some minimum characteristics[19] (Table 3).

Table 3

Minimum characteristics of SPMs[19]

Guantes	Two pairs of surgical gloves or one pair of gloves that meets the safety characteristics required for handling cytostatic agents. Double use, to protect both the patient and the professional. In case of contact with the HD, these should be immediately replaced.
Lab coat / overalls	With back opening / central zipper, elastic cuffs, and waterproof front area and sleeves. In case of contact with the HD, it must be replaced.
Respiratory protection	Self-filtering masks type FFP3. Surgical masks don't protect against cytostatic sprays.
Eye protection	Integral-frame panoramic goggles.

Therefore, staff protection must be adapted to each one of these activities and drug formulations, because the precautions to be taken are different in each case. For example, as stated in the NIOSH document from 20144, "in situations such as capsule opening, or tablet splitting or crushing, when there are no extraction cabinets, safety cabinets or isolators, at least double gloves should be used, as well as mask, lab coat, and working surface protection". Besides, as this list included a great variability of medications, from high-risk cytotoxic agents to medications that could only affect fertile-age staff to a lower degree, the actions to be determined should not be general; instead, there should be a case-by-case analysis, and therefore the following procedure should only be used as a reference.

This means that the list of medications stated in the publication by the NIOSH[4,5] can be used as a reference in order to determine specific measures for managing each HD, and each centre should adapt it to its own situation and needs, as well as keep it updated with the new medications, taking into account the recommendations by their manufacturers.

However, given the large number of HDs included in the list, it will be impossible to implement a procedure to ensure the correct and safe manipulation of each HD in the different procedures where it appears.

Therefore, a simplification is necessary in order to ensure an adequate identification. As a general rule, HDs should be identified during the process of their use, including the whole chain, from selection, reception, repackaging, storage, distribution, preparation, administration, and waste management; and medications should be classified in order to implement common measures of handling in each procedure, to ensure a correct and safe handling of each HD.

Conclusions

It has been impossible to determine clearly he toxic effects at long-term of exposure to these drugs, but there is evidence of their danger, the potential occupational risk represented by their handling, and the consequences derived. Therefore, it is imperative to adopt measures that will help to reduce this exposure, and guarantee optimal working conditions. In this sense, the most adequate activity will be prevention.

Different incidents associated with HDs have forced hospitals to prepare working procedures with higher or lower complexity or difficult to understand and follow by the staff. The classification and categorization designed for our working procedure has simplified to a great extent the identification and handling of HDS included in the hospital formulary, so that any healthcare professional will know how to act adequately and safely in any procedure involving HDs.

Moreover, the Hospital Administration should regulate the hazard level of medications through visual codes or symbols, in a way similar to

the one stated in this procedure. This will equally become a useful tool within the policies for occupational risk prevention in any healthcare centre.

In conclusion, the development and implementation of specific work procedures for the safe handling of drugs will allow hospital authorities to meet effectively all legal duties in prevention matters, as well as to provide staff with an adequate setting to avoid the potential risk posed by some medications.

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Appendix 1. General recommendations for hazardous drug handling

Table 4, Table 5 and Table 6 detail the recommendations for the SPMs to be used in different activities.

Table 4
Recommendations about the equipment to be used according to specific tasks in handling non-sterile hazardous drugs

FORMULATION	TYPE OF ACTIVITY	SPECIFIC HANDLING TASKS	GLOVES	WHITE COAT	GOGGLES	MASK
ORAL SOLID FORMULATIONS	Preparation	To prepare oral solid magistral formulas (to weigh, mix, dissolve, dilute…)	YES. Double pair	YES	YES. Except for use of BSC with front protection	YES
		To re-dose whole oral solid formulations (to split, cut, crush tablets, open capsules)	YES. Double pair	YES	YES. Except for use of BSC with front protection	YES
		To re-package whole oral solid formulations	YES. One pair	YES	NO	NO
		To re-package handled oral solid formulations.	YES. Double pair	YES	NO	NO
	Dispensing	Oral solid formulations prepared in single doses	YES. One pair	NO	NO	NO
		Count of whole solid oral formulations from multi-dose jars	YES. Double pair	YES	NO	NO
		Handled oral formulations	YES. Double pair	YES	YES	YES
		Whole packages of oral solid formulations.	YES. One pair	NO	NO	NO
		Whole packages of oral solid formulations with their secondary preparation	NO	NO	NO	NO
	Administration	Whole oral solid formulations prepared in single doses	YES. One pair	NO. Except for risk of splashing	NO	NO
		Handled oral solid formulations.	YES. Double pair	NO. Except for risk of splashing	NO	NO
		Inhaled powder / spray	YES. Double pair	YES	YES	YES

(*) It is considered that there is Risk of Splashing in the following situations: there is risk of resistance by the patient, administration diluted in liquid, and administration through feeding tube.

Table 5
Recommendations about the equipment to be used according to specific tasks in handling sterile hazardous drugs

FORMULATION	TYPE OF ACTIVITY	SPECIFIC HANDLING TASKS	GLOVES	WHITE COAT	GOGGLES	MASK
STERILE TOPICAL FORMULATIONS	Preparation	To prepare sterile topical magistral formulas (to weigh, mix, dilute, dissolve…)	YES. Double pair	YES	YES. Except for use of BSC with front protection	YES
	Dispensing	Sterile topical formulations prepared in single doses	YES. One pair	NO	NO	NO
		Whole packages of topical formulations with their secondary preparation	NO	NO	NO	NO
	Administration	Prepared sterile topical formulations	YES. Double pair	NO. Except for risk of splashing	NO. Except for risk of splashing	NO
		Solution for vesical instillation	YES. Double pair	YES. Except for use of closed system	YES. Except for use of closed system of administration	YES. Except for use of closed system

(*) It is considered that there is Risk of Splashing in the following situations: there is risk of resistance by the patient, administration diluted in liquid, and administration through feeding tube.

