SAFETY DATA SHEET

1. Identification

Product identifier **HYCAMTIN INJECTABLE**

Other means of identification Not available.

Synonym(s) HYCAMTIN INFUSION 1 MG/3 ML * HYCAMTIN INJECTION 1 MG/3 ML * HYCAMTIN INJECTION 4 MG/5 ML * HYCAMTIN INJECTION (CONTAINING 10% TOPOTECAN) * TOPOTECAN, FORMULATED PRODUCT

Recommended use Medicinal Product

This safety data sheet is written to provide health, safety and environmental information for people handling this formulated product in the workplace. It is not intended to provide information relevant to medicinal use of the product. In this instance patients should consult prescribing information/package insert/product label or consult their pharmacist or physician. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate safety data sheet for each ingredient.

Recommended restrictions No other uses are advised.

Manufacturer/Importer/Supplier/Distributor information

Manufacturer

GlaxoSmithKline US
5 Moore Drive
Research Triangle Park, NC 27709 USA
US General Information (normal business hours): +1-888-825-5249
Email Address: msds@gsk.com
Website: www.gsk.com
EMERGENCY PHONE NUMBERS -
TRANSPORT EMERGENCIES::
US / International toll call +1 703 527 3887
available 24 hrs/7 days; multi-language response

2. Hazard(s) identification

Classified hazards

Exempt from requirements - product regulated as a medicinal product, cosmetic product or medical device.

Label elements

Exempt from requirements - product regulated as a medicinal product, cosmetic product or medical device.

Hazard(s) not otherwise classified (HNOC)

Exempt from requirements - product regulated as a medicinal product, cosmetic product or medical device.

3. Composition/information on ingredients

Mixtures

Hazardous components

Chemical name	Common name and synonyms	CAS number	%
MANNITOL	D-MANNITOL 1,2,3,4,5,6-HEXANEHEXOL MANNA SUGAR MANNITE OSMITROL BP-686 MANNITOL, D- DIOSMOL MANITON-S MANNIDEX MANNIGEN MANNISTOL OSMOSOL D-MANNITE CORDYCEPIC ACID D-(-)-MANNITOL MANNITOLUM OSMOSAL ISOTOL C6H14O6 OHS13660 RTECS OP2060000	69-65-8	60
TARTARIC ACID	2,3-DIHYDROXY-(R-(R*, R*)BUTANEDIOIC ACID DEXTROTARTARIC ACID 2,3-DIHYDROXYBUTANEDIOIC ACID NATURAL TARTARIC ACID (+)-TARTARIC ACID L-TARTARIC ACID (+)-L-TARTARIC ACID L-(+)-TARTARIC ACID (R,R)-TARTARIC ACID (R,R)-(+)-TARTARIC ACID (2R,3R)-TARTARIC ACID L-THREOIC ACID L-2,3-DIHYDROXYBUTANEDIOIC ACID DIHYDROXYSUCCINIC ACID D-TARTARIC ACID (+)-(R,R)-TARTARIC ACID (2R,3R)-(+)-TARTARIC ACID 1,2-DIHYDROXYETHANE-1,2-DICARBOXYL ACID D-ALPHA,BETA-DIHYDROXYSUCCINIC ACID THREARIC ACID RTECS WW7875000 885 (GW ACN)	87-69-4	30
TOPOTECAN	(S)-10-((DIMETHYLAMINO)METHYL)-4-ETH DOLIZINO(1,2-B)QUINOLINE-3,14(4H,12H)-I MONOHYDROCHLORIDE SKF-104864-A TOPOTECAN HYDROCHLORIDE	119413-54-6	10

*Designates that a specific chemical identity and/or percentage of composition has been withheld as a trade secret.

4. First-aid measures

Inhalation
If not breathing, give artificial respiration. If breathing is difficult, trained personnel should give oxygen. Get medical attention immediately.

Skin contact
Immediately flush with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Get medical attention if symptoms occur.

Eye contact
In the case of contact with eyes, rinse immediately with plenty of water and seek medical advice. Get medical attention if irritation develops and persists.

Ingestion
Rinse mouth thoroughly. Call a physician or poison control center immediately. Only induce vomiting at the instruction of medical personnel. Never give anything by mouth to an unconscious person.

