NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
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Suggested Citation

NIOSH [2014]. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014. By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2014-138 (Supersedes 2012-150).

DHHS (NIOSH) Publication Number 2014-138 (Supersedes 2012-150)

September 2014

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Preamble:. The National Institute for Occupational Safety and Health (NIOSH) Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings was published in September 2004, http://www.cdc.gov/niosh/docs/2004-165/. In Appendix A of the Alert, NIOSH identified a sample list of major hazardous drugs. The list was compiled from information provided by four institutions that had generated lists of hazardous drugs for their respective institutions, as well as a list from the Pharmaceutical Research and Manufacturers of America (PhRMA). The 2004 list was updated in 2010 and 2012. The current update (2014) adds 27 drugs and includes a review of the 2004 list and the consequent removal of 12 drugs that did not meet the NIOSH criteria for hazardous drugs. In addition, a new format has been developed for the list of hazardous drugs, as described below. The review process for the addition of the new listings is described in the Federal Register: http://www.cdc.gov/niosh/docket/review/docket233/pdf/CDC-2013-0007.pdf.

Drugs Considered Hazardous

General Approach to Handling Hazardous Drugs

In the Alert (NIOSH 2004) and updates to the hazardous drug list (NIOSH 2012), NIOSH has recommended standard precautions or universal precautions be taken in handling hazardous drugs. Given the addition of many non-antineoplastic drugs and drugs in tablet and/or capsule form to the list, no single approach can cover the diverse potential occupational exposures to the drugs. The current NIOSH approach involves three groups of drugs:

- Group 1: Antineoplastic drugs (AHFS Classification 10:00) [ASHP/AHFS DI 2013]. Note that many of these drugs may also pose a reproductive risk for susceptible populations (Table 1).
- Group 2: Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug. Note that some of these drugs may also pose a reproductive risk for susceptible populations (Table 2).
- Group 3: Drugs that primarily pose a reproductive risk to men and women who are actively trying to conceive and women who are pregnant or breast feeding, because some of these drugs may be present in breast milk (Table 3).

The majority of the reproductive risks associated with the drugs listed in Table 3 are focused on women, but some can apply to men only (such as reduced fertility or sperm count) or to both men and women. Although all hazardous drugs should be handled accordingly, especially if they must be prepared aseptically, some populations of workers may not be at serious risk from handling drugs in Group 3. These include workers who are excluded from the susceptible populations for specific reasons such as age or infertility. In addition, drugs for which the manufacturer includes safe-handling guidance in the package insert are indicated. NIOSH carries out a hazard identification on each drug on the basis of the NIOSH criteria for a hazardous drug. No attempt has been made to perform risk assessments on each drug or to propose exposure limits. NIOSH has provided guidance for personal protective equipment and ventilated engineering controls for some of the various scenarios in which a drug may be handled in health care settings (Table 5). This guidance cannot cover all possible situations but provides general recommendations for the major handling events typically seen in health care.

Defining Hazardous Drugs

Hazardous drugs include those used for cancer chemotherapy, antiviral drugs, hormones, some bioengineered drugs, and other miscellaneous drugs. The definition of hazardous drugs used in the Alert is based on a definition originally developed in 1990 by the American Society of Hospital Pharmacists

[ASHP 1990], currently known as the American Society of Health-System Pharmacists. Thus, the definition may not accurately reflect the potential toxicity criteria associated with some of the newer-generation pharmaceuticals entering the health care setting. For example, bioengineered drugs target specific sites in the body, and although they may or may not pose a risk to health care workers, some may pose a risk to patients.

NIOSH and other organizations are still gathering data on the potential toxicity and health effects related to highly potent drugs and bioengineered drugs. Therefore, when working with any hazardous drug, health care workers should follow the approaches described in Table 5, along with any recommendations included in the manufacturer's Safety Data Sheet (SDS).

ASHP Definition of Hazardous Drugs

ASHP defines hazardous drugs in its 1990 revision of the Technical Assistance Bulletin on Handling Hazardous Drugs [ASHP 1990]. The bulletin gives criteria for identifying potentially hazardous drugs that should be handled in accordance with an established safety program [McDiarmid et al. 1991; Arrington and McDiarmid 1993; ASHP 2006; Massoomi et al. 2008; Eisenberg 2009; ONS 2011]. The criteria are prioritized to reflect the hierarchy of potential toxicity described below. Since the hazardous drugs covered by the Alert were designed as therapeutic agents for humans, human toxicity profiles should be considered superior to any data from animal models or *in vitro* systems. Additional guidance for defining hazardous drugs is available in the following sources: carcinogenicity [61 Fed Regist 17960–18011 (1996b); IARC 2014], teratogenicity [56 Fed Regist 63798–63826 (1991)], developmental toxicity [56 Fed Regist 63798–63826 (1991)], and reproductive toxicity [61 Fed Regist 56274–56322 (1996a)]. Physical characteristics of the agents (such as liquid versus solid or water versus lipid solubility) also need to be considered in determining the potential for occupational exposure.

NIOSH Revision of ASHP Definition

The 1990 ASHP definition of hazardous drugs* was revised by the NIOSH Working Group on Hazardous Drugs for the Alert. Drugs considered hazardous include those that exhibit one or more of the following six characteristics in humans or animals:

- Carcinogenicity
- Teratogenicity or other developmental toxicity†
- Reproductive toxicity†
- Organ toxicity at low doses†
- Genotoxicity‡
- Structure and toxicity profiles of new drugs that mimic existing drugs determined hazardous by the above criteria

*ASHP [1990] definition of hazardous drugs

1. Genotoxicity (i.e., mutagenicity and clastogenicity in short-term test systems)
2. Carcinogenicity in animal models, in the patient population, or both, as reported by the International Agency for Research on Cancer (IARC)
3. Teratogenicity or fertility impairment in animal studies or in treated patients
4. Evidence of serious organ or other toxicity at low doses in animal models or treated patients.

†All drugs have toxic side effects, but some exhibit toxicity at low doses. The level of toxicity reflects a continuum from relatively nontoxic to production of toxic effects in patients at low doses (for example, a few milligrams or less). For example, a daily therapeutic dose of 10 mg/day or a dose of 1 mg/kg per day in laboratory animals that produces serious organ toxicity, developmental toxicity, or reproductive toxicity has been used by the pharmaceutical industry to develop occupational exposure limits (OELs) of less than 10 μg/m^3 after applying appropriate uncertainty factors [Sargent and Kirk 1988; Naumann and Sargent 1997; Sargent et al. 2002]. OELs in this range are typically established for potent or toxic drugs in the pharmaceutical industry. Under all circumstances, an evaluation of all available data should be conducted to protect health care workers.

