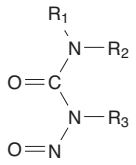
Nitrosourea Chemotherapeutic Agents



Generic nitrosourea structure

Introduction

Five nitrosourea chemotherapeutic agents are listed in the Report on Carcinogens as individual chemicals and not as a class. The generic structure for a nitrosourea is shown above (the simplest member of the nitrosourea class, *N*-nitrosourea, has hydrogen atoms for the R_1, R_2, and R_3 groups). The five nitrosourea chemotherapeutic agents share a common mechanism of action for their cytotoxicity and antitumor activity, which result from their nonenzymatic decomposition to produce products with alkylating and carbamoylating activities (Lemoine *et al.* 1991, Chabner *et al.* 2001). The 2-chloroethylnitrosoureas (CENUs) — 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU, lomustine), bis(chloroethyl) nitrosourea (BCNU, carmustine), 1-(2-chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea (methyl-CCNU, semustine), and chlorozotocin — degrade to form the 2-chloroethyl carbonium ion, which is a strong electrophile capable of alkylating guanine, cytidine, and adenine. If the chloride atom is displaced, intra- or inter-strand cross-links of DNA can result. Interstrand cross-links are considered to be associated with the cytotoxicity of nitrosoureas. Streptozotocin differs from the other four nitrosurea compounds in that it does not contain the 2-chloroethylnitrosourea group. Spontaneous degradation of nitrosourea compounds also can produce organic isocyanates that can carbamoylate lysine residues of proteins, and this reaction may inactivate some DNA repair enzymes. Of these five nitrosoureas, chlorozotocin and streptozotocin have low carbamoylating activity.

One of the nitrosourea compounds, methyl-CCNU, is listed as *known to be a human carcinogen*, and CCNU, BCNU, chlorozotocin, and streptozotocin are listed as *reasonably anticipated to be a human carcinogen*. In addition, two nitrosamines that share the nitrosourea structure, *N*-nitroso-*N*-methylurea and *N*-nitroso-*N*-ethylurea (see their profiles under Nitrosamines) are also listed as *reasonably anticipated to be a human carcinogen*.

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Lemoine A, Lucas C, Ings RMJ. 1991. Metabolism of the chloroethylnitrosoureas. *Xenobiotica* 21(6): 775-791.

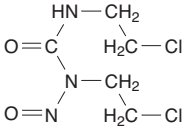
Bis(chloroethyl) Nitrosourea

CAS No. 154-93-8

Reasonably anticipated to be a human carcinogen

First listed in the *Fourth Annual Report on Carcinogens* (1985)

Also known as BCNU, carmustine, or *N*,*N*′-bis(2-chloroethyl) nitrosourea



Carcinogenicity

Bis(chloroethyl) nitrosourea (BCNU) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Exposure to BCNU by injection caused tumors in rats and mice at several different tissue sites. Lung tumors resulted from intraperitoneal injection of BCNU in rats of both sexes or intravenous injection in male rats, and tumors in the peritoneal cavity also were observed in male rats following intraperitoneal injection. Dermal exposure of mice to BCNU caused an early appearance of skin tumors induced by exposure to ultraviolet B radiation (IARC 1981, 1982).

Since BCNU was listed in the *Fourth Annual Report on Carcinogens,* an additional study in rats has been identified, in which BCNU administered by intravenous injection caused lung cancer (adenocarcinoma) and increased the incidence of neurogenic tumors (oligodendroglioma) (Eisenbrand 1984, Habs and Schmähl 1984).

Cancer Studies in Humans

The data available from studies in humans were inadequate to evaluate the relationship between human cancer and exposure specifically to BCNU. No epidemiological studies have evaluated exposure only to BCNU. However, BCNU is associated with the development of acute nonlymphocytic leukemia following its use with other anticancer therapies in the treatment of preexisting cancer (IARC 1987).

Properties

BCNU is bifunctional alkylating agent that is used as an antineoplastic agent. It is a chloroethyl nitrosourea compound that is an orange-yellow to light-yellow powder at room temperature (IARC 1981, Chabner *et al.* 2001, Akron 2009). BCNU is only slightly soluble in water and 50% ethanol, but is soluble in ethanol and lipids. It is sensitive to oxidation and hydrolysis at neutral pH with a half life of 98 minutes (IARC 1981). Physical and chemical properties of BCNU are listed in the following table.