Table 6
Individual Protection Equipment. Recommended SPMs for different handling of hazardous drugs

Formulation/Activity	Gloves	White coat / overalls	Eye Protection	Respiratory Protection	Cap and shoe covers
Spillage / recipient breakage	Yes (double gloves)	Yes	Yes	Yes	YES (If it is on the floor)
Patient care	Yes (single gloves)	Yes	Yes (If there is risk of splashing)	Yes (If there is risk of splashing)	No
Waste management (collection and transport)	Yes (single gloves)	Yes	No	No	No
Handling contaminated bed and floors	Yes (single gloves)	Yes	Yes (If there is risk of splashing)	Yes (If there is risk of splashing)	No
Maintenance of the sterile preparation room and ante-room	Yes (single gloves)	Yes	Yes (If there is risk of splashing)	Yes (If there is risk of splashing)	SI

Adapted from Source "Guía de Buenas Prácticas para Trabajadores Profesionalmente Expuestos a Agentes Citostáticos" ("Good Practice Guidelines for Workers Professionally Exposed to Cytostatic Agents") (Escuela Nacional de Medicina del Trabajo. Instituto de Salud Carlos III. Ministerio de Economía y Competitividad. Asociación Madrileña de Medicina del Trabajo en el Ámbito Sanitario (AMMTAS) 2014). Source: "Monografías de Farmacia Hospitalaria y Atención Primaria. Medicamentos Peligrosos." Issue 6. Year 2016.

1. Selection Criteria

Among other criteria, the following should be studied:

To choose those marketed formulations with contents better adapted to usual dosing, with the aim to minimize handling.

To choose the most adequate and easy-to-use strength (1, 2, 5, 10, 25 mg/ml).

Not mixing / preparing at the same time formulations of the same medication with different strengths.

To choose, if possible, and in case of hazardous drug, what appears in Appendix 1a and Appendix 1b, which are basically formulations with a design that guarantee their low external contamination. Thus, it is better to select:

Vials vs. ampoules.

Formulations as solution for immediate use vs. lyophilized formulations.

Drugs packaged in breakage-proof polypropylene vs. glass.

Certain compounds already pre-charged in syringes ready for administration.

To select among marketed formulations those with a more efficient sealing of the vial after puncture, because if there is an incomplete sealing when the needle is removed, there will be an increased risk of environmental contamination.

The presence or not of preservatives will affect the use-by date of the solution from its first use; and therefore it will determine, together with its physicochemical stability, the validity of the remaining fractions after preparing one treatment.

2. Reception and storage

All medications are received at the Pharmacy Unit in the Hospital Intermutual de Levante.

It is recommended to wear synthetic globes (nitrile, polyurethane, neoprene) for the manipulation and distribution of drugs in storage.

When opening the packaging of these drugs, attention should be paid to the presence of any broken packaging; in this case, the person must get adequate protection and follow the rules of action established against spillage.

Hazardous drugs must be stored with caution, in order to avoid any packaging breakage.

The fact that some drugs require low temperature for their storage must be taken into account (there is cold storage for these medications), and/or protection from the light (these must be kept in their original packaging).

Table 4, Table 5 and Table 6 show the recommendations for SPMs to be used in different activities.

3. Preparation

HDs must be prepared by authorized staff, and as far as possible this preparation should be centralized in the Pharmacy Unit.

In the working areas where medications are administered:

The staff must not eat, drink, chew gum or store food.

The staff must not use makeup or other cosmetic products that could lead to prolonged exposure in case of contamination.

Measures for adequate hand washing will be implemented, as well as working in a sterile area (if necessary), and the adequate SPMs will be used if necessary.

Any members of staff of reproductive age, and actively trying to conceive, who are handling drugs from List 3, must adopt all prevention measures recommended in this procedure.

This type of drugs might have restrictions for those professionals in the following situations:

Pregnant or breastfeeding women.

Staff considered at high-risk (with previous history of miscarriages or congenital malformations, previous treatments with cytostatic agents or ionizing radiations) and cutaneous allergies.

Fertile men and women actively trying to conceive.

Any of these situations should be reported to the Unit for Occupational Risk Prevention.

The number of persons handling HDs should be reduced as much as possible, through organization measures and the use of preparations that require the lowest level of handling.

4. Transportation and distribution

Transportation must be conducted in such a way as to avoid breakages or spillages.

No mechanical transportation systems will be used, such as pneumatic tubes.

In case any drug is not administered, it will be returned to the Pharmacy Unit through the same procedure and in the same packaging as it was delivered to the place of administration.

5. HD administration

Administration will include all techniques required for administering the treatment, regardless of its way of administration; the most frequently used are: intravenous, subcutaneous (SC), topical, intramuscular (IM) and oral.

Administration will be conducted following the recommendations in the product specifications for each drug, and always according to the Standard Operating Procedures (SOPs) or HIL Guidelines.

Oral Formulations

The selection of formulation will be conducted by prioritizing whole units (tablets, pills and/or capsules) and oral suspensions. If fragmented formulations are required, these must be prepared at the Pharmacy Unit.

When oral formulations are handled, direct contact with the drug should be avoided (see Section on SPMs).

When the medication is supplied in a package, or even packaged in single doses, and it is self-administered by the patient, it will ONLY be handled with single gloves, without any other measure required.

Topical Application

Creams or other topical formulations must be applied with the SPMs stated. During this technique, handling must be restricted to the lower extent, using a spatula or other application products in order to avoid contact with the product.

Subcutaneous (SC) and Intramuscular (IM) Administration

It will be preferred to prescribe drugs which are pre-charged and purged with closed drug transfer devices systems. In those cases where purge is

required, sterile gauze will be used, soaked in 70º alcohol, to prevent sprays and surface contamination.

A cloth with an absorbent upper side and a water-proof lower side should be placed under the administration line, with the aim to avoid contamination of bedclothes or the administration chair, in case of spillage.

Both in SC and IM administration, the needle won't be unattached to the syringe at any point; the connections must be luerlock to prevent any accidental disconnection, and discarded as one single piece in the adequate container. After the injection, extraction will be conducted with gauze soaked in 70º alcohol, to prevent any drug reflux or dripping.

During administration, individual protection equipment must be used (see Section on SPMs). Eye and respiratory protection will only be necessary if there is a reasonable risk of splashing, or if the patient's conditions could cause a potential accidental disconnection.

Intravenous Administration

It is recommended to implement closed drug transfer devices systems. This task must be conducted at preparation, so that no connection or disconnection are required during drug administration.

The system will be disposed of as one single piece in the specific container, the drugs used must not be disconnected.

The staff involved in this technique should be trained to ensure an adequate use of closed systems, in order to achieve an optimal performance and reduce to the lowest extent any risk of dripping, spillage, or spray.

During administration, individual protection equipment must be used (see Section on SPMs). Eye and respiratory protection will only be necessary if there is a reasonable risk of splashing, or if the patient's conditions could cause a potential accidental disconnection.