‡In evaluating mutagenicity for potentially hazardous drugs, responses from multiple test systems are needed before precautions can be required for handling such agents. The EPA evaluations include the type of cells affected and *in vitro* versus *in vivo* testing [51 Fed. Regist. 34006–34012 (1986)].

Determining Whether a Drug is Hazardous

Many hazardous drugs used to treat cancer (for example, alkylating agents) bind to or damage DNA. Other antineoplastic drugs, some antivirals, antibiotics, and bioengineered drugs interfere with cell growth or proliferation, or with DNA synthesis. In some cases, the nonselective actions of these drugs disrupt the growth and function of both healthy and diseased cells, resulting in toxic side effects for treated patients and their offspring. These nonselective actions can also cause adverse effects in health care workers who are inadvertently exposed to hazardous drugs.

Early concerns about occupational exposure to antineoplastic drugs first appeared in the 1970s. Although the antineoplastic drugs remain the principal focus of the Alert, other drugs may also be considered hazardous because they are potent (small quantities produce a physiological effect) or cause irreversible effects. As the use and number of these potent drugs increase, so do opportunities for hazardous exposures among health care workers. For example, antineoplastic drugs such as cyclophosphamide have immunosuppressant effects that proved beneficial for treating nonmalignant diseases such as rheumatoid arthritis and multiple sclerosis [Baker et al. 1987; Moody et al. 1987; Chabner et al. 1996; Abel 2000]. The lack of proper training for handling antineoplastic drugs in other specialty areas may be an issue that needs to be addressed [Polovich and Giesker 2011; Menonna-Quinn et al. 2013].

This document presents criteria and sources of information for determining whether a drug is hazardous. When a drug has been judged to be hazardous, the various precautions outlined in the Alert should be applied when handling that drug. Also included is a list of drugs that should be handled as hazardous. When applying the criteria for a hazardous drug as outlined above, NIOSH takes the following approach.

- NIOSH takes into account the dose for animal testing, for reproductive and developmental toxicity, and for carcinogenicity testing. If adverse effects are observed near, at, or below the maximum recommended human dose (MRHD), NIOSH considers it to be highly relevant. If doses producing an adverse effect are many times the MRHD, usually NIOSH does not consider them in its evaluation.
- In addition to dose, for carcinogenicity testing NIOSH looks for tumors in more than one species and sex. It looks for tumors in multiple organs and for tumors that are not rodent-specific. Any available human data are considered significant.
- For effects of genotoxicity, NIOSH looks at *in vivo* testing over *in vitro* testing. However, adverse outcomes in several *in vitro* tests will be considered in its evaluation.
- For reproductive and developmental effects, NIOSH notes if there was maternal toxicity, in addition to the dose. Effects on the fetus in the absence of maternal toxicity are considered relevant. Drugs with an FDA pregnancy category X rating are typically listed as hazardous. Drugs in Category D are often listed as hazardous, but it will depend on the individual drug. Any available human data are considered significant.
- For organ toxicity, the low dose criterion in the definition (a daily therapeutic dose of 10 mg/day or a dose of 1 mg/kg per day in laboratory animals) is used as a benchmark.
- Drugs with safe-handling guidelines from the manufacturer are automatically put on the list because the manufacturer has decided their properties warrant special handling.

In addition to using the list of hazardous drugs presented here, each organization should create its own list of drugs considered to be hazardous. This document presents guidance for making such a facility-specific list (see section entitled How to Generate Your Own List of Hazardous Drugs). Subsequently, newly purchased drugs should be evaluated against the organization's hazardous drug criteria and added to the list if they are deemed hazardous. Organizations have developed various approaches to identifying and classifying hazardous drugs [Chaffee et al. 2010; Badry et al. 2013; Kaestli et al. 2013]. Although the classification schemes may differ somewhat, the drugs listed as hazardous are quite similar.

Individual organizations may not have adequate resources for determining their own list of hazardous

drugs. If so, the list of hazardous drugs in this document will help employers and workers to determine when precautions are needed. However, reliance on such a published list is a concern because it quickly becomes outdated as new drugs continually enter the market or listed drugs are removed when additional information becomes available. NIOSH will update this list periodically, adding new drugs considered to be hazardous and removing those that require reclassification. This hazardous drug list will be posted on the NIOSH website at www.cdc.gov/niosh/topics/hazdrug/.

How to Generate Your Own List of Hazardous Drugs

The OSHA hazard communication standard [29 CFR 1910.1200] requires employers to develop a hazard communication program appropriate for their unique workplaces. An essential part of the program is the identification of all hazardous drugs a worker may encounter in the facility. Compliance with the OSHA hazard communication standard entails (1) evaluating whether these drugs meet one or more of the criteria for defining hazardous drugs and (2) posting a list of the hazardous drugs to ensure worker safety. Institutions may wish to compare their lists to the listing in this document or on the NIOSH website.

It is not likely that every health care provider or facility will use all drugs that have received U.S. Food and Drug Administration (FDA) approval, and the OSHA hazard communication standard does not mandate evaluation of every marketed drug. Instead, compliance requires practice-specific assessments for drugs used at any one time by a facility. However, hazardous drug evaluation is a continual process. Local hazard communication programs should provide for assessment of new drugs as they enter the marketplace and, when appropriate, reassessment of their presence on hazardous drug lists as toxicological data become available to support re-categorization. Toxicological data are often incomplete or unavailable for investigational drugs. However, if the mechanism of action suggests that there may be a concern, it is prudent to handle them as hazardous drugs until adequate information becomes available to exclude them.

With the increased availability of oral antineoplastic and other hazardous drugs, additional precautions are required in order to prevent worker exposure to these formulations. Some drugs defined as hazardous may not pose a significant risk of direct occupational exposure because of their dosage formulation (for example, coated tablets or capsules—solid, intact medications that are administered to patients without modifying the formulation). However, they may pose a risk if the formulations are altered, such as by crushing tablets or making solutions from them outside a ventilated cabinet [Simmons 2010; Goodin et al. 2011]. Uncoated tablets may present a risk of exposure from dust by skin contact and/or inhalation when the tablets are counted [Shahsavarani et al. 1993].

