SAFETY DATA SHEET

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1. Product identifier

Trade name or designation of the mixture	HYCAMTIN INJECTABLE
Registration number	-
Synonyms	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
Issue date	28-November-2013
Version number	27
Revision date	28-November-2013
Supersedes date	09-July-2013

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

Identified uses	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.
Uses advised against	No other uses are advised.

1.3. Details of the supplier of the safety data sheet

GlaxoSmithKline UK
980 Great West Road
Brentford, Middlesex TW8 9GS UK
UK General Information (normal business hours): +44-20-8047-5000
Email Address: msds@gsk.com
Website: www.gsk.com

1.4. Emergency telephone number

TRANSPORT EMERGENCIES::
UK In-country toll call: +(44)-870-8200418
International toll call: +1 703 527 3887
available 24 hrs/7 days; multi-language response

SECTION 2: Hazards identification

2.1. Classification of the substance or mixture

Classification according to Directive 67/548/EEC or 1999/45/EC as amended

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

Classification according to Regulation (EC) No 1272/2008 as amended

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

2.2. Label elements

Label according to Regulation (EC) No. 1272/2008 as amended

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

Supplemental label information Not applicable.

2.3. Other hazards Expected to be non-combustible.
Caution - Pharmaceutical agent. See section 11 for additional information on health hazards.

SECTION 3: Composition/information on ingredients

3.2. Mixtures

General information

Chemical name	%	CAS-No. / EC No.	REACH Registration No.	INDEX No.	Notes
MANNITOL	60	69-65-8 200-711-8	-	-	
Classification: **DSD:** -					
CLP: -					
TARTARIC ACID	30	87-69-4 201-766-0	-	-	
Classification: **DSD:** Xi;R36/37/38					
CLP: Skin Irrit. 2;H315, Eye Irrit. 2;H319, STOT SE 3;H335					
TOPOTECAN	10	119413-54-6 -	-	-	
Classification: **DSD:** Carc. Cat. 2;R45, Muta. Cat. 2;R46, Repr. Cat. 2;R60-61, T+;R28, R52-53					
CLP: Acute Tox. 2;H300, Muta. 1B;H340, Carc. 2;H351, Repr. 2;H361, STOT SE 1;H370, STOT RE 1;H372, Aquatic Chronic 3;H412					

CLP: Regulation No. 1272/2008.
DSD: Directive 67/548/EEC.
M: M-factor
vPvB: very persistent and very bioaccumulative substance.
PBT: persistent, bioaccumulative and toxic substance.
#: This substance has been assigned Community workplace exposure limit(s).

Composition comments The full text for all R- and H-phrases is displayed in section 16.

SECTION 4: First aid measures

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.

4.1. Description of 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 centre immediately. Only induce vomiting at the instruction of medical personnel. Never give anything by mouth to an unconsious person.

4.2. Most important symptoms and effects, both 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.

4.3. Indication of any immediate medical attention and special treatment needed Provide general supportive measures and treat symptomatically. Keep victim under observation. Symptoms may be delayed.

SECTION 5: Firefighting measures

General fire hazards Expected to be non-combustible.

5.1. Extinguishing media

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.

5.2. Special hazards arising from the substance or mixture By heating and fire, harmful vapours/gases may be formed.

5.3. Advice for firefighters

Special protective equipment for firefighters Self-contained breathing apparatus and full protective clothing must be worn in case of fire.

Special fire fighting procedures 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.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

For non-emergency personnel	Immediately evacuate personnel to safe areas. Keep people away from and upwind of spill/leak. Wear appropriate personal protective equipment. Do not touch or walk through spilled material. Ventilate closed spaces before entering them. Local authorities should be advised if significant spillages cannot be contained. For personal protection, see section 8.
For emergency responders	Keep unnecessary personnel away. Use personal protection recommended in Section 8 of the MSDS.
6.2. Environmental precautions	Avoid discharge into drains, water courses or onto the ground.
6.3. Methods and material for containment and cleaning up	Stop the flow of material, if this is without risk. Following product recovery, flush area with water.
6.4. Reference to other sections	For personal protection, see section 8. For waste disposal, see section 13.