Most important symptoms/effects, acute and delayed
The following adverse effects have been noted with therapeutic use of this material: temporary decrease in white blood cell count; gastrointestinal distress; fatigue; weakness; symptoms of hypersensitivity (such as skin rash, hives, itching). Additional effects of overexposure may occur.

Indication of immediate medical attention and special treatment needed	Provide general supportive measures and treat symptomatically. Keep victim under observation. Symptoms may be delayed.
General information	Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves. IF exposed or concerned: Get medical advice/attention.

5. Fire-fighting measures

Suitable extinguishing media	Water fog. Foam. Apply extinguishing media carefully to avoid creating airborne dust.
Unsuitable extinguishing media	Carbon dioxide or dry powder extinguishers may be ineffective.
Specific hazards arising from the chemical	By heating and fire, harmful vapors/gases may be formed.
Special protective equipment and precautions for firefighters	Self-contained breathing apparatus and full protective clothing must be worn in case of fire.
Fire-fighting equipment/instructions	In the event of fire, cool tanks with water spray. Move containers from fire area if you can do so without risk. Use standard firefighting procedures and consider the hazards of other involved materials.
Specific methods	Cool containers exposed to flames with water until well after the fire is out.

6. Accidental release measures

Personal precautions, protective equipment and emergency procedures	Keep unnecessary personnel away. Keep people away from and upwind of spill/leak. Keep out of low areas. Wear appropriate personal protective equipment. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Ensure adequate ventilation. Local authorities should be advised if significant spillages cannot be contained. For personal protection, see section 8 of the MSDS.
Methods and materials for containment and cleaning up	Stop the flow of material, if this is without risk. Prevent entry into waterways, sewer, basements or confined areas. Following product recovery, flush area with water. For waste disposal, see section 13 of the MSDS.
Environmental precautions	Avoid discharge into drains, water courses or onto the ground.

7. Handling and storage

Precautions for safe handling	Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Do not taste or swallow. Avoid contact during pregnancy/while nursing. Avoid prolonged exposure. Provide adequate ventilation. Wear appropriate personal protective equipment. Observe good industrial hygiene practices. When using, do not eat, drink or smoke. Wash hands thoroughly after handling.
Conditions for safe storage, including any incompatibilities	Store locked up. Store in original tightly closed container. Store in a cool, dry place out of direct sunlight. Store away from incompatible materials (see Section 10 of the MSDS).

8. Exposure controls/personal protection

Occupational exposure limits

GSK Components	Type	Value	Note
MANNITOL (CAS 69-65-8)	OHC	1	
TARTARIC ACID (CAS 87-69-4)	8 HR TWA	5000 mcg/m3	
	OHC	1	
TOPOTECAN (CAS 119413-54-6)	8 HR TWA	0.03 mcg/m3	
	OHC	5	REPRODUCTIVE HAZARD, CARCINOGEN

Biological limit values	No biological exposure limits noted for the ingredient(s).
Appropriate engineering controls	An Exposure Control Approach (ECA) is established for operations involving this material based upon the OEL/Occupational Hazard Category and the outcome of a site- or operation-specific risk assessment. Good general ventilation (typically 10 air changes per hour) should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels to an acceptable level.

Individual protection measures, such as personal protective equipment

Eye/face protection	Not normally needed.
Hand protection	The choice of an appropriate glove does not only depend on its material but also on other quality features and is different from one producer to the other. Glove selection must take into account any solvents and other hazards present.
Other	Use personal protective equipment as required.

Respiratory protection	No personal respiratory protective equipment normally required.
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.
General hygiene considerations	An occupational/industrial hygiene monitoring method has been developed for this material. For advice on suitable monitoring methods, seek guidance from a qualified environment, health and safety professional. New or expectant mothers are at greater risk if exposed to the active ingredient which is readily absorbed through the skin. They should not handle unpackaged product. Risk assessments must take this into consideration. Female employees anticipating pregnancy or with a confirmed pregnancy must be encouraged to notify an occupational health professional or their line manager. This will act as the trigger for individual re-assessment of the employee's work practices. Always observe good personal hygiene measures, such as washing after handling the material and before eating, drinking, and/or smoking. Routinely wash work clothing and protective equipment to remove contaminants.