All hazardous drugs, regardless of the formulation, should be labeled as such to prevent improper handling. Tablet and capsule forms of hazardous drugs should not be placed in automated counting machines, which subject them to stress and may introduce powdered contaminants into the work area. Counting and pouring of hazardous drugs should be done carefully, and clean equipment should be dedicated for use with these drugs. Crushing tablets or opening capsules should be avoided and liquid formulations should be used whenever possible. During the compounding of hazardous drugs (e.g., crushing, dissolving, or preparing a solution or an ointment), workers should wear non-permeable gowns and double gloves (Table 5). Guidelines for the safe compounding, administration, and disposal of hazardous drugs have been developed by several organizations [NIOSH 2004; ASHP 2006; ONS 2011; USP 2014].

Where to Find Information Related to Drug Toxicity

Practice-specific lists of hazardous drugs (usually developed by pharmacy or nursing departments) should be comprehensive, including all hazardous medications routinely used or very likely to be used

by a local practice. Here are some of the resources that employers can use to evaluate the hazard potential of a drug:

- Safety Data Sheets (SDSs, formally Material Safety Data Sheets)
- Product labeling approved by the U.S. FDA (drug package inserts)
- International Agency for Research on Cancer (IARC) http://www.iarc.fr
- Drugbank: http://www.drugbank.ca/
- DailyMed: http://dailymed.nlm.nih.gov/dailymed/
- Special health warnings from drug manufacturers, FDA, and other professional groups and organizations
- Reports and case studies published in medical and other health care profession journals
- Evidence-based recommendations from other facilities that meet the criteria defining hazardous drugs

Identification of Hazardous Drugs

The following list (Tables 1–3) contains those drugs that NIOSH has reviewed according to the criteria in the NIOSH definition of a hazardous drug. The list was compiled from the following:

- the original list published in 2004 (NIOSH 2004), which was a compilation of five lists available to NIOSH at the time (subsequently, the list was re-evaluated against the NIOSH criteria and several drugs were removed; Table 4a)
- the 2012 NIOSH update to the list
- the NIOSH 2014 update to the list, for which 27 drugs were added (including five with manufacturers' safe-handling warnings) and one drug, tetracycline, was deleted on the basis of re-evaluation and feedback from stakeholders (Table 4b).

The OSHA hazard communication standard requires hazardous drugs to be handled with use of special precautions. The mandate applies not only to health care professionals who provide direct patient care but also to others who support patient care by participating in product acquisition, storage, transportation, housekeeping, and waste disposal. Institutions may want to adopt this list or compare theirs with the list on the NIOSH website.

CAUTION: Drugs purchased and used by a facility may have entered the marketplace after the list below was assembled. Therefore, this list may not be all-inclusive.

If you use a drug that is not included in the list of hazardous drugs, check the available literature to see whether the unlisted drug should be treated as hazardous. Check the SDS from the manufacturer or the drug package insert. You may also check with other institutions that might be using the same drug. If any of the documents mention carcinogenicity, genotoxicity, teratogenicity (Section 13 in package insert), or reproductive or developmental toxicity (Section 8), or if the package insert contains safe-handling warnings (Section 16), use the precautions stipulated in the Alert. If the drug meets one or more of the criteria for hazardous drugs in the NIOSH definition, handle it as hazardous.

The list of hazardous drugs will be updated periodically on the website, hpp://www.cdc.gov/niosh/topics/hazdrug/.

This list supersedes both the 2004 list, http://www.cdc.gov/niosh/docs/2004-165/ and the 2012 list http://www.cdc.gov/niosh/docs/2012-150.

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Acknowledgments

This document was written by Thomas H. Connor, PhD; Barbara A. MacKenzie, BS; D. Gayle DeBord, PhD; Douglas B. Trout, MD, MHS; and James P. O'Callaghan, PhD, all of NIOSH.

Seleen Collins provided editorial services. Ryan Dufour, Nicole Romero, and Vanessa Williams provided graphic design and production services.

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NIOSH performs a hazard identification on each of the drugs in the following tables. The actual risk to health care workers depends on what is done with the drugs—how they are manipulated, how often they are handled, and what type of engineering controls and personal protective equipment (PPE) are used (see Table 5). For example,

- Dispensing a single tablet to a patient poses little to no risk to the healthcare worker. A single pair of gloves would be adequate.
- Repeatedly counting, cutting, or crushing tablets may pose a higher risk of worker exposure and contamination to the workplace if proper precautions are not in place. If a containment device such as a BSC (Class II biological safety cabinet) or CACI (compounding aseptic containment isolator) is not available, then double gloves, a protective gown, respiratory protection, and a disposable pad to protect the work surface should be used.
- Preparing a number of intravenous doses of an antineoplastic drug typically poses a higher potential risk to the worker. In addition to double gloving and a protective gown, an engineering control such as a BSC or CACI, possibly supplemented with a CSTD (closed system drug transfer device), is required to protect the drug, environment, and health care worker.

The drugs in Table 1 meet one or more of the NIOSH criteria for a hazardous drug. These drugs represent an occupational hazard to health care workers and should always be handled with use of recommended engineering controls and personal protective equipment (PPE), regardless of their formulation (IV [intravenous], SC [subcutaneous], topical, tablet, or capsule). Unopened, intact tablets and capsules may not pose the same degree of occupational exposure risk as injectable drugs, which usually require extensive preparation. Cutting, crushing or otherwise manipulating tablets and capsules will increase the risk of exposure to workers. In addition to many of these drugs being cytotoxic, the majority are hazardous to males or females who are actively trying to conceive, women who are pregnant or may become pregnant, or women who are breast feeding, because they may be present in breast milk. Manufacturers' safe-handling guidance (MSHG) is typically in Section 16 of the drug package insert. See Table 5 for safe-handling recommendations. AHFS = American Hospital Formulary Service; MHRD = maximum recommended human dose.

*Drugs in red font were added in 2014.

