SAFETY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/ UNDERTAKING

Contact information

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Product identifier

Abraxane® Powder for Suspension for Infusion (Albumin-bound paclitaxel for infusion)

Synonyms

Albumin-bound paclitaxel for infusion; ABI-007; Albumin-bound paclitaxel; *nab*-paclitaxel; 5β,20-epoxy-1,2α,4,7β,10β, 13α-hexahydroxytax-11-en-9-one 4,10-diacetate 2-benzoate 13-ester with (2R, 3S)-N-benzoyl-3-phenylisoserine.

Trade names

Abraxane®

Chemical family

Taxanes

Relevant identified uses of the substance or mixture and uses advised against

Bulk formulated pharmaceutical product/Formulated pharmaceutical product packaged in final form and intended for the final user; a microtubule stabilizer indicated for the treatment of certain types of cancer.

Note

The toxicological and ecological properties of this product have not been fully characterized. This SDS will be revisited as more data become available.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture

Drugs in the finished state and intended for the final user are not subject to labeling in the US, EU or Canada. Please consult the prescribing/packaging information. **The classification and labeling listed below is for the powder mixture (in vials).**

Globally Harmonized System [GHS]

Carcinogenic - Category 2. Germ Cell Mutagenicity - Category 2. Reproductive Toxicity - Category 1B. Specific Target Organ Toxicity (repeated exposure) - Category 1. Specific Target Organ Toxicity (single exposure) - Category 2.

Other/Supplemental

Hazard Classification (NOHSC) - CYTOTOXIC.

Label elements

GHS hazard pictogram

GHS signal word

Danger

GHS hazard statements

H341 - Suspected of causing genetic defects. H351 - Suspected of causing cancer. H360FD - May damage fertility. May damage the unborn child. H372 - Causes damage to lymphatic, cardiovascular, gastrointestinal, and nervous systems through prolonged or repeated exposure. H371 - May cause damage to bone marrow.

GHS precautionary statements

P201 - Obtain special instructions before use. P260 - Do not breathe dust. P264 - Wash hands thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. P281 - Use personal protective equipment as required. P309 + P311 - IF exposed or if you feel unwell: call a Poison Center or doctor/physician. P403 + P233 - Store in a well-ventilated place. Keep container tightly closed. P405 - Store locked up. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.

Additional elements

Other hazards

The most commonly reported adverse effect associated with therapeutic use of Abraxane® is reversible, dose-dependent bone marrow suppression, primarily in the form of neutropenia (decreased white blood cells). Other frequently reported effects include infections, hair loss, sensory neuropathy, increased blood pressure and electrocardiogram abnormalities, muscle/joint/chest pain, weakness, gastrointestinal disturbances (*e.g.,* nausea, diarrhea), and increased liver enzymes. Increased creatinine levels, ocular/visual disturbances, shortness of breath, and cough were also noted. Severe hypersensitivity reactions were rarely reported in

SECTION 2 - HAZARDS IDENTIFICATION …continued

Other hazards …continued

post-marketing surveillance.

Abraxane® contains albumin (human), a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. No cases of transmission of viral diseases or CJD have ever been identified for Abraxane®. Based on its mechanism of action and animal study results, a potential for Abraxane® to impair male fertility and harm a developing fetus cannot be excluded in the absence of definitive data.

Note

This substance is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA).

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ ELINCS#	Amount	GHS Classification
Albumin-bound paclitaxel	N/A	N/A	~100 %	RT1B: H360FD; Carc2: H351; GCM2: H341; STOT-S2: H371; STOT-R1: H372

Note

The ingredient(s) listed above are considered hazardous. The pharmacological and toxicological characteristics of this compound have not been fully characterized. See Section 16 for full text of GHS classifications.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed

Yes. If exposed or concerned: Get medical advice/attention.

Eye Contact

If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.

Skin Contact

Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.

Inhalation

Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.

Ingestion

Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.

SECTION 4 - FIRST AID MEASURES …continued

Protection of first aid responders	See Section 8 for Exposure Controls/Personal Protection recommendations.
Most important symptoms and effects, both acute and delayed	See Sections 2 and 11.
Indication of immediate medical attention and special treatment needed, if necessary	Abraxane® contains paclitaxel, a cytotoxic antineoplastic agent. Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective package or prescribing information for potential drug interactions.