Action in case of accidental spillage and exposures

Spillage

The worker must be protected with a waterproof lab coat, goggles or screen with lateral protection, shoe covers, and 2 pairs of gloves, one made of thick rubber and another one of non-powdered latex. In case the spillage has occurred outside the BSC, a FFP3-type mask for respiratory protection will also be used. These will be worn in the following order: shoe covers, lab coat, mask, first pair of gloves over the coat, second pair of gloves, and goggles or screen.

The spillage will be absorbed with cellulose or an absorbing cloth (dry if liquids and wet if dry powder) before proceeding to cleaning it. If there are rests of glass, these will never be collected with the hand, but with tweezers (or a collecting brush), and they will be placed in a small rigid container for sharp / cutting objects.

The dry surface must be cleaned afterwards with cellulose soaked in 70º alcohol. The area will be cleaned 3 times with soap and water or detergent cleaner / bleach, finally rinsing it with plenty of water, always going from the less contaminated to the most contaminated areas.

The protection equipment must be removed in this order: first pair of gloves, shoe covers, second pair of gloves, mask, lab coat and goggles. Everything should be discarded, except if eye-glasses are used; tweezers can be reused after being carefully washed with soap and water (hands should be protected with a clean pair of gloves in order to conduct this procedure).

All waste generated, as well as the materials used, will be treated as contaminated materials at the time of disposal.

Accidental exposure

If there is direct contact of the drug with the skin: The affected area will be immediately washed with soap and water, during approximately 10 minutes. If the skin appears irritated, it should be examined by a specialist.

If the drug splashes the eyes: rinse the affected eye with water or isotonic solution during at least 15 minutes, and then consult the specialist.

In case of accidental ingestion, it is necessary to see a doctor immediately.

In any of these cases, it will be reported to the Occupational Health area of the Prevention Unit to enable the specific pharmacovigilance.

7. Waste management

Drug waste must be treated in the Group III or Group IV containers, according to the current procedure for waste management.

8. Action by the Prevention Unit

Potential exposure to HDs in each of the activities described will depend on the set of preventive measures adopted; therefore, the potential exposure and its level must be established according to the risk evaluation conducted in each specific case.

The extent of the risk will depend on:

The toxicity inherent to each medication.

The level of exposure, associated with:

Workload.

Handling conditions.

Environmental protection.

Protection materials.

Handling technique, involving procedures, training and periodical assessment.

Time of exposure.

Stage of the process. There is higher risk in preparation and accidental spillage, though protection measures should include all stages of the process.

Characteristics of the handler (reproductive age, simultaneous exposure to other agents, etc.).

Another important aspect to be taken into account is the potential ways of penetration of these substances into the body, which are:

Inhalation of sprays and micro-drops emitted during the preparation of the hazardous drug solutions for administration, when vials are broken, while purging the system, etc.

Through direct contact, by penetration of the medication through the skin or mucosa.

Orally: ingestion of food and drinks, contaminated cigarettes.

Parenterally: through direct introduction of the medication by accidental needle sticks or cuts caused by vial breakage.

9. Individual protection equipment

The worker exposed should be qualified, aware of the risks taken if exposed to these drugs without an adequate protection, as well as of the conditions required for patient safety.

Thee requirements about the use of Individual Protection Equipment according to each medication have been stated in previous sections of this protocol (Appendix 2 and Appendix 3).

The SPM specifications for each activity are not the object of this document.

10. Information and training for the staff

With general application, and according to Articles 18 and 19 of the Law for Prevention of Occupational Risks[13], workers must receive adequate information and training about the risks derived of the presence of any hazardous chemical agent present in their working place, as well as about the prevention and protection measures to be adopted. In particular, the training of staff working with biohazardous drugs is a key aspect to prevent occupational risks.

Appendix 2. Hazardous Drugs (HDs) included in the hospital formulary. Specific recommendations for handling

Medications with risk for the healthcare staff	Formulation	Basic recommendations for handling* (meeting the safety rule)	NIOSH List
Acenocoumarol (Sintrom®) *GREEN*	Tablet	Preparation: No protection required, except if it must be split and the handler is in reproductive risk situation; in this case, this will be done in a Class II B2 BSC with double gloves, lab coat and mask. Report to the Occupational Risk Prevention Unit. Administration: It only affects staff at reproductive risk, who must administer with single gloves, without splitting or crushing.	3 (due to similarity with warfarin)
Azathioprine (Imurel®) *GREEN*	Tablet	Preparation**: No preparation required. Administration: Administer with single gloves. If it is necessary to split or crush***, use the oral Magistral Formula suspension.	2
Azatihioprine *BLUE*	Oral suspension (MF)	Production: In a Class II B2 BSC with double gloves, lab coat and mask. Preparation: If single doses must be prepared, this will be conducted in a Class II B2 BSC with double gloves, lab coat and mask. Administration: Double gloves and lab coat; use eye and respiratory protection if administered through catheter or the patient does not collaborate.	2
Cabergoline (Dostinex®) *GREEN*	Tablet	Preparation**: No preparation required. Administration: It only affects staff at reproductive risk, who must administer with single gloves, without splitting or crushing.	3

* Preparation of liquid oral formulations refers to re-dosing (charging the syringe), not to the production of the medication. ** Whenever possible, the original blister will be kept at re-packaging. *** Use preferably the liquid oral formulation. If no liquid oral formulation is available, splitting will be done at the Pharmacy Unit in a Class II B2 BSC. MF: Magistral Formula; ORPU: Occupational Risk Prevention Unit; Class II B2 BSC: Class II Type B2 Biological Safety Cabinet. Since the display

of this article is not in color, the words green, yellow, blue and red have been recorded in the tables below each medication. This color indicates the category of protection of that drug according to the color code from the lowest to the highest degree of protection during the preparation and administration (green, yellow, blue and red) as explained in the procedure described".

Appendix 3. Summary of Hazardous Drugs (HDs) included in the hospital formulary. Recommendations for preparation and administration

There is a summary below of the Hazardous Drugs (HDs) included in the formulary of the HIL.