**International Agency for Research on Cancer (www.iarc.fr).

***BCG, although classified as a vaccine, is used in the treatment of certain cancers. BCG should be prepared with aseptic techniques. To avoid cross-contamination, parenteral drugs should not be prepared in areas where BCG has been prepared. A separate area for the preparation of BCG suspension is recommended. All equipment, supplies, and receptacles in contact with BCG should be handled and disposed of as biohazardous. If preparation cannot be performed in a containment device, then respiratory protection, gloves, and a gown should be worn to avoid inhalation or contact with BCG organisms.

Table 1. Antineoplastic drugs including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
abiraterone*	10:00 antineoplastic agents		Women who are pregnant or women who may be pregnant should not handle without protection (e.g., gloves); FDA Pregnancy Category X	DailyMed; DrugBank
ado-trastuzumab emtansine	10:00 antineoplastic agents	yes	Conjugated monoclonal antibody; FDA Pregnancy Category D	DailyMed; DrugBank
altretamine	10:00 antineoplastic agents	yes	FDA Pregnancy category D	DailyMed; DrugBank
amsacrine	NA antineoplastic agents	yes	IARC Group 2B	DrugBank
anastrozole	10:00 antineoplastic agents		FDA Pregnancy category X	DailyMed; DrugBank
arsenic trioxide	10:00 antineoplastic agents	yes	IARC Group 1 carcinogen**; FDA Pregnancy Category D	DailyMed; DrugBank
azacitidine	10:00 antineoplastic agents	yes	IARC Group 2A carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank

(continued)

Table 1 (Continued). Antineoplastic drugs including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
bacillus calmette Guerin (BCG)***	80:12 vaccines	yes	See special handling requirements**; FDA Pregnancy Category C	DailyMed
bendamustine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed;
bexarotene	10:00 antineoplastic agents		FDA Pregnancy Category X	DailyMed; DrugBank
bicalutimide	10:00 antineoplastic agents		FDA Pregnancy Category X	DailyMed; DrugBank
bleomycin	10:00 antineoplastic agents	yes	IARC Group 2B; FDA Pregnancy Category D	DailyMed; DrugBank
bortezomib	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
brentuximab vedotin	10:00 antineoplastic agents	yes	Conjugated monoclonal antibody; FDA Pregnancy Category D	DailyMed; DrugBank
busulfan	10:00 antineoplastic agents	yes	IARC Group 1 carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
cabazitaxel	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
capecitabine	10:00 antineoplastic agents	yes	Metabolized to 5-fluorouracil; FDA Pregnancy Category D	DailyMed; DrugBank
carboplatin	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
carmustine	10:00 antineoplastic agents	yes	IARC Group 2A carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
chlorambucil	10:00 antineoplastic agents	yes	IARC Group 1 carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
cisplatin	10:00 antineoplastic agents	yes	IARC Group 2A carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
cladribine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
clofarabine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
crizotinib	10:00 antineoplastic agents		FDA Pregnancy Category D	DailyMed
cyclophosphamide	10:00 antineoplastic agents	yes	IARC Group 1 carcinogen; FDA Pregnancy Category D	DailyMed; Drugbank
cytarabine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank

(continued)

Table 1 (Continued). Antineoplastic drugs including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
dacarbazine	10:00 antineoplastic agents	yes	FDA Pregnancy Category C	DailyMed; Drugbank
dactinomycin	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
dasatinib	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; Drugbank
daunorubicin	10:00 antineoplastic agents	yes	IARC Group 2B, AKA daunomycin; FDA Pregnancy Category D	DailyMed; Drugbank
decitabine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; Drugbank
degarelix	10:00 antineoplastic agents	yes	FDA Pregnancy Category X	DailyMed; Drugbank
docetaxel	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
doxorubicin	10:00 antineoplastic agents	yes	IARC Group 2A carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
epirubicin	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; Drugbank
eribulin	10:00 antineoplastic agents		FDA Pregnancy Category D	DailyMed; DrugBank
erlotinib	10:00 antineoplastic agents		FDA Pregnancy Category D	DailyMed; DrugBank
estramustine	10:00 antineoplastic agents	yes	FDA Pregnancy Category X	DailyMed; Drugbank
etoposide	10:00 antineoplastic agents	yes	IARC Group 1 carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
everolimus	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; Drugbank
exemestane	10:00 antineoplastic agents		FDA Pregnancy Category X	DailyMed; DrugBank
floxuridine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
fludarabine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
fluorouracil	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
flutamide	10:00 antineoplastic agents		Indicated only for men; FDA Pregnancy Category D	DailyMed; DrugBank
fulvestrant	10:00 antineoplastic agents		FDA Pregnancy Category D	DailyMed; DrugBank
gemcitabine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
gemtuzumab ozogamicin	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank

(continued)

Table 1 (Continued). Antineoplastic drugs including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
goserelin	10:00 antineoplastic agents		FDA Pregnancy Category X	DailyMed; Drugbank
hydroxyurea	10:00 antineoplastic agents	yes	Special warning on handling bottles and capsules FDA Pregnancy Category D	DailyMed; DrugBank
idarubicin	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
ifosfamide	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
imatinib	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
irinotecan	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
ixabepilone	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
letrozole	10:00 antineoplastic agents		FDA pregnancy Category X	DailyMed; DrugBank
leuprolide	10:00 antineoplastic agents	yes	FDA Pregnancy Category X	DailyMed; Drugbank
lomustine	10:00 antineoplastic agents	yes	IARC Group 2A carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
mechloreth-amine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
megestrol	10:00 antineoplastic agents		Nursing should be discontinued if megestrol is required. Women at risk of pregnancy should avoid exposure; FDA Pregnancy Category X	DailyMed; DrugBank
melphalan	10:00 antineoplastic agents	yes	IARC Group 1 carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
mercaptopurine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
methotrexate	10:00 antineoplastic agents	yes	FDA Pregnancy Category X	DailyMed; DrugBank
mitomycin	10:00 antineoplastic agents	yes	IARC Group 2B; FDA Pregnancy Category D	DailyMed; DrugBank
mitotane	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
mitoxantrone	10:00 antineoplastic agents	yes	IARC Group 2B; FDA Pregnancy Category D	DailyMed; DrugBank
nelarabine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank

(continued)

