



SAFETY DATA SHEET

1. Identification

Product identifier

ALKERAN TABLETS

Other means of identification

Synonyms

ALKERAN TABLETS 2 MG * ALKERAN TABLETS 5 MG * GR 64466X TABLETS * ALKERANA TABLETS * MELPHALAN, 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

Chemical name	Common name and synonyms	CAS number	%
MICROCRYSTALLINE CELLULOSE	AVICEL PH MICROCRYSTALLINE CELLULOSE ALPHA-CELLULOSE AVICEL PH101 AVICEL PH102 AVICEL PH103 AVICEL PH105 AVICEL PH112 AVICEL PH200 CELLULOSE (8CI9CI) CELLULOSE CRYSTALLINE CELLULOSE, FOOD GRADE CRYSTALLINE CELLULOSE	9004-34-6	96 - < 98

Chemical name	Common name and synonyms	CAS number	%
MELPHALAN	MELFALAN L-PHENYLALANINE NITROGEN MUSTARD GR 64466X 4-(BIS(2-CHLOROETHYL)AMINO)-L-PHENYLALANINE L-SARCOLYSIN ALANINE, 3-(P-BIS(2-CHLOROETHYL)AMINO)PHENYL-, L-	148-82-3	2
MAGNESIUM STEARATE	STEARIC ACID, MAGNESIUM SALT MAGNESIUM DISTEARATE DIBASIC MAGNESIUM STEARATE MAGNESIUM DISTEARATE, PURE	557-04-0	< 1
POLYVINYLPIRROLIDONE	1-ETHENYL-2-PYRROLIDINONE HOMOPOLYMER POLY(N-VINYLPYRROLIDONE) POVIDONE PLASDONE PLASDONE K29/32	9003-39-8	< = 1
SILICA, AMORPHOUS, FUMED	SILICA, AMORPHOUS, FUMED, CRYSTALLINE FREE FUMED SILICA, CRYSTALLINE-FREE FUMED SYNTHETIC AMORPHOUS SILICA PYROGENIC COLLOIDAL SILICA SYNTHETIC AMORPHOUS SILICA AMORPHOUS FUMED SILICA RTECS VV7310000	112945-52-5	< 0.5

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

4. First-aid measures

Inhalation	Move to fresh air. If breathing is difficult, trained personnel should give oxygen. Call a physician if symptoms develop or persist. Under normal conditions of intended use, this material is not expected to be an inhalation hazard.
Skin contact	Immediately flush skin with plenty of water. Take off contaminated clothing and wash before reuse. Get medical attention if symptoms occur.
Eye contact	Rinse thoroughly with plenty of water for at least 15 minutes and consult a physician.
Ingestion	If swallowed, rinse mouth with water (only if the person is conscious). If ingestion of a large amount does occur, call a poison control center immediately. Do not induce vomiting without advice from poison control center.
Most important symptoms/effects, acute and delayed	Accidental exposure or contact might produce: Nausea, vomiting, symptoms of hypersensitivity (such as skin rash, hives, itching), anaemia, diarrhoea.
Indication of immediate medical attention and special treatment needed	No specific antidotes are recommended. Treat according to locally accepted protocols. For additional guidance, refer to the current prescribing information or to the local poison control information center.
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. The need for pre-placement and periodic health surveillance must be determined by risk assessment. Following assessment, if the risk of exposure is considered significant then a health record should be maintained for exposed individuals to document periods of exposure. This record should be retained for at least 30 years after exposure ceases (or according local regulatory requirements if more stringent).

5. Fire-fighting measures

Suitable extinguishing media	Water. Foam. Dry chemical powder. Carbon dioxide (CO2).
Unsuitable extinguishing media	None known.
Specific hazards arising from the chemical	During fire, gases hazardous to health 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	Move containers from fire area if you can do so without risk.

Specific methods Use standard firefighting procedures and consider the hazards of other involved materials.
General fire hazards No unusual fire or explosion hazards noted.

6. Accidental release measures

Personal precautions, protective equipment and emergency procedures Keep unnecessary personnel away. Keep people away from and upwind of spill/leak. Wear appropriate protective equipment and clothing during clean-up. 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 SDS.

Methods and materials for containment and cleaning up Large Spills: Stop the flow of material, if this is without risk. Dike the spilled material, where this is possible. Cover with plastic sheet to prevent spreading. Absorb in vermiculite, dry sand or earth and place into containers. Following product recovery, flush area with water.

Small Spills: Wipe up with absorbent material (e.g. cloth, fleece). Clean surface thoroughly to remove residual contamination.