COLOUR	RECOMMENDATIONS (Meeting the safety rule)	Medication (Classification by the NIOSH)
GREEN	Preparation[1]: No preparation required. Administration: Single gloves. No splitting or crushing. If it is necessary to split or crush the dose: - It would be of choice to use liquid oral formulations (consult with the Pharmacy Unit). - If no liquid oral formulation available, splitting will be done at the Pharmacy Unit, in a Class II B2 BSC with double gloves, lab coat / overalls and mask.	**Acenocoumarol tablets** (Sintrom®) (3), **Azathioprine tablets** (Imurel®) (2), **Cabergoline tablets** (Dostinex®) (3), **Carbamezapine tablets** (Tegretol®) (2), **Clonazepam tablets** (Rivotril®) (3), **Colchicine tablets** (Colchimax®) (3), **Spironolactone tablets** (Aldactone®) (2), **Phenytoine tablets** (Epanutin®) (2), **Phenoxybenzamine capsules** (Dibenzyran®) (2), **Fluconazole capsules** (3), **Oxcarbazepine tablets** (Trileptal®) (2), **Paroxetine tablets** (3), **Risperidone tablets** (Risperdal®) (2), **Topiramate tablets / capsules** (3), **Valproic Acid tablets** (Depakine®) (3), **Voriconazole tablets** (Vfend®) (3)
YELLOW	As a general rule, they should not be manipulated by personnel under reproductive risk[2,3]. Preparation: single gloves. Administration: Double gloves and lab coat; in case of risk of splashing, accidental disconnection of the system, administration through catheter, or patient who does not collaborate, use eye protection (goggles) and respiratory protection (mask). **In the exceptional case in which these must be PREPARED by staff at reproductive risk, they must be protected with double gloves, lab coat, goggles and mask.**	**Clonazepam oral solution** (Rivotril®) (3), **Clonazepam ampoules** (Rivotril®) (3), **Fluconazole vial for perfusion** (Diflucan®) (3), **Fluconazole oral solution** (Diflucan®) (3), **Topiramate oral suspension** (FM) (3), **Valproic Acid oral solution** (Depakine®) (3), **Valproic Acid vial** (Depakine®) (3), **Voriconazole oral suspension** (Vfend®) (3), **Voriconazole vial** (Vfend®) (3), **Zoledronic Acid bag for perfusion** (3)
BLUE	Preparation: In the Pharmacy Unit, in Class II B2 BSC with double gloves, lab coat and mask. **In the exceptional case in which it is not possible to prepare in Class II B2 BSC, use double gloves, lab coat, eye protection (goggles) and respiratory protection (mask).** Administration: Double gloves and lab coat; in case of risk of splashing, accidental disconnection of the system, administration through catheter, or patient who does not collaborate, use eye protection (goggles) and respiratory protection (mask).	**Azathioprine oral suspension** (MF) (2), **Carbamazepine oral suspension** (MF) (2), **Chloramphenicol ophthalmic ointment** (Colircusi de Icol®) (2), **Spironolactone oral suspension** (FM) (2), **Phenytoine oral suspension** (Epanutin®) (2), **Phenoxybenzamine suspension** (MF) (2), **Oxcarbazepine oral suspension** (Trileptal®) (2), **Risperidone oral solution** (Risperdal®) (2)
RED	Preparation: At the Pharmacy Unit in Class II B2 BSC with closed systems for preparation and administration. Double gloves, protective lab coat (preferable overalls) and masks. If not possible to prepare in Class II B2 BSC, use eye protection (goggles) and respiratory protection (mask). Administration: Closed systems of administration, double gloves, lab coat / overalls, and eye protection (if risk of splashing) and mask (if risk of inhalation).	**Phenytoine vial** (Magistral formula) (2), **Risperidone vial + pre-charged syringe** (Risperdal®) (2)

The number between brackets corresponds to the number of the NIOSH list in which this medication is included. Acenocoumarol by similarity with warfarin (not included in NIOSH) List 1: Antineoplastic or cytostatic agents. List 2: Non-antineoplastic medications that meet one or more NIOSH criteria to be considered of risk. List 3: Non-antineoplastic medications with effects on reproduction, and that can affect men and women who are trying actively to conceive, and pregnant or breastfeeding women, but that don't represent a risk for the rest of the staff. 1 Whenever possible, the original blister will be kept at re-packaging 2 Staff at reproductive risk: men and women who are actively trying to conceive, and pregnant or breastfeeding women. 3 For treatments prescribed continuously and that need to be prepared, this will be done at the Pharmacy Unit (PU) in CSBIIB2. Exceptional treatmetns will be prepared according to the protection measures already mentioned and, in case of persistence, their preparation will be similarly assumed by the PU. MG: Magistral Formula; Class II B2 BSC: Class II Type B2 Biological Safety Cabinet; CLDT: Closed System for Drug Transfer. Since the display of this article is not in color, the words green, yellow, blue and red have been recorded in the tables below each medication. This

color indicates the category of protection of that drug according to the color code from the lowest to the highest degree of protection during the preparation and administration (green, yellow, blue and red) as explained in the procedure described"

Apéndice 1. Recomendaciones generales para el manejo de medicamentos peligrosos

En la Tabla 4, Tabla 5 y Tabla 6 se detallan las recomendaciones de EPIs a utilizar en las diferentes actividades.

Tabla 4
Recomendaciones de equipo a utilizar según tareas específicas en la manipulación de medicamentos peligrosos no estériles

FORMA FARMACÉUTICA	TIPO DE ACTIVIDAD	TAREAS ESPECÍFICAS DE MANIPULACIÓN	GUANTE	BATA	GAFAS	MASCARILLA
FORMAS SÓLIDAS ORALES	Preparación	Elaborar fórmulas magistrales sólidas orales (pesar, mezclar, disolver, diluir…)	SI. Doble par	SI	SI. Salvo uso de CSB con protección frontal	SI
		Redosificar formas sólidas orales íntegras (partir, cortar, triturar comprimidos, abrir cápsulas)	SI. Doble par	SI	SI. Salvo uso de CSB con protección frontal	SI
		Reenvasar formas sólidas orales integras	SI. Un par	SI	NO	NO
		Reenvasar formas sólidas orales manipuladas	SI. Doble par	SI	NO	NO
	Dispensación	Formas sólidas orales acondicionadas en dosis unitarias	SI. Un par	NO	NO	NO
		Contaje de formas sólidas orales íntegras a partir de frascos multidosis	SI. Doble par	SI	NO	NO
		Formas orales manipuladas	SI. Doble par	SI	SI	SI
		Envases enteros de formas sólidas orales	SI. Un par	NO	NO	NO
		Envases enteros de formas sólidas orales con su acondicionamiento secundario	NO	NO	NO	NO
	Administración	Formas sólidas orales íntegras acondicionadas en dosis unitarias	SI. Un par	NO. Salvo riesgo de salpicadura	NO	NO
		Formas sólidas orales manipuladas	SI. Doble par	NO. Salvo riesgo de salpicadura	NO	NO
		Polvo por inhalación/ aerosol	SI. Doble par	SI	SI	SI

(*) Se considera que existe riesgo de salpicadura en las siguientes situaciones: existe riesgo de resistencia por parte de paciente, administración desleída en líquido y administración por sonda de alimentación.