Table 1 (Continued). Antineoplastic drugs including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
nilotinib	10:00 antineoplastic agents		FDA Pregnancy Category D	DailyMed; DrugBank
omacetaxin	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
oxaliplatin	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
paclitaxel	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
pazopanib	10:00 antineoplastic agents		FDA Pregnancy Category D	DailyMed; DrugBank
pemetrexed	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
pentostatin	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
pralatrexate	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
procarbazine	10:00 antineoplastic agents	yes	IARC Group 2A carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
romidepsin	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed
sorafenib	10:00 antineoplastic agents		FDA Pregnancy Category D	DailyMed; DrugBank
streptozocin	10:00 antineoplastic agents	yes	IARC Group 2B; FDA Pregnancy Category D	DailyMed; DrugBank
sunitinib	10:00 antineoplastic agents		FDA Pregnancy Category D	DailyMed; DrugBank
tamoxifen	10:00 antineoplastic agents		IARC Group 1 carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
temozolomide	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
temsirolimus	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
teniposide	10:00 antineoplastic agents	yes	IARC Group 2A carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
thioguanine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
thiotepa	10:00 antineoplastic agents	yes	IARC Group 1 carcinogen; FDA Pregnancy Category D	DailyMed; DrugBank
topotecan	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
toremifene	10:00 antineoplastic agents		FDA Pregnancy Category D	DailyMed; DrugBank
trimetrexate	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
triptorelin	10:00 antineoplastic agents		FDA Pregnancy Category X	DailyMed

(continued)

Table 1 (Continued). Antineoplastic drugs including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
valrubicin	10:00 antineoplastic agents	yes	FDA Pregnancy Category C	DailyMed; DrugBank
vandetanib	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
vemurafenib	10:00 antineoplastic agents		FDA Pregnancy Category D	DailyMed; DrugBank
vinblastine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
vincristine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; Drugbank
vinorelbine	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; DrugBank
vorinostat	10:00 antineoplastic agents	yes	FDA Pregnancy Category D	DailyMed; Drugbank

The drugs in Table 2 meet one or more of the NIOSH criteria for a hazardous drug. Unopened, intact tablets and capsules may not pose the same degree of occupational exposure risk as injectable drugs, which usually require extensive preparation. Cutting, crushing, or otherwise manipulating tablets and capsules will increase the risk of exposure to workers. Some of these drugs may represent an occupational hazard to males or females who are actively trying to conceive, women who are pregnant or may become pregnant, or women who are breast feeding, because they may be present in breast milk. Manufacturers' safe-handling guidance (MSHG) is typically in Section 16 of the drug package insert. See Table 5 for safe-handling recommendations. AHFS = American Hospital Formulary Service; MHRD = maximum recommended human dose.

*Drugs in red font were added in 2014.

**International Agency for Research on Cancer, www.iarc.fr

***Drugs in blue font meet one or more additional criteria for a hazardous drug and also pose a potential reproductive hazard.

Table 2. Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
abacavir*	8:18.08.20 nucleoside and reverse transcriptase inhibitors		FDA Pregnancy Category C; malignant tumors observed in male and female mice and rats; genotoxic in *in vivo* micronucleus test.	DailyMed; DrugBank
alefacept	84:92 skin and mucous membrane agents, miscellaneous		Increased frequency of malignancies observed in treated patients; FDA Pregnancy Category B	DailyMed; DrugBank
apomorphine	28:36.20.08 Nonergot-derivative dopamine receptor agonists		FDA Pregnancy Category C; genotoxic in several *in vitro* assays.	DailyMed; DrugBank
azathioprine	92:44 immunosuppressant agents	yes	IARC Group 1 carcinogen**; FDA Pregnancy Category D***	DailyMed; DrugBank
carbamazepine	28:12:92 anticonvulsants, miscellaneous		Black Box warning for aplastic anemia; congenital malformations in offspring of mothers who took drug; rapid transplacental passage; FDA Pregnancy Category D	DailyMed; Drugbank

(continued)

Table 2 (Continued). Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
chloramphenicol	8:12:08 chloramphenicols		IARC Group 2A carcinogen; FDA Pregnancy Category C	DailyMed; DrugBank
cidofovir	8:18:32 nucleoside and nucleotides	yes	FDA Pregnancy Category C	DailyMed; Drugbank
cyclosporine	92:44 immunosuppressive agents		IARC Group 1 carcinogen; FDA pregnancy Category C	DailyMed; Drugbank
deferiprone	64:00 Heavy metal antagonists		Genotoxic *in vitro* and *in vivo*; FDA Pregnancy Category D	DailyMed; DrugBank
dexrazoxane	92:56 protective agents	yes	FDA Pregnancy Category C; secondary malignancies observed in patients treated long term with Razoxane (a racemic mixture containing dexrazane); genotoxic *in vitro* and *in vivo*; in laboratory studies, testicular atrophy observed at or below the human dose	DailyMed; DrugBank
diethylstilbestrol	NA		IARC Group 1 carcinogen; FDA Pregnancy Category X	DrugBank
divalproex	28:12:92 anticonvulsants, miscellaneous		Black Box warning for teratogenicity; FDA Pregnancy Category D; tumors seen in laboratory studies at doses below MRHD	DailyMed
entecavir	8:18:32 nucleosides and nucleotides	yes	FDA Pregnancy Category C	DailyMed; DrugBank

(continued)

Table 2 (Continued). Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
estradiol	68:16:04 estrogens		Black Box warning for malignant neoplasms; increased risk of endometrial cancer, breast cancer, and ovarian cancer; in laboratory studies, increased frequency of carcinomas of the breast, uterus, cervix, vagina, testis, and liver; present in breast milk; FDA Pregnancy Category X	DailyMed; DrugBank
estrogen/ progesterone combinations	68:12 contraceptives		IARC Group 1 carcinogen; FDA Pregnancy Category X	DailyMed
estrogens, conjugated	68:16:04 estrogens		Black Box warning for endometrial cancer and cardiovascular risks; long-term use in women and laboratory studies increases frequency of several cancers; FDA Pregnancy Category X	DailyMed
estrogens, esterified	68:16:04 estrogens		Black Box warning for endometrial cancer and cardiovascular risks: FDA Pregnancy Category X	DailyMed
estropipate	68:16:04 estrogens		Black Box warning for endometrial carcinoma in postmenopausal women and use during pregnancy; FDA Pregnancy Category X	DailyMed; DrugBank
fingolimod	92:20 biologic response modifiers		FDA Pregnancy Category C; in laboratory studies, increased malformations and embryo-fetal deaths at less than the RHD; malignant lymphomas observed in male and female mice.	DailyMed; DrugBank