SECTION 7: Handling and storage

7.1. 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.
7.2. 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).
7.3. Specific end use(s)	Medicinal Product

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

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).
Recommended monitoring procedures	Follow standard monitoring procedures.
Derived No Effect Level (DNEL)	Not available.
Predicted no effect concentrations (PNECs)	Not available.

8.2. Exposure controls

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

General information	Follow all local regulations if personal protective equipment (PPE) is used in the workplace. Personal protection equipment should be chosen according to the CEN standards and in discussion with the supplier of the personal protective equipment.
Eye/face protection	Not normally needed.
Skin protection	
- 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. With respect to the above precautions select suitable chemical resistant protective gloves (EN 374) with a protective index 6 (>480min permeation time).
- Other	Wear suitable protective clothing. (EN 14605 for splashes, EN ISO 13982 for dust)

Respiratory protection	No personal respiratory protective equipment normally required.
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.
Hygiene measures	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.
Environmental exposure controls	
Hazard guidance and control recommendations	Environmental manager must be informed of all major releases.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Appearance	
Physical state	Solid.
Form	Lyophilised powder.
Colour	Not available.
Odour	Not available.
Odour 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.
Vapour pressure	Not available.
Vapour 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.
Explosive properties	Not available.
Oxidizing properties	Not available.
9.2. Other information	No relevant additional information available.

SECTION 10: Stability and reactivity

10.1. Reactivity	The product is stable and non-reactive under normal conditions of use, storage and transport.
10.2. Chemical stability	Material is stable under normal conditions.
10.3. Possibility of hazardous reactions	No dangerous reaction known under conditions of normal use.
10.4. Conditions to avoid	Contact with incompatible materials.
10.5. Incompatible materials	Strong oxidising agents.

10.6. Hazardous decomposition products Chlorine compounds.

SECTION 11: Toxicological information

General information Occupational exposure to the substance or mixture may cause adverse effects.

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 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.

11.1. 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 sensitisation Not established.

Skin sensitisation Health injuries are not known or expected under normal use.

Germ cell mutagenicity The ingredient topotecan hydrochloride has caused genetic toxicity in laboratory studies.

Germ cell mutagenicity

Mutagenicity

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.

Reproductive toxicity

Reproductivity

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 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.

Mixture versus substance information Not available.

Other information Not available.

SECTION 12: Ecological information

12.1. Toxicity

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.

12.2. Persistence and degradability

Persistence and degradability

Photolysis

Half-life (Photolysis-aqueous)

TOPOTECAN	2.51 Minutes Measured

Hydrolysis

Half-life (Hydrolysis-neutral)

TOPOTECAN	35 years Measured

Biodegradability

Percent degradation (Aerobic biodegradation-inherent)

TARTARIC ACID	34 - 75.2 %, 5 days BOD5, Activated sludge

Percent degradation (Aerobic biodegradation-ready)

TOPOTECAN	0 %, 28 days Batch activated sludge (BAS), Residential sludge

12.3. Bioaccumulative potential

Partition coefficient n-octanol/water (log Kow)

MANNITOL	-3.1
TOPOTECAN	-0.3 (Calculated).

Bioconcentration factor (BCF)

MANNITOL	1 Estimated

12.4. 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

12.5. Results of PBT and vPvB assessment Not available.

12.6. Other adverse effects Not available.

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Residual waste 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.

EU waste code The Waste code should be assigned in discussion between the user, the producer and the waste disposal company.

Disposal methods/information 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.

Special precautions Dispose in accordance with all applicable regulations.

SECTION 14: Transport information

ADR

14.1. UN number	UN3249
14.2. UN proper shipping name	Medicine, solid, toxic, n.o.s. (HYCAMTIN INJECTION (CONTAINING 10% TOPOTECAN))
14.3. Transport hazard class(es)	6.1(PGIII)
Subsidiary class(es)	-
14.4. Packing group	III
14.5. Environmental hazards	No
Tunnel code	E
Labels required	6.1
Additional information:	
LTD QTY index	LQ9
Special Provisions	221, 274, 601

IATA

14.1. UN number	UN3249
14.2. UN proper shipping name	Medicine, solid, toxic, n.o.s. (HYCAMTIN INJECTION (CONTAINING 10% TOPOTECAN))
14.3. Transport hazard class(es)	6.1(PGIII)
Subsidiary class(es)	-
14.4. Packing group	III
Labels required	Not available.