Tabla 5

Recomendaciones del equipo a utilizar según tareas específicas en la manipulación de medicamentos peligrosos estériles

FORMA FARMACÉUTICA	TIPO DE ACTIVIDAD	TAREAS ESPECÍFICAS DE MANIPULACIÓN	GUANTE	BATA	GAFAS	MASCARILLA
FORMAS TÓPICAS ESTÉRILES	Preparación	Elaborar fórmulas magistrales tópicas estériles (pesar, mezclar, diluir, disolver…)	SI. Doble par	SI	SI. Salvo uso de CSB con protección frontal	SI
	Dispensación	Formas tópicas estériles acondicionadas en dosis unitarias	SI. Un par	NO	NO	NO
		Envases enteros de formas tópicas con su acondicionamiento secundario	NO	NO	NO	NO
	Administración	Formas tópicas estériles preparadas	SI. Doble par	NO. Salvo riesgo de salpicadura	NO. Salvo riesgo de salpicadura	NO
		Solución para instilación vesical	SI. Doble par	SI. Salvo uso de sistema cerrado	SI. Salvo uso de sistema cerrado de administración	SI. Salvo uso de sistema cerrado

(*) Se considera que existe riesgo de salpicadura en las siguientes situaciones: existe riesgo de resistencia por parte de paciente, administración desleída en líquido y administración por sonda de alimentación.

Tabla 6

Equipos de protección individual - EPI recomendados para las diferentes manipulaciones de Medicamentos Peligrosos.

Forma farmacéutica/ actividad	Guantes	Bata/Mono	Protección ocular	Protección respiratoria	Gorro y Calzas
Derrames / rotura de recipientes	Sí (doble guante)	Sí	Sí	Sí	SI (si está en el suelo)
Cuidados de pacientes	Sí (guante simple)	Sí	Sí (si existe riesgo de salpicadura)	Sí (si existe riesgo de salpicadura)	No
Gestión de residuos (recogida y transporte)	Sí (guante simple)	Sí	No	No	No
Manipulación de cama y suelos contaminados	Sí (guante simple)	Sí	Sí (si existe riesgo de salpicadura)	Sí (si existe riesgo de salpicadura)	No
Mantenimiento de la sala de preparación estéril y antesala	Sí (guante simple)	Sí	Sí (si existe riesgo de salpicadura)	Sí (si existe riesgo de salpicadura)	SI

Adaptación de Fuente Guía de Buenas Prácticas para Trabajadores Profesionalmente Expuestos a Agentes Citostáticos (Escuela Nacional de Medicina del Trabajo. Instituto de Salud Carlos III. Ministerio de Economía y Competitividad. Asociación Madrileña de Medicina del Trabajo en el Ámbito Sanitario (AMMTAS) 2014) Fuente: Monografías de Farmacia Hospitalaria y Atención Primaria. Medicamentos Peligrosos. Número 6. Año 2016.

1. Criterios de selección

Entre otros criterios, se deben estudiar los siguientes:

Elegir las presentaciones comerciales cuyo contenido se adapte mejor a las dosis habituales, con objeto de minimizar la manipulación.

Elegir la concentración más apropiada y de fácil manejo (1, 2, 5, 10, 25 mg/ml).

No mezclar/preparar al mismo tiempo presentaciones de un mismo medicamento con diferentes concentraciones.

Elegir, si es posible y en caso de fármaco peligroso lo indicado en el Apéndice 1a y Apéndice 1b, que básicamente son presentaciones cuyo diseño garantice la baja contaminación exterior de las mismas. De esta forma, son preferibles:

Los viales frente a las ampollas.

Las presentaciones en solución para uso inmediato frente a los liofilizados.

Las presentaciones con envase de polipropileno a prueba de rotura, frente al cristal.

Ciertos compuestos ya precargados en jeringas listas para la administración.

Seleccionar entre las presentaciones comerciales aquellas en las que el sellado del vial tras la punción sea más eficiente, ya que en el caso de que este sellado sea incompleto al retirar la aguja, el riesgo de contaminación ambiental aumenta.

La presencia o no de conservantes afecta a la caducidad de la solución a partir de su primera utilización y, por tanto, junto con la estabilidad físico-química, condiciona la validez de las fracciones sobrantes tras la preparación de un tratamiento.

2. Recepción y almacenaje

La recepción de todos los medicamentos, se realiza en el Servicio de Farmacia del Hospital Intermutual de Levante.

Se recomienda utilizar guantes sintéticos (nitrilo, poliuretano, neopreno) para la manipulación y distribución de medicamentos en almacén.

Al abrir los paquetes de estos medicamentos se prestará atención por si hubiera algún envase roto en cuyo caso la persona se protegerá adecuadamente y seguirá las normas de actuación establecidas frente a derrames.

El almacenamiento de los medicamentos peligrosos se realizará con precaución de modo que se eviten roturas de los envases.

Se tendrán en cuenta todos aquellos medicamentos que requieren bajas temperaturas para su conservación (se dispone de cámaras frigoríficas para estos medicamentos) y/o protección de la luz (se mantendrán en su envase original).

En la Tabla 4, Tabla 5 y Tabla 6 se detallan las recomendaciones de EPIs a utilizar en las diferentes actividades.

3. Preparación

La preparación de MP debe realizarse por personal autorizado y se centralizarán en la medida de lo posible en el Servicio de Farmacia.

En las áreas de trabajo donde se administren los medicamentos:

El personal no deberá comer, beber, masticar chicle ni almacenar alimentos.

El personal no utilizará maquillaje ni otros productos cosméticos que puedan provocar una exposición prolongada en caso de contaminación.

Se implementarán medidas de lavado de manos adecuado, trabajo en zona estéril (en caso necesario) y se utilizarán si es necesario los EPI adecuados, lavado de manos.

El personal que se encuentre en edad reproductiva y que esté intentando concebir de forma activa y manipule fármacos de la lista 3, deberá adoptar todas las medidas de prevención recomendadas en este procedimiento.

Este tipo de medicamentos pueden tener restricciones para los profesionales que se encuentren en las siguientes situaciones:

Mujeres embarazadas o en período de lactancia.

Personal considerado de alto riesgo (con antecedentes de abortos o malformaciones congénitas, tratamientos previos con citostáticos o radiaciones ionizantes) y alergias cutáneas.

Hombres y mujeres fértiles intentando concebir de forma activa.