SECTION 5 - FIREFIGHTING MEASURES

Extinguishing media	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
Specific hazards arising from the substance or mixture	No information identified. May emit carbon monoxide, carbon dioxide, and oxides of nitrogen.
Flammability/ Explosivity	No explosivity or flammability data identified. High concentrations of finely divided airborne organic particles can potentially explode if ignited.
Advice for firefighters	Wear full protective clothing and a self-contained breathing apparatus with a full facepiece operated in the pressure demand or other positive pressure mode. Decontaminate all equipment after use.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. Do not breathe dust.
Environmental precautions	Do not empty into drains. Avoid release to the environment.
Methods and material for containment and cleaning up	If vials are crushed/broken: DO NOT RAISE DUST. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize entry of powder into the air. Add excess liquid to allow the material to enter solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container suitable for disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice.
Reference to other sections	See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling

If vials are crushed or broken, dust containing drug substance may be released. Minimize dust generation and accumulation. Follow recommendations for handling potent and cytotoxic pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid breathing dust. Wash thoroughly after handling. Avoid exposure to light.

Conditions for safe storage including any incompatibilities

Store at controlled room temperature (20- 25°C) away from incompatible materials. Excursions are permitted to 15-30°C. Store out of direct sunlight in dark, dry conditions.

Specific end use(s)

No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note

Dispose of broken vials/syringes in a sharps container.

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Albumin-bound paclitaxel	Celgene	TWA-8 HR	2 µg/m³

Exposure/Engineering controls

None required for normal handling of packaged product. If vials are crushed/ broken: Open handling should not be performed when handling potent substances or substances of unknown toxicity. Control exposures to below the OEL (if available). Otherwise, selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Material should be handled inside a closed process, ventilated enclosure, isolator or device of equivalent or better control that is suitable for dusts and/or aerosols.

Respiratory protection

None required for normal handling of packaged product. If vials are crushed/ broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine powder handling tasks, an approved and properly worn powered air-purifying respirator equipped with HEPA filters or combination filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where air purifying respirators may not provide adequate protection.

Hand protection

Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

Skin protection

Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Eye/face protection	Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.
Environmental Exposure Controls	Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.
Other protective measures	Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	Lyophilized cake/powder in vials
Color	White to off-white
Odor	Odorless
Odor threshold	No information identified.
pH	6.0-7.5 (reconstituted)
Melting point/ freezing point	~216 °C
Initial boiling point and boiling range	No information identified.
Flash point	No information identified.
Evaporation rate	No information identified.
Flammability (solid, gas)	No information identified.
Upper/lower flammability or explosive limits	No information identified.
Vapor pressure	No information identified.
Vapor density	No information identified.
Relative density	No information identified.
Water solubility	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Solvent solubility	No information identified.
Partition coefficient (*n-octanol/water*)	No information identified.
Auto-ignition temperature	No information identified.
Decomposition temperature	No information identified.
Viscosity	No information identified.
Explosive properties	No information identified.
Oxidizing properties	No information identified.

Other information

Molecular formula	$C_{47}H_{51}NO_{14}$
Molecular weight	853.9 (paclitaxel); ~67 kDa (albumin)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	Stable under normal temperatures and pressures.
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	Light
Incompatible materials	Strong oxidizers, acids, bases.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note **The following data describe Abraxane® and/or paclitaxel.**

Information on toxicological effects

Route of entry Intended for IV use. Large protein are unlikely to be absorbed through inhalation, skin contact, or ingestion.

Acute toxicity

Compound	Type	Route	Species	Dose
Albumin-bound paclitaxel	LD_{50}	Intravenous	Mouse	12 mg/kg (paclitaxel)
	LD_{50}	Intravenous	Rat	85 mg/kg (paclitaxel)