Additional Information:

Passenger & cargo	Allowed.
Packaging Instruction	670
Pkg Inst cargo only	677
Pkg Inst pasenger & cargo	Y645
LQ	
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

14.1. UN number	UN3249
14.2. UN proper shipping name	MEDICINE, SOLID, TOXIC, N.O.S. (HYCAMTIN INJECTION (CONTAINING 10% TOPOTECAN))
14.3. Transport hazard class(es)	6.1(PGIII)
Subsidiary class(es)	-
14.4. Packing group	III
14.5. Environmental hazards	
Marine pollutant	No
Labels required	Not available.
EmS	F-A, S-A
14.6. 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.
14.7. Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code	Not applicable.

ADR; IATA; IMDG

SECTION 15: Regulatory information

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

EU regulations

Regulation (EC) No. 1005/2009 on substances that deplete the ozone layer, Annex I

Not listed.

Regulation (EC) No. 1005/2009 on substances that deplete the ozone layer, Annex II

Not listed.

Regulation (EC) No. 850/2004 On persistent organic pollutants, Annex I as amended

Not listed.

Regulation (EC) No. 689/2008 concerning the export and import of dangerous chemicals, Annex I, part 1 as amended

Not listed.

Regulation (EC) No. 689/2008 concerning the export and import of dangerous chemicals, Annex I, part 2 as amended

Not listed.

Regulation (EC) No. 689/2008 concerning the export and import of dangerous chemicals, Annex I, part 3 as amended

Not listed.

Regulation (EC) No. 689/2008 concerning the export and import of dangerous chemicals, Annex V as amended

Not listed.

Regulation (EC) No. 166/2006 Annex II Pollutant Release and Transfer Registry

Not listed.

Regulation (EC) No. 1907/2006, REACH Article 59(1) Candidate List as currently published by ECHA

Not listed.

Authorisations

Regulation (EC) No. 1907/2006, REACH Annex XIV Substances subject to authorization, as amended

Not listed.

Restrictions on use

Regulation (EC) No. 1907/2006, REACH Annex XVII Substances subject to restriction on marketing and use as amended

Not listed.

Directive 2004/37/EC: on the protection of workers from the risks related to exposure to carcinogens and mutagens at work

Not listed.

Directive 92/85/EEC: on the safety and health of pregnant workers and workers who have recently given birth or are breastfeeding

Not listed.

Other EU regulations

Directive 96/82/EC (Seveso II) on the control of major-accident hazards involving dangerous substances

Not listed.

Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work

Not listed.

Directive 94/33/EC on the protection of young people at work

Not listed.

Other regulations	The product is classified and labelled in accordance with EC directives or respective national laws. This Safety Data Sheet complies with the requirements of Regulation (EC) No 1907/2006. Pregnant women should not work with the product, if there is the least risk of exposure.
National regulations	Young people under 18 years old are not allow to work with this product according to the EU Directive 94/33/EC on the protection of young people at work. Follow national regulation for work with chemical agents.
15.2. Chemical safety assessment	No Chemical Safety Assessment has been carried out.

SECTION 16: Other information

List of abbreviations	Not available.
References	GSK Hazard Determination
Information on evaluation method leading to the classification of mixture	The classification for health and environmental hazards is derived by a combination of calculation methods and test data, if available.
Full text of any statements or R-phrases and H-statements under Sections 2 to 15	R28 Very toxic if swallowed. R36/37/38 Irritating to eyes, respiratory system and skin. R45 May cause cancer. R46 May cause heritable genetic damage. R52 Harmful to aquatic organisms. R53 May cause long term adverse effects in the aquatic environment. R60 May impair fertility. R61 May cause harm to the unborn child. H300 Fatal if swallowed. H315 Causes skin irritation. H319 Causes serious eye irritation. H335 May cause respiratory irritation. H340 May cause genetic defects. H351 Suspected of causing cancer. H361 Suspected of damaging fertility or the unborn child. H370 Causes damage to organs. H372 Causes damage to organs through prolonged or repeated exposure. H412 Harmful to aquatic life with long lasting effects.
Revision information	Regulatory Information: United States
Training information	Follow training instructions when handling this material.
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.