Property	Information
Molecular weight	214.0[a]
Melting point	31°C[b]
Log K_{ow}	1.53[b]
Water solubility	4 g/L at 25°C[b]
Vapor pressure	3.69×10^{-5} mm at Hg 25°C[b]
Dissociation constant (pK_a)	10.19[a]

Sources: [a]Akron 2009, [b]ChemIDplus 2009.

Use

BCNU has been used since 1971 as an anticancer drug and in 1977 was approved by the U.S. Food and Drug Administration, as carmustine, to be marketed for the treatment of Hodgkin disease, non-Hodgkin lymphoma, multiple myeloma, and primary or metastatic brain tumors (IARC 1981, FDA 2009a, MedlinePlus 2009). It has also been used to treat malignant melanoma, breast cancer, gastrointestinal cancer, Ewing sarcoma, and Burkitt lymphoma and to be applied to the skin to treat mycosis fungoides (MedlinePlus 2009). BCNU may be used alone or in combination with other antineoplastic agents (ClinicalTrials 2009).

Production

No data on production volumes of BCNU were found. In 2009, BCNU was available from nine suppliers worldwide, including seven U.S. suppliers (ChemSources 2009). Carmustine is the active ingredient

in two pharmaceutical products, an intracranial implant and an injectable drug, which are available from two different pharmaceutical companies (FDA 2009b). The injectable product is available in 100-mg vials, and the implantable product comes in a 7.7-mg size.

Exposure

The primary routes of human exposure to BCNU are injection, implantation (FDA 2009b), and dermal contact in patients (MedlinePlus 2009). Reported doses of the injectable drug are 100 to 250 mg/m^2 of body surface area daily by intravenous injection for two or three days (IARC 1981). In 2009, 159 clinical trials involving BCNU alone or in combination with other antineoplastic agents and treatments were in progress or recently completed (ClinicalTrials 2009). Health professionals and support staff (including custodians) may be exposed to BCNU by dermal contact, inhalation, and accidental ingestion during drug preparation, administration, or cleanup of medical waste, including excretions from treated patents (Zimmerman *et al.* 1981, NIOSH 2004). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 14,122 health-services workers, including 10,338 women, potentially were exposed to BCNU (NIOSH 1990).

Regulations

Food and Drug Administration (FDA)

Carmustine is a prescription drug subject to labeling and other requirements.

Guidelines

National Institute for Occupational Safety and Health (NIOSH)

A comprehensive set of guidelines has been established to prevent occupational exposures to hazardous drugs in health-care settings.

Occupational Safety and Health Administration (OSHA)

A comprehensive set of guidelines has been established to prevent occupational exposures to hazardous drugs in health-care settings.

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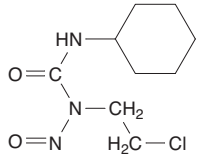
1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea

CAS No. 13010-47-4

Reasonably anticipated to be a human carcinogen

First listed in the *Fourth Annual Report on Carcinogens* (1985)

Also known as CCNU or lomustine



Carcinogenicity

1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Exposure to CCNU by injection caused tumors in rodents. Lung tumors resulted from intraperitoneal injection of CCNU in rats of both sexes or intravenous injection in male rats (IARC 1981, 1982). Following intraperitoneal injection of CCNU, a slight increase in the incidence of malignant lymphoma (lymphosarcoma) was observed in mice of both sexes.

Cancer Studies in Humans

The data available from studies in humans were inadequate to evaluate the relationship between human cancer and exposure specifically to CCNU. In several reported cases, cancer patients who received CCNU developed leukemia; however, all but one of these patients had also been treated with other cytotoxic agents and/or irradiation (IARC 1981, 1982).

Properties

CCNU is a bifunctional alkylating agent that is used as an antineoplastic agent. It is a chloroethyl nitrosourea compound that is a yellow powder at room temperature. It is practically insoluble in water, soluble in ethanol, 0.1 N hydrochloric acid, and sodium hydroxide, and highly soluble in lipids. It may be oxidized or hydrolyzed at room temperature and neutral pH with a half-life of 117 minutes (IARC 1981, 1987, HSDB 2009). Physical and chemical properties of CCNU are listed in the following table.