Cualquiera de dichas situaciones se deberá comunicar al Servicio de prevención de riesgos laborales.

Debe reducirse al máximo el número de personas que manejan MP, mediante medidas organizativas y la utilización de preparaciones que requieran la menor manipulación posible.

4. Transporte y distribución

El transporte se debe realizar de forma que se eviten roturas o derrames.

No se emplearán sistemas mecánicos de transporte tipo tubos neumáticos.

En caso de que algún medicamento no se administre, se devolverá al Servicio de Farmacia por el mismo procedimiento y en el mismo envase que se entregó en el lugar de administración.

5. Administración de MP

La administración comprenderá todas las técnicas necesarias para la aplicación del tratamiento, independientemente de la vía de administración, siendo las más utilizadas la vía intravenosa, la vía subcutánea (SC), la vía tópica, la vía intramuscular (IM) y la vía oral.

La administración se realizará siguiendo las recomendaciones de las fichas técnicas de cada fármaco y siempre según los Procedimientos Normalizados de Trabajo (PNT) o Guías del HIL.

Formas orales

La elección de presentación se realizará priorizando las unidades completas (comprimidos, grageas y/o cápsulas) y las suspensiones orales. En el caso de precisar formas fragmentadas, estas deberán ser preparadas en el Servicio de Farmacia.

Cuando se manipulen formas orales, se debe evitar el contacto directo con el fármaco (ver apartado EPI).

Cuando el medicamento se suministre envasado o incluso envasado en unidosis y la administración sea por parte del propio enfermo ÚNICAMENTE se manipulará con guantes simples, no siendo necesaria ninguna otra medida.

Aplicación tópica

Las cremas u otras formas tópicas deben aplicarse con los EPI indicados. Durante la técnica se restringe la manipulación a lo mínimo posible,

utilizando espátulas u otros productos de aplicación que eviten el contacto con el producto.

Administración subcutánea (SC) e intramuscular (IM)

Preferentemente se pautarán fármacos precargados y purgados con sistemas cerrados de transferencia. En el caso de precisar purgado se utilizará una gasa estéril empapada en alcohol de 70º, para impedir la formación de aerosoles y contaminación de superficies.

Disponer, bajo la vía de administración, un paño absorbente por su cara superior e impermeable por la inferior, con objeto de evitar que se contamine la ropa de cama o el sillón de administración, si se produce algún derrame.

Tanto en la administración SC como en la IM, en ningún momento se desconectará aguja de la jeringa, las conexiones deben ser luer-lock que impida la desconexión accidental, siendo desechadas como una sola pieza en el contenedor apropiado.

Finalizada la inyección, la extracción se realizará con una gasa impregnada en alcohol de 70º para evitar reflujos de medicación o goteo.

Durante la administración se utilizarán equipos de protección individual (ver apartado EPI). La protección ocular y respiratoria solo será necesaria si existe riesgo razonable de salpicadura o si por las condiciones del paciente se pudiera prever una desconexión accidental.

Administración intravenosa

Se recomienda la aplicación de sistemas cerrados de transferencia. Esta labor se tiene que llevar a cabo en la preparación, para que no sea necesario realizar ninguna conexión o desconexión durante la administración.

El sistema se eliminará como si fuera una sola pieza en el contenedor de específico, no se deben desconectar los fármacos utilizados.

El personal implicado en la técnica, debe ser formado para asegurar la utilización adecuada de los sistemas cerrados para lograr un óptimo funcionamiento, y reducir al mínimo el riesgo de goteos, derrames o creación de aerosoles.

Durante la administración se utilizarán equipos de protección individual (ver apartado EPI). La protección ocular y respiratoria solo será necesaria si existe riesgo razonable de salpicadura o si por las condiciones del paciente se pudiera prever una desconexión accidental.

Actuación ante derrames y exposiciones accidentales

Derrame

El trabajador se protegerá con bata impermeable, gafas o pantalla con protección lateral, calzas y 2 pares de guantes, uno de goma grueso y otro de látex sin polvo. En el caso de que el derrame se haya producido en el exterior de la CSB, se utilizará además mascarilla de protección respiratorio tipo FFP3. El orden de colocación será: calzas, bata, mascarilla, 1er par de guantes sobre la bata, 2º par de guantes y gafas ó pantalla.

Se empapará el derrame con celulosa o un paño absorbente (seco si se trata de líquidos y húmedo si es un polvo seco) antes de proceder a su limpieza. Si existen restos de cristales nunca se recogerán con la mano

sino con la ayuda de unas pinzas (o cepillo recogedor), y se meterán en un contenedor pequeño rígido para objetos punzantes/cortantes.

La superficie seca debe limpiarse después con celulosa empapada de alcohol 70%. Se lavará la zona 3 veces con agua y jabón o limpiador detergente-lejía aclarando finalmente con abundante agua, siempre de las zonas menos contaminadas a las más contaminadas.

Retirarse los equipos de protección por este orden: 1er par de guantes, calzas, 2º par de guantes, mascarilla, bata y gafas. Desechar todo salvo si se utilizan gafas y las pinzas que podrán ser reutilizadas después de lavarlas cuidadosamente con agua y jabón (protegerse las manos con un par de guantes limpios para realizar esta operación).

Todos los residuos generados, así como el material empleado se tratarán como material contaminado a la hora de la eliminación.

Exposición accidental

Si el medicamento contacta directamente con la piel: se lavará inmediatamente la zona afectada con agua y jabón, durante unos 10 minutos. Si la piel se encontraba irritada, deberá ser examinada por un especialista.

Si el medicamento salpica los ojos: enjuagar el ojo afectado con agua o solución isotónica durante al menos 15 minutos y luego acudir al especialista.

En caso de ingestión accidental, es necesario acudir inmediatamente al médico.

En cualquiera de los casos, se comunicará al área de Salud Laboral del Servicio de Prevención para la realización de la vigilancia médica específica.

7. Tratamiento de residuos

Los residuos de los medicamentos se tratarán en los contenedores del Grupo III o Grupo IV, según el procedimiento de residuos vigente.

8. Actuación del servicio de prevención

La exposición potencial a MP en cada una de las actividades descritas dependerá del conjunto de medidas preventivas que se adopten, por lo que la posible exposición y su grado deberán establecerse en base a la evaluación de riesgos que se realice en cada caso concreto.

La magnitud del riesgo dependerá de:

La toxicidad inherente de cada medicamento.

El nivel de exposición, que se relaciona con:

La carga de trabajo.

Las condiciones de manipulación.

Protección ambiental.

Material de protección.