9. Physical and chemical properties

Appearance	
Physical state	Solid.
Form	Lyophilised powder.
Color	Not available.
Odor	Not available.
Odor threshold	Not available.
pH value	Not available.
Melting point/freezing point	Not available.
Initial boiling point and boiling range	Not available.
Flash point	Not available.
Evaporation rate	Not available.
Flammability (solid, gas)	Not available.
Upper/lower flammability or explosive limits	
Flammability limit - lower (%)	Not available.
Flammability limit - upper (%)	Not available.
Explosive limit - lower (%)	Not available.
Explosive limit - upper (%)	Not available.
Vapor pressure	Not available.
Vapor density	Not available.
Relative density	Not available.
Solubility(ies)	Not available.
Partition coefficient (n-octanol/water)	Not available.
Auto-ignition temperature	Not available.
Decomposition temperature	Not available.
Viscosity	Not available.

10. Stability and reactivity

Reactivity	The product is stable and non-reactive under normal conditions of use, storage and transport.
Chemical stability	Material is stable under normal conditions.
Possibility of hazardous reactions	No dangerous reaction known under conditions of normal use.
Conditions to avoid	Contact with incompatible materials.
Incompatible materials	Strong oxidizing agents.
Hazardous decomposition products	Chlorine compounds.

11. Toxicological information

Information on likely routes of exposure

Ingestion	Toxic if swallowed.

Inhalation	Knowledge about health hazard is incomplete. Inhalation of dusts may cause respiratory irritation.
Skin contact	Knowledge about health hazard is incomplete. Dust or powder may irritate the skin.
Eye contact	Knowledge about health hazard is incomplete. Dust or powder may irritate eye tissue.
Symptoms related to the physical, chemical and toxicological characteristics	The following adverse effects have been noted with therapeutic use of this material: temporary decrease in white blood cell count; gastrointestinal distress; fatigue; weakness; symptoms of hypersensitivity (such as skin rash, hives, itching). Additional effects of overexposure may occur.

Information on toxicological effects

Acute toxicity Toxic if swallowed.

Components	Species	Test Results
MANNITOL (CAS 69-65-8)		
Acute		
Oral		
LD50	Rat	13.5 g/kg
TOPOTECAN (CAS 119413-54-6)		
Acute		
Oral		
LD50	Rat	5 - 50 mg/kg
Chronic		
Oral		
LD	Rat	1 mg/kg/day, 180 day study

* Estimates for product may be based on additional component data not shown.

Skin corrosion/irritation	May be irritating to the skin.
Serious eye damage/eye irritation	Dust or powder may irritate eye tissue.
Respiratory sensitization	Not established.
Skin sensitization	Health injuries are not known or expected under normal use.
Germ cell mutagenicity	The ingredient topotecan hydrochloride has caused genetic toxicity in laboratory studies.

TOPOTECAN	Ames Assay, GLP assay Result: Negative Chromosomal Aberration Assay In Vitro, human lymphocytes Result: Positive GreenScreen Assay Result: Positive Micronucleus Assay, GLP assay; NOEL between 0.01 and 0.04 mg/kg; single intravenous dose Result: Positive Species: Mouse Mouse Lymphoma Cell (L5178Y) Mutation Assay, GLP assay Result: Positive Sister Chromatid Exchange, V79 cells Result: Positive

Carcinogenicity	Suspect cancer hazard.
TOPOTECAN	SAR / QSAR, carcinogenicity anticipated based on pharmacology Result: Positive
Reproductive toxicity	The ingredient topotecan hydrochloride has caused adverse effects to fertility in animal studies. The ingredient topotecan hydrochloride has caused adverse effects on the development of unborn offspring in animal studies.
TOPOTECAN	Embryo-foetal development - Intravenous Result: LOAEL (maternal) = 4 mg/m2 (body surface area)/day (mortality, weight loss); maternal NOAEL = 1.25 mg/m2/day; foetal LOAEL = 1.25 mg/m2/day (embryolethality); foetal NOAEL = 0.125 mg/m2/day Species: Rabbit Embryo-foetal development - Intravenous Result: LOAEL = 0.59 mg/m2/day, maternal and foetal adverse effects (maternal toxicity, increased pre- and post-implantation loss, malformations, decreased foetal weight); NOAEL = 0.059 mg/m2/day Species: Rat

TOPOTECAN	Fertility, Female Result: LOAEL = 1.36 mg/m2/day, maternal and foetal effects (maternal toxicity, increased pre-implantation loss, foetal lethality and ocular malformation); NOAEL (maternal and foetal) = 0.136 mg/m2/day Species: Rat Fertility, Male Result: NOAEL / fertility = 0.68 mg/m2/day intravenous; (maximum dose) Species: Rat

Specific target organ toxicity - single exposure Not established.