Property	Information
Molecular weight	233.7[a]
Melting point	88°C to 90°C[b]
Log K_{ow}	2.83[b]
Water solubility	111 mg/L at 25°C[b]
Vapor pressure	1.01×10^{-5} mm Hg at 25°C[b]

Sources: [a]HSDB 2009; [b]ChemIDplus 2009.

Use

CCNU is an oral anticancer drug that was approved by the U.S. Food and Drug Administration in 1976 for marketing, as lomustine (FDA 2009a). CCNU is used alone or in combination with other antineoplastic agents, including procarbazine and vincristine, etoposide and prednimustine, and other combinations (IARC 1981, HSDB 2009). It is used primarily in the treatment of Hodgkin disease and brain tumors, but it has also been used to treat other cancer, including lung cancer, non-Hodgkin lymphoma, malignant melanoma, breast cancer, kidney cancer, and cancer of the gastrointestinal tract (MedlinePlus 2009). It has also been applied to the skin to treat mycosis fungoides and psoriasis.

Production

CCNU was first synthesized in 1966 (IARC 1981). In 2009, it was produced by two manufacturers, one in China and one in Europe (SRI 2009), and was available from eighteen suppliers, including nine U.S. suppliers (ChemSources 2009). CNNU (lomustine) is the active ingredient in three products (capsules in strengths of 10, 40, and 100 mg) from a single pharmaceutical company (FDA 2009b).

Exposure

The primary route of human exposure to CCNU is ingestion during its use as a pharmaceutical product; however, exposure potentially can also occur through inhalation and dermal contact (Akron 2009, MedlinePlus 2009). The recommended dose for adults and children is 130 mg/m^2 of body surface, given as a single oral dose every six weeks (IARC 1981). In 2009, 45 clinical trials involving CCNU were in progress or recently completed, including 12 that had not completed patient recruitment (ClinicalTrials 2009). Health professionals and support staff (including custodians) may be exposed by dermal contact, inhalation, or accidental ingestion during drug preparation, administration, or cleanup of medical waste, including excretions from treated patents (Zimmerman *et al.* 1981, NIOSH 2004). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 2,457 health-services workers, including 1,069 women, potentially were exposed to CCNU (NIOSH 1990).

Regulations

Consumer Product Safety Commission (CPSC)

Any orally administered prescription drug for human use requires child-resistant packaging.

Food and Drug Administration (FDA)

Lomustine is a prescription drug subject to labeling and other requirements.

Guidelines

National Institute for Occupational Safety and Health (NIOSH)

A comprehensive set of guidelines has been established to prevent occupational exposures to hazardous drugs in health-care settings.

Occupational Safety and Health Administration (OSHA)

A comprehensive set of guidelines has been established to prevent occupational exposures to hazardous drugs in health-care settings.

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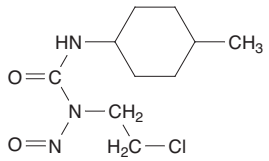
1-(2-Chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea

CAS No. 13909-09-6

Known to be a human carcinogen

First listed in the *Sixth Annual Report on Carcinogens* (1991)

Also known as methyl-CCNU, MeCCNU, or semustine



Carcinogenicity

1-(2-Chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea (methyl-CCNU) is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans.

Cancer Studies in Humans

An increased relative risk (over 12-fold) for nonlymphocytic leukemia was found among patients with gastrointestinal cancer who were treated with methyl-CCNU in several clinical trials; 14 cases of leukemic disorders were reported among 2,067 patients given methyl-CCNU, compared with only 1 case of acute nonlymphocytic leukemia among 1,566 patients given other therapies (Boice *et al.* 1983). A later analysis of this study found that the risk of leukemia increased with increasing cumulative dose of methyl-CCNU, reaching a relative risk of about 40-fold, adjusted for survival time, among patients treated with the highest dose (Boice *et al.* 1986, IARC 1987).