(continued)

Table 2 (Continued). Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
fluoxymesterone	68:08 androgens		Tumors in mice and rats and possibly humans; FDA Pregnancy Category X	DailyMed; DrugBank
fosphenytoin	28:12.12 hydantoins		Metabolized to phenytoin; FDA Pregnancy Category D	DailyMed; DrugBank
ganciclovir	8:18:32 nucleosides and nucleotides	yes	FDA Pregnancy Category C	DailyMed; DrugBank
leflunomide	92:36 disease-modifying antirheumatic agents		Teratogenic in laboratory studies at 1/10 HD; marked postnatal survival at 1/100 HD; FDA Pregnancy Category X; severe liver injury reported in patients; carcinogenicity observed at doses below HD	DailyMed; DrugBank
lenalidomide	92:20 biologic response modulators	yes	Analog of thalidomide; FDA Black box warnings for limb abnormalaties; pregnancy Category X; in laboratory studies, caused thalidomide-type limb defects in monkey offspring	DailyMed; DrugBank
liraglutide recombinant	68:20.06 incretin mimetics		FDA Pregnancy Category C; Black Box warning for thyroid C-cell tumors, with supporting evidence in laboratory studies; also in laboratory studies, teratogenic at or below the MRHD.	DailyMed; DrugBank
medroxyprogesterone acetate	68:32 progestins	yes	IARC Group 2B; FDA Pregnancy Category X	DailyMed; DrugBank

(continued)

Table 2 (Continued). Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
mycophenolate mofetil	92:44 immunosuppressive agents		Black Box warning for embryo fetal toxicity, malignancies and serious infections; Increased risk of first-trimester pregnancy loss and increased risk of congenital malformations; FDA Pregnancy Category D; Special warning: tablets should not be crushed and capsules should not be opened or crushed. Avoid inhalation or direct contact with skin or mucous membranes of the powder contained in capsules and oral suspension (before or after constitution). If such contact occurs, wash thoroughly with soap and water; rinse eyes with plain water.	DailyMed; DrugBank
mycophenolic acid	92:44 immunosuppressive agents		Black Box warning for first trimester pregnancy loss and an increased risk of congenital malformations; FDA Pregnancy Category D; Black Box warning for lymphomas and other malignancies; genotoxic *in vitro* and *in vivo*	DailyMed; DrugBank
nevirapine	8:18.08.16 nonnucleoside reverse transcriptase inhibitors		FDA Pregnancy Category B; in laboratory studies, hepatocellular adenomas and carcinomas at doses lower than human dose.	DailyMed; DrugBank
oxcarbazepine	28:12:92 anticonvulsants, miscellaneous		Tumors observed in laboratory studies at 1/10 MRHD; FDA Pregnancy Category C	DailyMed; Drugbank

(continued)

Table 2 (Continued). Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
palifermin	84:16 cell stimulants and proliferants		FDA Pregnancy Category C; potential for stimulation of tumor growth	DailyMed; Drugbank
phenoxybenzamine	12:16:04:04 non-selective alpha-andrenergic blocking agents		IARC Group 2B; FDA Pregnancy Category C	DailyMed; DrugBank
phenytoin	28:12.12 hydantoins		IARC 2B; FDA Pregnancy Category D	DailyMed; DrugBank
pipobroman	NA		FDA Pregnancy Category D	Drugbank
progesterone	68:32 progestins		IARC Group 2B	DailyMed; Drugbank
progestins	68:12 contraceptives		FDA Pregnancy Category X	
propylthiouracil	68:36.08 antithyroid agents		IARC 2B; FDA Pregnancy Category D	DailyMed; DrugBank
raloxifene	68:16:12 estrogen agonists-antagonists		Abortion and developmental abnormalities seen at low doses in laboratory studies; evidence of tumors at low doses in laboratory studies; FDA Pregnancy Category X	DailyMed; Drugbank
rasagiline	28:36 antiparkinsonian agents		FDA Pregnancy Category C	DailyMed; Drugbank
risperidone	28:16:08:04 atypical antipsychotics		Evidence of tumors at low doses in laboratory studies; may be prolactin-mediated; FDA Pregnancy Category C	DailyMed; DrugBank
sirolimus	92:44 immunosuppressive agents		AKA rapamycin; increased risk of lymphomas and other malignancies; embryotoxic and fetotoxic at 0.2 HD; FDA Pregnancy Category C	DailyMed; DrugBank

(continued)

Table 2 (Continued). Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug including those with manufacturers' safe handling guidance (MSHG)

Drug	AHFS classification	MSHG	Reason for listing	Links
spironolactone	24:32.20 mineralocorticoid receptor antagonists		FDA Pregnancy Category C; black box warning for tumorogenicity in laboratory studies.	DailyMed; DrugBank
tacrolimus	92:44 immunosuppressive agents		Increased risk of lymphomas and other malignancies; reproductive effects seen in laboratory studies below the MRHD; excreted in breast milk; FDA Pregnancy Category C	DailyMed; DrugBank
thalidomide	92:20 biologic response modulators	yes	FDA Pregnancy Category X	DailyMed; DrugBank
uracil mustard	NA	yes	FDA Pregnancy Category D	DrugBank
valganciclovir	8:18:32 nucleosides and nucleotides	yes	FDA Pregnancy Category C	DailyMed; DrugBank
zidovudine	8:18:08 antiretroviral agents		IARC Group 2B; FDA Pregnancy Category C	DailyMed; DrugBank

The drugs in Table 3 primarily meet the NIOSH criteria for reproductive hazards. They represent a potential occupational hazard to males or females who are actively trying to conceive, women who are pregnant or may become pregnant, or breast feeding as they may be present in breast milk. Unopened, intact tablets and capsules may not pose the same degree of occupational risk as injectable drugs that usually require extensive preparation. Cutting, crushing or otherwise manipulating tablets and capsules will increase the risk of exposure to workers. Manufacturers' safe handling guidance (MSHG) is typically in Section 16 of the drug package insert. See Table 5 for safe handling recommendations.

*Drugs in red font were added in 2014.