Specific target organ toxicity - repeated exposure Causes damage to organs through prolonged or repeated exposure.

Aspiration hazard Not available.

Chronic effects May cause damage to organs through prolonged or repeated exposure.

12. Ecological information

Ecotoxicity

Components		Species	Test Results
TOPOTECAN (CAS 119413-54-6)			
Aquatic			
Acute			
Crustacea	EC50	Water flea (Daphnia magna)	61.8 mg/L, 48 hours, Static test, OECD 202
Fish	EC50	Fathead minnow (Adult Pimephales promelas)	45.7 mg/L, 96 hours, Static test, OECD 203
	NOEC	Fathead minnow (Adult Pimephales promelas)	25 mg/L, 96 hours, Static test
Microtox	EC50	Microtox	102 mg/L, 15 minutes

* Estimates for product may be based on additional component data not shown.

Persistence and degradability

Photolysis

Half-life (Photolysis-aqueous)

TOPOTECAN	2.51 Minutes Measured

Hydrolysis

Half-life (Hydrolysis-neutral)

TOPOTECAN	35 Years Measured

Bioaccumulative potential

Partition coefficient n-octanol / water (log Kow)

TOPOTECAN	-0.3 (Calculated).
MANNITOL	-3.1

Bioconcentration factor (BCF)

MANNITOL	1 Estimated

Mobility in soil

Adsorption

Sludge/biomass distribution coefficient - log Kd

TOPOTECAN	2.28 Measured

Soil/sediment sorption - log Koc

MANNITOL	0.7 Estimated

Mobility in general

Volatility

Henry's law

MANNITOL	0 atm m3/mol
TARTARIC ACID	0 atm m^3/mol Estimated

Other adverse effects Not available.

13. Disposal considerations

Disposal instructions	Collect and reclaim or dispose in sealed containers at licensed waste disposal site. This material and its container must be disposed of as hazardous waste. Do not allow this material to drain into sewers/water supplies. Do not contaminate ponds, waterways or ditches with chemical or used container. Dispose of contents/container in accordance with local/regional/national/international regulations.
Local disposal regulations	Dispose in accordance with all applicable regulations.
Hazardous waste code	The waste code should be assigned in discussion between the user, the producer and the waste disposal company.
Waste from residues / unused products	Dispose of in accordance with local regulations. Empty containers or liners may retain some product residues. This material and its container must be disposed of in a safe manner (see: Disposal instructions).
Contaminated packaging	Empty containers should be taken to an approved waste handling site for recycling or disposal. Since emptied containers may retain product residue, follow label warnings even after container is emptied.

14. Transport information

DOT

UN number	UN3249
UN proper shipping name	Medicine, solid, toxic, n.o.s. (HYCAMTIN INJECTION (CONTAINING 10% TOPOTECAN))
Transport hazard class(es)	6.1(PGIII)
Subsidiary class(es)	Not available.
Packing group	III
Special precautions for user	Consumer Commodity, ORM-D may apply.See 173.153
Labels required	6.1
Special provisions	T1, TP33
Packaging exceptions	153
Packaging non bulk	213
Packaging bulk	240
Qty limits cargo	200 kg
Qty limits passenger	100 kg

IATA

UN number	UN3249
UN proper shipping name	Medicine, solid, toxic, n.o.s. (HYCAMTIN INJECTION (CONTAINING 10% TOPOTECAN))
Transport hazard class(es)	6.1(PGIII)
Subsidiary class(es)	-
Packaging group	III
Labels required	Not available.
ERG Code	6L
Passenger & cargo	Allowed.
Additional Information:	
Packaging Instruction	670
Pkg Inst cargo only	677
Pkg Inst passenger & cargo	Y645
SP see 44	A3,A801
Max net qty pkg	100 kg
Max net qty pkg cargo only	200 kg
Max net qty pkg LQ	5 kg

ID 8000, Consumer Commodity, may apply. See Packing Instruction Y963.