Cancer Studies in Experimental Animals

There is limited evidence for the carcinogenicity of methyl-CCNU in experimental animals (Weisburger 1977). Methyl-CCNU admin-

istered by intravenous injection caused lung tumors in male rats. Administered by intraperitoneal injection, it increased the total incidence of all tumors in male rats and slightly increased the incidence of leukemia and malignant lymphoma (lymphosarcoma) in female mice (IARC 1987).

Properties

Methyl-CCNU is a direct-acting bifunctional alkylating agent that has been tested for use as an antineoplastic agent. It is a chloroethyl nitrosourea compound that is a light-yellow powder at room temperature (IARC 1987, Akron 2009). It is practically insoluble in water (ChemIDplus 2009). Physical and chemical properties of methyl-CCNU are listed in the following table.

Property	Information
Molecular weight	247.7[a]
Melting point	70°C[b]
Log K_{ow}	3.3[a]
Water solubility	0.037 g/L at 25°C[a]
Vapor pressure	5.61×10^{-6} mm Hg at 25°C[a]

Sources: [a]ChemIDplus 2009, [b]Akron 2009.

Use

Methyl-CCNU is an investigational chemotherapy drug that has been used in clinical trials to treat several types of cancer, including brain cancer, malignant melanoma, lung cancer, and gastrointestinal-tract cancer (Boice *et al.* 1983). As of 2009, it had not been approved by the U.S. Food and Drug Administration for any uses (FDA 2009).

Production

No data on U.S. production, imports, or exports of methyl-CCNU were found. In 2009, methyl-CCNU was available from eight suppliers worldwide, including six U.S. suppliers (ChemSources 2009).

Exposure

The most direct exposure to methyl-CCNU is of cancer patients participating in clinical trials of treatment regimens that include methyl-CCNU. In 2009, two completed clinical trials involving methyl-CCNU were identified (ClinicalTrials 2009). The typical oral dose is 125 to 200 mg/m^2 of body surface area, repeated every six weeks (Parfitt 1999). Health professionals and support staff (including custodians) may be exposed to methyl-CCNU by dermal contact, inhalation, or accidental ingestion during drug preparation, administration, or cleanup of medical waste, including excretions from treated patents (Zimmerman *et al.* 1981, NIOSH 2004). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 229 workers, including 82 women, potentially were exposed to methyl-CCNU (NIOSH 1990).

Regulations

No specific regulations or guidelines relevant to reduction of exposure to methyl-CCNU were identified.

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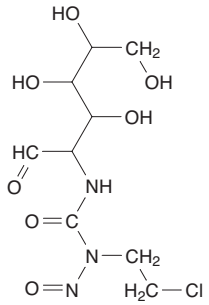
Chlorozotocin

CAS No. 54749-90-5

Reasonably anticipated to be a human carcinogen

First listed in the *Eighth Report on Carcinogens* (1998)



Carcinogenicity

Chlorozotocin is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals and because it is a member of a well-defined, structurally related class of substances listed in the Report on Carcinogens as either *known to be a human carcinogen* or *reasonably anticipated to be a human carcinogen*.

Cancer Studies in Experimental Animals

Exposure to chlorozotocin caused tumors at several different tissue sites in rats. Chlorozotocin administered to male rats by intravenous injection caused cancer of the nervous system, lungs, and forestomach. Intraperitoneal injection of chlorozotocin caused tumors in the abdominal cavity (sarcoma or mesothelioma) in rats of both sexes (IARC 1990).

Cancer Studies in Humans

No epidemiological studies were identified that evaluated the relationship between human cancer and exposure specifically to chlorozotocin.

Studies on Mechanisms of Carcinogenesis

Chlorozotocin is structurally related to other chloroethyl nitrosoureas, one of which, 1-(2-chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea, is listed in the Report on Carcinogens as *known to be a human carcinogen*, and two of which, bis(chloroethyl) nitrosourea and 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea, are listed in the Report on Carcinogens as *reasonably anticipated to be a human carcinogen.* Chlorozotocin exerts its adverse effects through the formation of mono- and bi-functional alkylating agents. It causes genetic damage in a wide variety of bacterial and mammalian cellular assays, inducing mutations in bacteria, yeast, insects, and cultured mammalian cells and DNA damage in human, mouse, and Chinese hamster cells *in vitro* and in bone-marrow cells in rats exposed *in vivo* (IARC 1990). In rats subcutaneously implanted with rhabdomyosarcoma cells, chlorozotocin administered by intraperitoneal injection increased metastasis to the lungs (Pauwels *et al.* 1985). There is no evidence to suggest that the mechanisms by which chlorozotocin causes tumors in experimental animals would not also operate in humans.