Table 3. Non-antineoplastic drugs that primarily have adverse reproductive effects

Drug	AHFS classification	Reason for listing	Links
acitretin	88:04 vitamin A	Black Box warning on adverse reproductive effects; FDA Pregnancy Category X	DailyMed; DrugBank
alitretinoin	84:92 skin and mucous membrane agents, miscellaneous	FDA Pregnancy Category D	DailyMed; DrugBank
ambrisentan	24:12:92 vasodilating agents, miscellaneous	Black Box warning on adverse reproductive effects; reduced sperm counts in patients; FDA Pregnancy Category X	DailyMed;
bosentan	24:12:92 vasodilating agents, miscellaneous	Black Box warning on adverse reproductive effects; FDA Pregnancy Category X	DailyMed; DrugBank
cabergoline	28:36:20:04 ergot-derivative dopamine receptor agonists	Inhibition of conception and embryo fetal effects at doses below recommended human dose; FDA Pregnancy Category B	DailyMed; DrugBank
cetrorelix	92:40 gonadotropin-releasing hormone anagonists	FDA Pregnancy Category X	DailyMed; DrugBank
choriogonadotropin	68:18 gonadotropins	FDA pregnancy Category X; may cause fetal harm when administered to a pregnant woman.	DailyMed; DrugBank

(continued)

Table 3 (Continued). Non-antineoplastic drugs that primarily have adverse reproductive effects

Drug	AHFS classification	Reason for listing	Links
clonazepam	28:12:08 benzodiapines	Increased risk of congenital abnormalities when taken in first trimester; FDA Pregnancy Category D	DailyMed; DrugBank
colchicine	92:16 antigout agents	FDA Pregnancy Category C; published animal reproduction and development studies indicate it causes embryofetal toxicity, teratogenicity, and altered postnatal development at exposures within or above the clinical therapeutic range	DailyMed; DrugBank
dinoprostone	76:00 oxytocics	Hazardous only for women in late pregnancy; FDA Pregnancy Category C	DailyMed; DrugBank
dronedarone	24:04:04 antiarrythmics	Teratogenic in laboratory studies at ½ MRHD; FDA Pregnancy Category X	DailyMed; DrugBank
dutasteride	92:08 5-alpha reductase inhibitors	Women warned not to handle; FDA Pregnancy Category X	DailyMed; DrugBank
ergonovine/methylergonovine	76:00 oxytocics	Use is contraindicated during pregnancy because of its uterotonic effects; FDA Pregnancy Category C	DailyMed; DrugBank; DrugBank
finasteride	92:08 5-alpha reductase inhibitors	Women should not handle crushed or broken finasteride tablets when they are pregnant or may potentially be pregnant due to potential risk to a male fetus; FDA Pregnancy Category X	DailyMed; Drugbank

(continued)

Table 3 (Continued). Non-antineoplastic drugs that primarily have adverse reproductive effects

Drug	AHFS classification	Reason for listing	Links
fluconazole	8:18.08 azoles	FDA Pregnancy Category C; case reports describe congenital anomalies in infants exposed in utero to maternal fluconazole (400–800 mg/day) during most or all of the first trimester, similar to those seen in animal studies	DailyMed; DrugBank
ganirelix	92:40 gonadotropin-eleasing hormone antagonists	FDA Pregnancy Category X	DailyMed
gonadotropin, chorionic	68:18 gonadotropins	Defects of forelimbs and central nervous system and alterations in sex ratio have been reported in laboratory studies; FDA pregnancy Category C	DailyMed; DrugBank7
icatibant	92:32 complement inhibitors	FDA Pregnancy Category C; in laboratory studies, premature birth and abortion rates increased at a dose that was less than 1/40th the MRHD and delayed parturition and fetal death occurred at 0.5 and 2-fold, respectively, the MRHD	DailyMed; DrugBank
mentropins	68:18 gonadotropins	FDA Pregnancy Category X	Drugbank
methyltestosterone	68:08 androgens	FDA Pregnancy Category X	DailyMed; DrugBank
mifepristone	76:00 oxytocics	When given to pregnant women results in termination of pregnancy; FDA Pregnancy Category X	DailyMed; DrugBank
misoprostol	56:28.28 prostaglandins	FDA Pregnancy Category X	DailyMed; DrugBank

(continued)

Table 3 (Continued). Non-antineoplastic drugs that primarily have adverse reproductive effects

Drug	AHFS classification	Reason for listing	Links
nafarelin	68:18 gonadotropins	Note: Given only as nasal spray; no potential for occupational exposure; FDA Pregnancy Category X	DailyMed; DrugBank
oxytocin	76:00 oxytocics	Hazardous only for women in 3rd trimester; FDA Pregnancy Category C	DailyMed; DrugBank
paroxetine	28:16:04:20 selective serotonin uptake inhibitors	Increased risk of congenital abnormalities when taken in first trimester; complications in pregnancy when taken in third trimester; FDA Pregnancy Category D	DailyMed; Drugbank
pentetate calcium trisodium	NA	Severe teratogenic effects in laboratory studies in dogs: supplied in ampule which can lead to occupational exposure; FDA Pregnancy Category C	DailyMed
plerixafor	20:16 hematopoietic agents	Teratogenic in laboratory studies; FDA Pregnancy Category D	DailyMed; DrugBank
ribavirin	8:18:32 nucleosides and nucleotides	Teratogenic and embryotoxic effects in several laboratory studies; contraindicated in women who are pregnant and in the male partners of women who are pregnant; FDA Pregnancy Category X	DailyMed; DrugBank
telavancin	8:12:28 glycopeptides	Black Box warning for potential risk to fetus and adverse reproductive outcomes; reduced fetal weights and increased rates of digit and limb malformations in three species at clinical doses; FDA Pregnancy Category C	DailyMed; Drugbank

(continued)

Table 3 (Continued). Non-antineoplastic drugs that primarily have adverse reproductive effects*