IMDG

UN number	UN3249
UN proper shipping name	MEDICINE, SOLID, TOXIC, N.O.S. (HYCAMTIN INJECTION (CONTAINING 10% TOPOTECAN))
Transport hazard class(es)	6.1(PGIII)
Subsidiary class(es)	-
Packaging group	III
Environmental hazards	
Marine pollutant	No
Labels required	Not available.
EmS	F-A, S-A
Special precautions for user	May be able to ship as an Excepted or Limited Quantity. Review all HazMat Table packaging exceptions and instructions to identify options.

May be able to ship as an Excepted or Limited Quantity. Review all HazMat Table packaging exceptions and instructions to identify options.

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code Not applicable.

DOT

IATA; IMDG

15. Regulatory information

US federal regulations This product is a "Hazardous Chemical" as defined by the OSHA Hazard Communication Standard, 29 CFR 1910.1200.

TSCA Section 12(b) Export Notification (40 CFR 707, Subpt. D)

Not regulated.

CERCLA Hazardous Substance List (40 CFR 302.4)

Not listed.

US. OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not listed.

SARA 304 Emergency release notification

Not regulated.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

Hazard categories Immediate Hazard - Yes
Delayed Hazard - Yes
Fire Hazard - No
Pressure Hazard - No
Reactivity Hazard - No

SARA 302 Extremely hazardous substance No

SARA 311/312 Hazardous chemical No

NFPA ratings Health: 3
Flammability: 1
Instability: 0

HMIS® ratings Health: 3*
Flammability: 1
Physical hazard: 0

Other federal regulations

Clean Air Act (CAA) Section 112 Hazardous Air Pollutants (HAPs) List

Not regulated.

Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130)

Not regulated.

Safe Drinking Water Act (SDWA) Not regulated.

Food and Drug Administration (FDA) Not regulated.

US state regulations

US. Massachusetts RTK - Substance List

Not regulated.

US. New Jersey Worker and Community Right-to-Know Act

Not regulated.

US. Pennsylvania RTK - Hazardous Substances

Not regulated.

US. Rhode Island RTK

Not regulated.

US. California Proposition 65

California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): This material is not known to contain any chemicals currently listed as carcinogens or reproductive toxins.

International Inventories

Country(s) or region	Inventory name	On inventory (yes/no)*
Australia	Australian Inventory of Chemical Substances (AICS)	No
Canada	Domestic Substances List (DSL)	No
Canada	Non-Domestic Substances List (NDSL)	No
China	Inventory of Existing Chemical Substances in China (IECSC)	No
Europe	European Inventory of Existing Commercial Chemical Substances (EINECS)	No
Europe	European List of Notified Chemical Substances (ELINCS)	No
Japan	Inventory of Existing and New Chemical Substances (ENCS)	No
Korea	Existing Chemicals List (ECL)	No
New Zealand	New Zealand Inventory	No
Philippines	Philippine Inventory of Chemicals and Chemical Substances (PICCS)	No
United States & Puerto Rico	Toxic Substances Control Act (TSCA) Inventory	No

*A "Yes" indicates that all components of this product comply with the inventory requirements administered by the governing country(s)
A "No" indicates that one or more components of the product are not listed or exempt from listing on the inventory administered by the governing country(s).

16. Other information, including date of preparation or last revision

Issue date	11-28-2013
Revision date	11-28-2013
Version #	27
Further information	This material has not been assessed for HMIS or NFPA ratings. HMIS® is a registered trade and service mark of the NPCA.
HMIS® ratings	Health: 3* Flammability: 1 Physical hazard: 0
NFPA ratings	Health: 3 Flammability: 1 Instability: 0
References	GSK Hazard Determination
Disclaimer	The information and recommendations in this safety data sheet are, to the best of our knowledge, accurate as of the date of issue. Nothing herein shall be deemed to create any warranty, express or implied. It is the responsibility of the user to determine the applicability of this information and the suitability of the material or product for any particular purpose.
Revision Information	Regulatory Information: United States