Técnica de manipulación. Implica procedimientos, adiestramiento y evaluación periódica.

El tiempo de exposición.

La fase del proceso. Hay mayor riesgo en la preparación y los derrames accidentales, aunque las medidas de protección deben incluir todas las fases del proceso.

Características del manipulador (edad reproductiva, exposición simultánea a otros agentes, etc.).

Otro aspecto importante a tener en cuenta es las posibles vías de penetración en el organismo de estas sustancias, que son:

Inhalación de los aerosoles y micro gotas que se desprenden durante la preparación de las soluciones de medicamentos peligrosos durante su administración, por rotura de ampollas, al purgar el sistema, etc.

Por contacto directo, por penetración del medicamento a través de la piel o de las mucosas.

Por vía oral: ingestión de alimentos, bebidas, cigarrillos contaminados.

Por vía parenteral: por introducción directa del medicamento a través de pinchazos accidentales o cortes producidos por rotura de ampollas.

9. Equipos de protección individual

El trabajador expuesto deberá estar cualificado, con conocimiento de los riesgos que corre si se expone sin la protección adecuada a estos medicamentos, así como de las condiciones que se exigen para la seguridad del paciente.

En apartados anteriores de este protocolo se han establecido las necesidades en cuanto a la utilización de Equipos de Protección Individual en función de cada medicamento (Apéndice 2 y Apéndice 3).

Las especificaciones que deben tener los EPIs en cada actividad no es el objeto de este documento.

10. Información y Formación e a los trabajadores

Con carácter general y de conformidad con los artículos 18 y 19 de la Ley de Prevención de Riesgos Laborales[13], los trabajadores deben recibir una información y formación adecuadas sobre los riesgos derivados de la presencia de cualquier agente químico peligroso en el lugar de trabajo, así como sobre las medidas de prevención y protección que hayan de adoptarse. En particular, la formación del personal que trabaja con medicamentos biopeligrosos es un aspecto clave para evitar los riesgos laborales.

Apéndice 2. Medicamentos Peligrosos (MP) incluidos en la en guía farmacoterapéutica GFT. Recomendaciones específicas de manejo

Medicamentos de Riesgo para Personal Sanitario	Forma farmacéutica	Recomendaciones básicas de manejo* (atender a la norma de seguridad)	Lista NIOSH
Acenocumarol (Sintrom®) *VERDE*	Comprimido	Preparación: No precisa protección salvo que se tenga que fraccionar y el manipulador esté situación de riesgo reproductivo que se hará en CSB II B2 con doble guante, bata y mascarilla. Comunicar al SPRL. Administración: Sólo afecta a personal en riesgo reproductivo, que deberán administrar con guante simple, no fraccionar ni triturar.	3 (por similitud con warfarina)
Azatioprina (Imurel®) *VERDE*	Comprimido	Preparación**: no precisa preparación. Administración: Administrar con guante simple. Si es necesario fraccionar o triturar***, utilizar la suspensión oral Fórmula Magistral.	2
Azatioprina *AZUL*	Suspensión oral (FM)	Elaboración: en CSB II B2 con doble guante, bata y mascarilla. Preparación: Si hay que preparar dosis unitarias hacerlo en CSB II B2 con doble guante, bata y mascarilla. Administración: doble guante y bata; utilizar protección ocular e inhalatoria si se administra por sonda o el paciente no colabora.	2
Cabergolina (Dostinex®) *VERDE*	Comprimido	Preparación**: no precisa preparación. Administración: Sólo afecta a personal en riesgo reproductivo, que deberán administrar con guante simple, no fraccionar ni triturar.	3
Carbamazepina (Tegretol®) *VERDE*	Comprimido	Preparación**: no precisa preparación. Administración: Administrar con guante simple. Si es necesario fraccionar o triturar***, utilizar la suspensión oral Fórmula Magistral.	2
Carbamazepina *AZUL*	Suspensión oral (FM)	Elaboración: en CSB II B2 con doble guante, bata y mascarilla. Preparación: Si hay que preparar dosis unitarias hacerlo en CSB II B2 con doble guante, bata y mascarilla. Administración: doble guante y bata; utilizar protección ocular e inhalatoria si se administra por sonda o el paciente no colabora.	2
Clonazepam (Rivotril®) *AMARILLO*	Ampolla	Preparación: No se precisa protección salvo que el manipulador esté en situación de riesgo reproductivo (no abrir las ampollas), en cuyo caso debe contactar con el SPRL. Administración: Sólo afecta a personal en riesgo reproductivo, que deberán administrar con doble guante y bata; utilizar protección ocular cuando exista riesgo de salpicadura y respiratoria si hay posibilidad de inhalación. Contactar con SPRL.	3
Clonazepam (Rivotril®) *VERDE*	Comprimido	Preparación**: no precisa preparación. Administración: Sólo afecta a personal en riesgo reproductivo, que deberán administrar con guante simple, no fraccionar ni triturar***. Si es necesario fraccionar o triturar, utilizar la solución oral.	3
Clonazepam (Rivotril®) *AMARILLO*	Solución oral	Preparación: No necesita preparación. No se precisa protección salvo que el manipulador esté en situación de riesgo reproductivo, que, si tienen que preparar dosis unitarias, deben hacerlo en CSB II B2 con doble guante, bata y mascarilla, y contactar con SPRL. Administración: Sólo afecta a personal en riesgo reproductivo, que deberán administrar con doble guante y bata; utilizar protección ocular e inhalatoria si se administra por sonda o el paciente no colabora.	3
Cloranfenicol (Colircusi de Icol®) *AZUL*	Pomada oftálmica	Preparación: no precisa preparación. Administración: Administrar con doble guante y bata; utilizar protección ocular cuando exista riesgo de salpicadura y respiratoria si hay posibilidad de inhalación.	2
Colchicina (Colchimax®) *VERDE*	Comprimido	Preparación**: no precisa preparación. Administración: Sólo afecta a personal en riesgo reproductivo, que deberán administrar con guante simple, no fraccionar ni triturar.	3

* La preparación de formas orales líquidas se refiere a la redosificación (cargar la jeringa), no a la elaboración del medicamento. ** Siempre que sea posible, en el reenvasado, se mantendrá el blíster original. *** Utilizar preferentemente forma oral líquida. En caso de no disponer de forma oral líquida, el fraccionamiento se realizará en Servicio de Farmacia en CSB II B2. FM: Fórmula magistral; SPRL: Servicio de Prevención de Riesgos Laborales; CSB II B2: Cabina de Seguridad Biológica Tipo II Clase B2. "Dado que la visualización de éste artículo no es en color, se han hecho constar las palabras: verde, amarillo, azul y rojo en las tablas debajo de cada

medicamento. Este color indica la categoría de protección de ese medicamento según el código de colores de menor a mayor grado de protección durante la preparación y administración (verde, amarillo, azul y rojo) tal y como se explica en el procedimiento descrito".