Properties

Chlorozotocin is a nitrosourea compound that exists as ivory-colored crystals at room temperature. It is soluble in water and is stable in solution at room temperature for up to 3 hours and under refrigeration for 24 hours. The powder form of chlorozotocin is stable under refrigeration for two years. The spontaneous, nonenzymatic degradation of chlorozotocin results in formation of DNA-alkylating and protein-carbamoylating moieties (Chabner *et al.* 2001). Physical and chemical properties of chlorozotocin are listed in the following table.

Property	Information
Molecular weight	265.7[a]
Melting point	147°C to 148°C (decomposes with evolution of gas)[b]
Log K_{ow}	–1.02[b]
Water solubility	1.8 g/L at 25°C[a]
Vapor pressure	3.98×10^{-14} mm Hg at 25°C[a]
Dissociation constant (pK_a)	9.08[c]

Sources: [a]ChemIDplus 2009, [b]HSDB 2009, [c]Akron 2009.

Use

Chlorozotocin is a cytostatic agent that has been used to treat melanoma and multiple myeloma and cancer of the stomach, large intestine, pancreas, and lung (IARC 1990). As of 2009, no products containing chlorozotocin as an active ingredient had been approved for use by the U.S. Food and Drug Administration (FDA 2009).

Production

Synthesis of chlorozotocin occurs by nitrosation of the urea derivative prepared from D-glucosamine and 2-chloroethyl isocyanate. Chlorozotocin was reported to be produced in the United States (IARC 1990), but no production data were found, nor any data on U.S. imports or exports of chlorozotocin, and no U.S. suppliers were identified.

Exposure

The primary route of potential human exposure to chlorozotocin is intravenous administration. Chlorozotocin has been given intravenously at doses of 100 to 225 mg/m^2 of body surface area (IARC 1990). Health professionals and support staff (including custodians) may be exposed to chlorozotocin by dermal contact, inhalation, or accidental ingestion during drug preparation, administration, or cleanup of medical waste, including excretions from treated patients (NIOSH 2004, Zimmerman *et al.* 1981). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 267 health-services workers, including 223 women, potentially were exposed to chlorozotocin (NIOSH 1990).

Regulations

No specific regulations or guidelines relevant to reduction of exposure to chlorozotocin were identified.

Guidelines

National Institute for Occupational Safety and Health (NIOSH)

A comprehensive set of guidelines has been established to prevent occupational exposures to hazardous drugs in health-care settings.

Occupational Safety and Health Administration (OSHA)

A comprehensive set of guidelines has been established to prevent occupational exposures to hazardous drugs in health-care settings.

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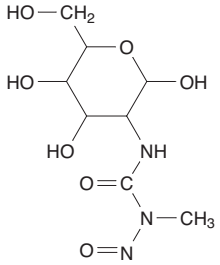
Streptozotocin

CAS No. 18883-66-4

Reasonably anticipated to be a human carcinogen

First listed in the *Second Annual Report on Carcinogens* (1981)



Carcinogenicity

Streptozotocin is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Exposure to streptozotocin by injection caused tumors at several different tissue sites in three rodent species. Administration of strep-

tozotocin by intraperitoneal injection caused kidney tumors in rats and mice of both sexes. In mice, it also caused lung tumors in both sexes and uterine tumors in females. In rats, it also caused pancreatic tumors in both sexes, liver tumors in females, and cancer of the abdominal cavity (sarcoma of the peritoneum) in males. In hamsters, it caused tumors of the liver (hepatocellular carcinoma) or bile duct (cholangioma) in both sexes (IARC 1978). A single intravenous injection of streptozotocin caused malignant or benign kidney tumors (adenocarcinoma, sarcoma, or adenoma) in rats of both sexes (IARC 1974, 1978, Rakieten and Gordon 1975).

