


Defining a Hazardous Agent

TXCH Global HOPE




1

Objectives

By the end of this presentation, the participant should be able to:

- Identify guidelines which define hazardous agents/drugs
- Describe the characteristics which classify an agent/drug as hazardous
- Design a list of agents/drugs which are considered hazardous



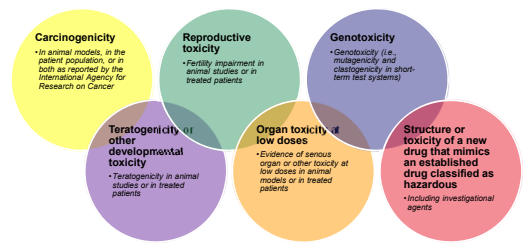
2

Relevant International Guidelines


Guideline/Recommendation	Group; Year Updated
United States Pharmacopoeia (USP) Chapter <800>	United States Pharmacopoeia; 2019
ASHP Guidelines on Handling Hazardous Drugs	American Society of Health System Pharmacists (ASHP); 2018
OSHA technical Manual: Controlling Occupational Exposure to Hazardous Drugs	Occupational Safety & Health Administration (OSHA); 2014
Safe Handling of Hazardous Chemotherapy Drugs in Limited-Resource Settings	Pan American Health Organization of the WHO; 2013
Chemotherapy Administration Safety Standards	American Society of Clinical Oncology & Oncology Nursing Society; 2013
ISMP International Medication Safety Self assessment for Oncology	Institute for Safe Medication Practices (ISMP); 2012
QuapoS 4: Quality Standard for the Oncology Pharmacy Service with Commentary, DGOP e.V	German Society of Oncology Pharmacy
ISOPP Standards of practice	International Society of Oncology Pharmacy Practitioners (ISOPP); 2007
Bonnes Pratiques de préparation (BPP)	Agence française de sécurité sanitaire de produits de santé (Afsaps); 2007
Supvapro: sécurité dans l'emploi des cytostatiques	Swiss Accident Insurance Fund; 2004

3

Hazardous Drug Criteria/Characteristics




All characteristics must be considered. A drug does not need to meet all criteria to be considered "hazardous" - it may be hazardous by only meeting 1 of the criteria above. The handling approach may vary based on the risk criteria.



4

USP <800> Implementation Details

- **A single designated person must oversee hazardous drug handling in the institution**
 - Must have proper knowledge, training, and qualifications
- **A health system must establish a hazardous drugs list**
 - Must be based on the model list by NIOSH
 - NIOSH classifies agents into one of 3 categories based on personnel risk
 - Must be updated annually
- **When implementing safe handling guidelines, the institution must also annually evaluate the following**
 - NIOSH classification of each agent
 - Dosage forms used
 - Need for manipulation based on presentation/patient population
 - Manufacturer's packaging
 - The overall risk of exposure



5

NIOSH Hazardous Drugs List (2016)

Group 1

- Antineoplastic drugs
- Identified by American Hospital Formulary Service (AHFS) Classification 10:00


Group 2

- Non-antineoplastic drugs that meet one or more of the 6 NIOSH criteria

Group 3

- Drugs that pose a reproductive risk for men and women who are actively trying to conceive and women who are pregnant or breastfeeding (as some agents may be present in breast milk)

The NIOSH list has been updated about every 2 years since first published in 2004. The next update is pending for 2019.



6

Group 1: Antineoplastic Drugs

Select agents based on Pediatric Hematology/Oncology use; *not a comprehensive list*

Agent	Additional Details	Agent	Additional Details
Arsenic trioxide	IARC Group 1 carcinogen; NTP: FDA Pregnancy Cat D	Fluorouracil	FDA Pregnancy Category D
Bleomycin	IARC Group 2B carcinogen; FDA Pregnancy Category D	Hydroxyurea	FDA Pregnancy Category D
Carboplatin	FDA Pregnancy Category D	Ifosfamide	FDA Pregnancy Category D
Cisplatin	IARC Group 2A carcinogen; NTP: FDA Pregnancy D	Imatinib	FDA Pregnancy Category D
Cyclophosphamide	IARC Group 1 carcinogen; NTP: FDA Pregnancy Cat D	Mercaptopurine	FDA Pregnancy Category D
Cytarabine	FDA Pregnancy Category D	Methotrexate	FDA Pregnancy Category X
Dacarbazine	NTP: FDA Pregnancy Category C	Paclitaxel	FDA Pregnancy Category D
Dactinomycin	FDA Pregnancy Category D	Procarbazine	IARC Group 2A carcinogen; NTP: FDA Pregnancy Category D
Daunorubicin	IARC Group 2B carcinogen; FDA Pregnancy Category D	Temozolomide	FDA Pregnancy Category D
Doxorubicin	IARC Group 2A carcinogen; NTP: FDA Pregnancy Category D	Vinblastine	FDA Pregnancy Category D
Etoposide	IARC Group 1 carcinogen; FDA Pregnancy Category D	Vincristine	FDA Pregnancy Category D