Drug	AHFS classification	Reason for listing	Links
testosterone	68:08 androgens	Children should avoid contact with unwashed or unclothed application sites on skin; FDA Pregnancy Category X	DailyMed; DrugBank
topiramate	28:12.92 anticonvulsants, miscellaneous	FDA Pregnancy Category D	DailyMed; DrugBank
tretinoin	84:16 cell stimulants and proliferants	Black Box warning for severe birth defects; Special FDA distribution system; FDA Pregnancy Category X	DailyMed; DrugBank
ulipristal	68:12 contraceptives	FDA Pregnancy Category X	DailyMed
valproate/valproic acid	28:12:92 anticonvulsants, miscellaneous	Black Box warning for teratogenicity; congenital malformations including neural tube defects and others; teratogenic in multiple species; FDA Pregnancy Category D	DailyMed; DailyMed; DrugBank
vigabatrin	28:12:92 anticonvulsants, miscellaneous	Malformations seen in laboratory studies below the MRHD; FDA Pregnancy Category C	DailyMed; Drugbank
voriconazole	8:14.08 azoles	FDA Pregnancy Category D	DailyMed; DrugBank
warfarin	20:12.04.08 coumarin derivatives	FDA Pregnancy Category D	DailyMed; DrugBank
ziprasidone	28:16:08:04 atypical antipsychotics	Developmental toxicity, including possible teratogenic effects at doses similar to human therapeutic doses; an increase in the number of pups born dead and a decrease in postnatal survival at less than MRHD; FDA Pregnancy Category C	DailyMed; Drugbank

(continued)

Table 3 (Continued). Non-antineoplastic drugs that primarily have adverse reproductive effects*

Drug	AHFS classification	Reason for listing	Links
zoledronic acid	92:24 bone resorption inhibitors	Number of stillbirths increased and survival of neonates decreased in laboratory studies at low doses; FDA Pregnancy Category D	DailyMed; DrugBank
zonisamide	28:12:92 anticonvulsants, miscellaneous	Teratogenic in multiple animal species; FDA Pregnancy Category C	DailyMed; DrugBank

Table 4 lists drugs that were deleted from the 2004 and 2012 NIOSH hazardous drug lists. The 2004 list was a composite of five separate lists. When the drugs on that list were reviewed against the NIOSH criteria for hazardous drugs, these 11 drugs did not meet the criteria. Tetracycline was removed from the 2012 list on the basis of feedback from stakeholders.

*AHFS = American Hospital Formulary Service.

Table 4a. Drugs deleted from the 2004 hazardous drug list for not meeting the NIOSH criteria for hazardous drugs

Drug	AHFS Classification*
aldesleukin	10:00 antineoplastic agents
asparaginase	10:00 antineoplastic agents
denileukin	10:00 antineoplastic agents
estrone	68:16.04 estrogens
nilutamide	10:00 antineoplastic agents
pegaspargase	10:00 antineoplastic agents
pentamidine isethionate	8:40 miscellaneous anti-infectives
podofilox/podophyllum resin	84:36 miscellaneous skin and mucous membrane agents (mitotic inhibitor)
testolactone	10:00 antineoplastic agents
trifluridine	52:04.06 antivirals
vidarabine	52:04.06 antivirals

Table 4b. Drugs deleted from the 2012 list on the basis of stakeholder comments

Drug	AHFS Classification*
Tetracycline	8:12.24 tetracyclines

Table 5 provides general guidance for some of the possible scenarios that may be encountered in health care settings where hazardous drugs are handled, but it cannot cover all possible situations. This guidance applies to the drugs in Tables 1–3. For more detailed information on safe-handling practices, see the reference list [NIOSH 2004; ASHP 2006; USP 2008; ONS 2011].

Table 5. Personal protective equipment and engineering controls for working with hazardous drugs in healthcare settings*

Formulation	Activity	Double gloves	Protective gown	Eye protection	Respiratory protection	Ventilated engineering controls
Intact tablet or capsule	Administration from unit-dose package	no (single glove should be used)	no	no	no	N/A
Tablets or capsules	Cutting, crushing or otherwise manipulating tablets or capsules	yes	yes	no	yes, if not done in a control device	yes†
	Administration	yes	yes	no[2]	yes, if powder generated	N/A
Oral liquid drug	Compounding	yes	yes	yes, if not done in a control device	yes, if not done in a control device	yes†
	Administration	yes	yes	no‡	no‡	N/A
Topical drug	Compounding	yes	yes	yes	yes, if not done in a control device	yes†
	Administration	yes	yes	yes, if liquid that could splash‡	yes, if inhalation potential	N/A
Ampoule	Opening	yes	yes	yes, if not done in a control device	yes, if not done in a control device	yes, BSC or CACI

(continued)

Table 5 (Continued). Personal protective equipment and engineering controls for working with hazardous drugs in healthcare settings*

Formulation	Activity	Double gloves	Protective gown	Eye protection	Respiratory protection	Ventilated engineering controls
Subcutaneous, intramuscular injection	Preparation (withdrawing from vial or ampoule)	yes	yes	yes, if not done in a control device	yes, if not done in a control device	yes, BSC or CACI
	Administration from prepared syringe	yes	yes	yes, if liquid that could splash‡	yes, if inhalation potential‡	N/A
Intravenous solution	Compounding	yes	yes	yes, if not done in a control device	yes, if not done in a control device	yes, BSC or CACI; recommend use of CSTD
	Administration of prepared solution§	yes	yes	yes, if liquid that could splash‡	yes, if inhalation potential‡	N/A; recommend use of CSTD
Solution for irrigation	Compounding	yes	yes	yes, if not done in a control device	yes, if not done in a control device	yes, BSC or CACI; recommend use of CSTD
	Administration (bladder, HIPEC, limb perfusion, etc.)	yes	yes	yes	yes	N/A
Powder/ solution for inhalation	Inhalation	yes	yes	yes	yes	yes, when applicable

*The table provides general guidance for some of the possible scenarios that may be encountered in healthcare settings, but cannot cover all possible situations. For more detailed information on safe handling practices, see the reference list [NIOSH 2004; ASHP 2006; USP 2008, and ONS 2011]. BSC = Class II biological safety cabinet; CACI = compounding aseptic containment isolator; CSTD = closed system drug transfer device; HIPEC = hyperthermic intraperitoneal chemotherapy.

†For nonsterile preparations, an engineering control such as a fume hood or Class I BSC is sufficient. It is recommended that these activities be carried out in a control device, but it is recognized that under some circumstances, it is not possible. If the activity is performed in an engineering control that is used for sterile intravenous preparations, a thorough cleaning is required following the activity.

‡Required if patient may resist (infant, unruly patient, veterinary patient) or if administered by feeding tube.

§Intravenous tubing already attached and primed.

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DHHS (NIOSH) Publication No. 2014-138 (Supersedes 2012-150)

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