Irritation/Corrosion	No data available.
Sensitization	No data available.
STOT-single exposure	Myelosuppression was observed in rats following single Abraxane® doses (details not specified). In another study, single doses ≥9 mg/m^2 IV resulted in necrosis/ diffuse degeneration of the testes doses. Testicular degeneration/atrophy was seen in dogs at 175 mg/m^2, in addition to serum sickness.
STOT-repeated exposure/Repeat-dose toxicity	Administration of 100 mg/m^2 Abraxane® IV to monkeys on a weekly schedule for 3 weeks led to myelosuppression, organ weight changes (increased spleen weight, decreased thymus, pituitary, testes, liver, and thyroid), and microscopic changes in the thymus, heart, male reproductive organs, and liver. Administration of ≥10 mg/kg IV to rats resulted in mortality, atrophic changes in the lymphatic/hematopoietic tissues, male reproductive organs, and skin, in addition to degenerative changes in the nervous system and eyes. Effects were mostly reversible following a 4-week recovery period, except for those in the reproductive organs, central nervous system, and eye. A NOAEL for Abraxane was not identified.
Reproductive toxicity	In a 12-week study in male rats, weekly IV doses of Abraxane® caused decreased litter sizes at 7 mg/kg and irreversible sterility at 16 mg/kg. A NOAEL of 2 mg/kg/ week was established for effects on male fertility.
Developmental toxicity	Daily IV Abraxane® injections of 1-2 mg/kg in pregnant rats increased the number of fetal deaths, resorptions, malformations, and was maternally toxic. A NOAEL of 0.5 mg/kg/day was established for fetal/maternal toxicity.
Genotoxicity	Paclitaxel was negative for mutagenicity in a bacterial Ames assay, a mutation assay in Chinese hamster ovary cells, and a *Drosophila* wing somatic mutation and recombination test, but was positive for clastogenicity in an *in vitro* cytogenetics assay in primary human lymphocytes and an *in vivo* mouse bone marrow micronucleus assay.
Carcinogenicity	Long-term carcinogenicity studies with Abraxane® have not been conducted. This substance is not listed by NTP, IARC, ACGIH or OSHA as a carcinogen.
Aspiration hazard	No data available.
Human health data	See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Albumin-bound paclitaxel	LC_{50} (time not specified)	Daphnia magna	>0.7 mg/L (paclitaxel)
	LC_{50} (time not specified)	Activated sludge	>1000 mg/L (paclitaxel)

Persistence and Degradability No data available.

Bioaccumulative potential No data available.

Mobility in soil No data available.

Results of PBT and vPvB assessment Not performed.

Other adverse effects No data available.

Note The environmental characteristics of the substance have not been fully investigated. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods Dispose of wastes by appropriately permitted chemical waste incinerator in accordance to prescribed federal, state, and local guidelines. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, *e.g.*, appropriately permitted municipal or onsite wastewater treatment facility.

SECTION 14 - TRANSPORT INFORMATION

Transport Based on the available data, this substance is not regulated as a hazardous material/ dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, IMDG, or ADG Code. No special transport conditions are necessary unless required by other regulations.

UN number None assigned.

UN proper shipping name None assigned.

Transport hazard classes and packing group None assigned.

Environmental hazards Based on the available data, this substance is not regulated as an environmental hazard or a marine pollutant.

SECTION 14 - TRANSPORT INFORMATION …continued

Special precautions for users	Cytotoxic - Handle with Care.
Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code	Not applicable.
Hazardchem Code/HIN	None assigned.

SECTION 15 - REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture	This SDS generally complies with the requirements listed under current guidelines in the US, EU, Canada and Australia. Consult your local or regional authorities for more information.
Chemical safety assessment	Not conducted.
TSCA status	Not listed
SARA section 313	Not listed.
California proposition 65	Contains paclitaxel which is listed as a developmental toxicant and a reproductive toxicant (male and female).
Additional information	SUSMP: Schedule 4 (prescription only medicine)

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications	GCM2 - Germ Cell Mutagenicity Category 2. H341 - Suspected of causing genetic defects. Carc2 - Carcinogenicity Category 2. H351 - Suspected of causing cancer. RT1B - Reproductive toxicity Category 1B. H360FD - May damage fertility. May damage the unborn child. STOT-R1 - Specific Target Organ Toxicity Following Repeated Exposure Category 1. H372 - Causes damage to lymphatic, cardiovascular, gastrointestinal, and nervous systems through prolonged or repeated exposure.
Sources of data	Information from published literature and internal company data.
Abbreviations	ACGIH - American Conference of Government Industrial Hygienists; ADG - Australian Dangerous Goods Code; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AHSEL - Australian health, safety and environmental legislation; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified

SECTION 16 - OTHER INFORMATION …continued

Abbreviations …continued

Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; HIN - Hazard Identification Number (Australia); IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NOHSC - National Occupational Health & Safety Commission; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STEL - Short Term Exposure Limit; STOT - Specific Target Organ Toxicity; SUSMP - Standard for the Uniform Scheduling of Medicines and Poisons; TDG - Transport Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System

Issue Date

11 April 2018

Revisions

Updated synonyms in Section 1, classifications in Section 2, and data in Section 11

Disclaimer

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a potent pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.