FDA: U.S. Food & Drug Administration; IARC: International Agency for Research on Cancer; Group 1 = Carcinogenic; Group 2A = Probably Carcinogenic; Group 2B = Possibly Carcinogenic; NTP = National Toxicology Program "Known or "Reasonably Accepted as Human Carcinogens; MHRD = maximum recommended human dose



7

Group 2: Other Drugs Meeting NIOSH Criteria

Select agents based on Pediatric Hematology/Oncology use; *not a comprehensive list*
Agents meeting ≥1 NIOSH criteria & agents with manufacturer's safe-handling guidance

Agent	Additional Details	Agent	Additional Details
Carbamazepine	Boxed warning for aplastic anemia; congenital malformations in offspring; rapid transplacental passage; FDA Pregnancy Category D	Lenalidomide	Analogy of thalidomide; Black Box warning/animal data for limb abnormalities; FDA Pregnancy Category X
Chloramphenicol	IARC Group 2A carcinogen; NTP: FDA Pregnancy C	Medroxyprogesterone acetate	IARC Group 2B; FDA Pregnancy Category X
Idotolvir	FDA Pregnancy Category C	Myophenolate mesylate	Black Box warning for embryo fetal toxicity, malignancies, serious infections; increased risk of first trimester loss and congenital malformations; FDA Pregnancy Category D
Cyclosporine	IARC Group 1 carcinogen; NTP: FDA Pregnancy Category C	Nevirapine	FDA Pregnancy Category B; hepatocellular adenomas and carcinomas at doses lower than human dose
Desazoxane	FDA Pregnancy Category C; secondary malignancies; genotoxic in vitro and in vivo; testicular atrophy at or below human dose (in lab studies)	Oxcarbazepine	Tumors in lab studies at 1/10 the MHRD; FDA Pregnancy Category C
Estrogens	IARC Group 1 carcinogen; NTP: Pregnancy Category X (see specific agent for more details)	Sirolimus	Increased risk of lymphomas and other malignancies; embryonic and fetotoxic at 0.2 human doses; FDA Pregnancy Category C
Fosphenytoin & phenytoin	IARC Group 2B; NTP: FDA Pregnancy Category D	Tacrolimus	Increased risk of lymphomas and other malignancies; reproductive effects in lab studies below MHRD; increased in breast risk; FDA Pregnancy Category C
Ganciclovir & valganciclovir	FDA Pregnancy Category C	Zidovudine	IARC Group 2B; FDA Pregnancy Category C

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8

Group 3: Agents with Adverse Reproductive Effects

Select agents based on Pediatric Hematology/Oncology use; *not a comprehensive list*

Agent	Additional Details
Fluconazole	FDA Pregnancy Category C; case reports of congenital anomalies in infants exposed in utero to maternal fluconazole during the first trimester
Ribavirin	Teratogenic and embryotoxic effects in lab studies; contraindicated in women who are pregnant and male partners of women who are pregnant; FDA Pregnancy Category X
Tretinoin	Black Box warning for severe birth defects; FDA Pregnancy Category X
Valproate/valproic acid	Black Box warning for teratogenicity; congenital malformations, including neural tube defects; FDA Pregnancy Category D
Voriconazole	FDA Pregnancy Category D
Warfarin	FDA Pregnancy Category D
Zoledronic acid	Increased number of still births and decreased neonatal survival in lab studies at low doses; FDA Pregnancy Category D



9

Hazardous Agents: Next Steps

- An institutional approach to classifying and handling hazardous agents must be established
 - The NIOSH model list must be used as a starting point
- The approach to safe handling will vary based on the drug dosage form, preparation approach, toxicity characteristics, and more
- Additional details on safe handling of hazardous agents are discussed in other modules



10

What's Next?

- Complete practice questions
- Review answer file



11

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12