Since streptozotocin was listed in the *Second Annual Report on Carcinogens,* additional studies in rodents have been identified. Intravenous injection of streptozotocin increased the incidence of benign or malignant kidney tumors in mice of both sexes (Hard 1985, Delahunt *et al.* 1995) and the incidence of benign tumors of the kidney, pancreas, liver, bile duct, and testis in male rats (Feldman *et al*. 1977, Kazumi *et al.* 1978, Okawa and Doi 1983). Pancreatic tumors (islet-cell adenoma, ductular adenoma, or insulinoma) also were observed in hamsters of both sexes after a single intravenous injection of streptozotocin (Pour and Patil 1983) and in male hamsters after intraperitoneal injection (Pour *et al.* 1990).

Cancer Studies in Humans

The data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure specifically to streptozotocin.

Properties

Streptozotocin is a nitrosourea compound that exists as pale-yellow or ivory pointed platelets or prisms at room temperature (HSDB 2009). It is soluble in water, lower alcohols, and ketones, slightly soluble in most other polar organic solvents, and insoluble in nonpolar organic solvents. Streptozotocin is sensitive to humidity and light and decomposes rapidly at temperatures over 70°C (IARC 1974). It is most stable in acidic solutions and decomposes rapidly in alkaline solutions. Physical and chemical properties of streptozotocin are listed in the following table.

Property	Information
Molecular weight	265.2[a]
Melting point	115°C[b]
Log K_{ow}	–1.45[b]
Water solubility	5.070 g/L at 25°C[b]
Vapor pressure	1.74×10^{-12} mm Hg at 25°C[b]
Dissociation constant (pK_a)	1.35[a]

Sources: [a]HSDB 2009; [b]ChemIDplus 2009.

Use

Streptozotocin was approved by the U.S. Food and Drug Administration in 1982, as Zanosar, to be marketed for treatment of pancreatic cancer (FDA 2009a). It has also been used to induce and study diabetes, because it has a specific toxic action on pancreatic β-cells (IARC 1974, 1978). Streptozotocin has been investigated as a potential antibacterial agent, but has never been used commercially for this purpose. It is used to treat pancreatic islet-cell cancer, pancreatic adenocarcinoma, Hodgkin disease, colorectal cancer, liver cancer (hepatocellular carcinoma), adrenal-gland cancer (pheochromocytoma), lung cancer (epidermoid carcinoma), lymphocytic lymphoma, Burkitt lymphoma, acute lymphocytic leukemia, malignant melanoma, metastatic sarcoma, and malignant carcinoid tumors (IARC 1978, MedlinePlus 2009).

Production

Streptozotocin is derived from the bacterium *Streptomyces achromogenes* and has been synthesized by three different procedures (IARC 1978, HSDB 2009). In 2009, it was produced by one manufacturer worldwide, in the United States (SRI 2009), and was available from 24 suppliers, including 15 U.S. suppliers (ChemSources 2009). No data on U.S. imports or exports of streptozotocin were found.

Exposure

Streptozotocin is available as an injectable product in 1-g vials from a single U.S. pharmaceutical company (FDA 2009b). In 2009, eight clinical trials using streptozotocin in combination with other antineoplastic agents as treatment for pancreatic, brain, colorectal, adrenal cortical, or various other endocrine tumors were in progress or recently completed (ClinicalTrials 2009). Health professionals and support staff (including custodians) may be exposed to streptozotocin by dermal contact, inhalation, or accidental ingestion during drug preparation, administration, or cleanup of medical waste, including excretions from treated patients (Zimmerman *et al.* 1981, NIOSH 2004). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 2,074 workers, including 1,713 women, potentially were exposed to streptozotocin (NIOSH 1990).

Regulations

Environmental Protection Agency (EPA)

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 1 lb.

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste code for which the listing is based wholly or partly on the presence of streptozotocin = U206.

Listed as a hazardous constituent of waste.

Food and Drug Administration (FDA)

Streptozotocin is a prescription drug subject to labeling and other requirements.

Guidelines

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Occupational Safety and Health Administration (OSHA)

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