Apéndice 3. Resumen de Medicamentos Peligrosos (MP) incluidos en la GFT. Recomendaciones en la preparación y administración

A continuación, se muestran resumidos los Medicamentos Peligrosos (MP) incluidos en guía farmacoterapéutica (GFT) del HIL.

COLOR	RECOMENDACIONES (Atender a la norma de seguridad)	Medicamento (clasificación NIOSH)
VERDE	Preparación[1]: no precisan preparación. Administración: guante simple. No fraccionar ni triturar. En caso de ser necesario fraccionar o triturar la dosis: - Será de elección la utilización de formas orales líquidas (consultar con el Servicio de Farmacia). - En caso de no disponer de forma oral líquida, el fraccionamiento se realizará en el Servicio de Farmacia en CSB II B2 con doble guante, bata/mono y mascarilla.	**Acenocumarol comprimidos** (Sintrom®) (3), **Azatioprina comprimidos** (Imurel®) (2), **Cabergolina comprimidos** (Dostinex®) (3), **Carbamezapina comprimidos** (Tegretol®) (2), **Clonazepam comprimidos** (Rivotril®) (3), **Colchicina comprimidos** (Colchimax®) (3), **Espironolactona comprimidos** (Aldactone®) (2), **Fenitoína comprimidos** (Epanutin®) (2), **Fenoxibenzamina** cápsulas (Dibenzyran®) (2), **Fluconazol** cápsulas (3), **Oxcarbazepina comprimidos** (Trileptal®) (2), **Paroxetina comprimidos** (3), **Risperidona comprimidos** (Risperdal®) (2), **Topiramato comprimidos / cápsulas** (3), **Valproico Acido comprimidos** (Depakine®) (3), **Voriconazol comprimidos** (Vfend®) (3)
AMARILLO	Como norma general, no deben manipularse por personal en riesgo reproductivo[2,3]. Preparación: guante simple. Administración: doble guante y bata, en caso de riesgo de salpicadura, desconexión accidental del sistema, administración por sonda o paciente no colaborador, utilizar protección ocular (gafas) e inhalatoria (mascarilla). **En el caso excepcional de que deban de ser PREPARADOS por personal en riesgo reproductivo, lo harán protegidos mediante doble guante, bata, gafas y mascarilla**	**Clonazepam solución oral** (Rivotril®) (3), **Clonazepam ampollas** (Rivotril®) (3), **Fluconazol frasco para perfusión** (Diflucan®) (3), **Fluconazol solución oral** (Diflucan®) (3), **Topiramato suspensión oral** (FM) (3), **Valproico Acido solución oral** (Depakine®) (3), **Valproico Acido vial** (Depakine®) (3), **Voriconazol suspensión oral** (Vfend®) (3), **Voriconazol vial** (Vfend®) (3), **Zoledrónico Acido bolsa para perfusión** (3)
AZUL	Preparación: en el Servicio de Farmacia en CSB II B2 con doble guante, bata y mascarilla. **En el caso excepcional de que no sea posible preparar en CSB II B2, utilizar doble guante, bata, protección ocular (gafas) y respiratoria (mascarilla).** Administración: doble guante y bata; en caso de riesgo de salpicadura, desconexión accidental del sistema, administración por sonda o paciente no colaborador, utilizar protección ocular (gafas) e inhalatoria (mascarilla).	**Azatioprina suspensión oral** (FM) (2), **Carbamezapina suspensión oral** (FM) (2), **Cloranfenicol pomada oftálmica** (Colircusi de Icol®) (2), **Espironolactona suspensión oral** (FM) (2), **Fenitoína suspensión oral** (Epanutin®) (2), **Fenoxibenzamina suspensión** (FM) (2), **Oxcarbazepina suspensión oral** (Trileptal®) (2), **Risperidona solución oral** (Risperdal®) (2)
ROJO	Preparación: En el Servicio de Farmacia en CSB II B2 con sistemas cerrados de preparación y administración. Doble guante, bata protectora (preferible mono) y mascarilla. Si no es posible preparar en CSB II B2, utilizar: protección ocular (gafas) y respiratoria (mascarilla). Administración: sistemas cerrados de administración, doble guante, bata/mono, y protección ocular (si riesgo de salpicaduras) y mascarilla (si riesgo de inhalación).	**Fenitoína vial** (Fórmula magistral) (2), **Risperidona vial+jeringa precargada** (Risperdal®) (2)

El número entre paréntesis corresponde al número de lista de NIOSH en el que ese medicamento se encuentra incluido. Acenocumarol por similitud con warfarina (no incluido en NIOSH). Lista 1: medicamentos antineoplásicos o citostáticos. Lista 2: medicamentos no antineoplásicos que cumplen con uno o más criterios NIOSH para ser considerados de riesgo. Lista 3: medicamentos no antineoplásicos que tienen efectos sobre la reproducción. y que pueden afectar a hombres y mujeres que están intentando concebir de forma activa, y mujeres embarazadas o en periodo de lactancia, pero que no comportan riesgo para el resto del personal. 1 Siempre que sea posible, en el reenvasado, se mantendrá el blíster original. 2 Personal en riesgo reproductivo: hombres y mujeres que están intentando concebir de forma activa, y mujeres embarazadas o en periodo de lactancia. 3 En los tratamientos instaurados de forma continuada que requieran preparación, serán preparados en el Servicio de Farmacia(SF) en CSBIIB2. Los tratamientos excepcionales se prepararán según medidas de protección mencionadas, y en caso de continuidad, igualmente se asumirá la preparación en el SF. FM: Fórmula magistral; CSB II B2: Cabina de seguridad biológica Clase II Tipo B2; SCTM: sistema cerrado de transferencia de medicamentos. "Dado que la visualización de éste artículo no es en color, se han hecho constar las palabras: verde, amarillo, azul y rojo en las tablas debajo de cada medicamento. Este

color indica la categoría de protección de ese medicamento según el código de colores de menor a mayor grado de protección durante la preparación y administración (verde, amarillo, azul y rojo) tal y como se explica en el procedimiento descrito".

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Conflict of interest declaration

Conflict of interests

The authors declare not having any conflict of interests.