Never return spills to original containers for re-use. For waste disposal, see section 13 of the SDS. Avoid discharge into drains, water courses or onto the ground.

Environmental precautions

7. Handling and storage

Precautions for safe handling Obtain special instructions before use. Avoid breaking or crushing tablets. Do not handle until all safety precautions have been read and understood. Avoid breathing dust/fume/gas/mist/vapors/spray. Avoid contact with eyes, skin, and clothing. Avoid prolonged exposure. Do not taste or swallow. When using, do not eat, drink or smoke. Pregnant or breastfeeding women must not handle this product. Should be handled in closed systems, if possible. Provide adequate ventilation. Wear appropriate personal protective equipment. Wash hands thoroughly after handling. Observe good industrial hygiene practices.

Conditions for safe storage, including any incompatibilities Store locked up. Store in original tightly closed container. Store away from incompatible materials (see Section 10 of the SDS).

8. Exposure controls/personal protection

Occupational exposure limits

GSK

Components	Type	Value	Note
MELPHALAN (CAS 148-82-3)	8 HR TWA	1 mcg/m ³	
	OHC	5	REPRODUCTIVE HAZARD
		5	SKIN SENSITISER
		5	CARCINOGEN

US. OSHA Table Z-1 Limits for Air Contaminants (29 CFR 1910.1000)

Components	Type	Value	Form
MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)	PEL	5 mg/m ³	Respirable fraction.
		15 mg/m ³	Total dust.

US. OSHA Table Z-3 (29 CFR 1910.1000)

Components	Type	Value
SILICA, AMORPHOUS, FUMED (CAS 112945-52-5)	TWA	0.8 mg/m ³
		20 mppcf

US. ACGIH Threshold Limit Values

Components	Type	Value
MAGNESIUM STEARATE (CAS 557-04-0)	TWA	10 mg/m ³
MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)	TWA	10 mg/m ³

US. NIOSH: Pocket Guide to Chemical Hazards

Components	Type	Value	Form
MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)	TWA	5 mg/m ³	Respirable.
SILICA, AMORPHOUS, FUMED (CAS 112945-52-5)	TWA	10 mg/m ³ 6 mg/m ³	Total

Biological limit values No biological exposure limits noted for the ingredient(s).

Exposure guidelines**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. Ventilate as needed to control airborne dust. Use explosion-proof ventilation equipment if airborne dust levels are high. It is strongly advised that dedicated areas and containment, such as glove boxes, isolators, and enclosed material transfer systems be used to prevent personnel exposure and spread of contamination. Special considerations apply in the planning, design, review and implementation of controls - seek specialist assistance from local occupational hygienist or safety department.

Individual protection measures, such as personal protective equipment

Eye/face protection Not normally needed. If contact is likely, safety glasses with side shields are recommended.

Skin protection**Hand protection**

Glove selection must take into account any solvents and other hazards present. 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.

Other

Wear suitable protective clothing as protection against splashing or contamination.

Respiratory protection

Use a NIOSH/MSHA approved respirator if there is a risk of exposure to dust/fume at levels exceeding the exposure limits. When workers are facing concentrations above the exposure limit they must use appropriate certified respirators.

Thermal hazards

Wear appropriate thermal protective clothing, when necessary.

General hygiene considerations

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. For advice on suitable monitoring methods, seek guidance from a qualified environment, health and safety professional. Strict control of access to the working area is essential. New or expectant mothers might be at greater risk from overexposure. 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.

9. Physical and chemical properties**Appearance**

Physical state Solid.
Form Tablet.
Color Not available.

Odor Not available.

Odor threshold Not available.

pH 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)	
Solubility (water)	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. Fluorine.
Hazardous decomposition products	None known. Irritating and/or toxic fumes and gases may be emitted upon the product's decomposition.

11. Toxicological information

Information on likely routes of exposure

Inhalation	Under normal conditions of intended use, this material is not expected to be an inhalation hazard.
Skin contact	Health injuries are not known or expected under normal use.
Eye contact	Health injuries are not known or expected under normal use.
Ingestion	Health injuries are not known or expected under normal use.

Symptoms related to the physical, chemical and toxicological characteristics	Accidental exposure or contact might produce: symptoms of hypersensitivity (such as skin rash, hives, itching), anaemia, Nausea, vomiting., diarrhoea.
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Information on toxicological effects

Acute toxicity	Health injuries are not known or expected under normal use.
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Components	Species	Test Results
MAGNESIUM STEARATE (CAS 557-04-0)		
<u>Acute</u>		
Oral		
LD50	Rat	> 2000 mg/kg
MELPHALAN (CAS 148-82-3)		
<u>Acute</u>		
Oral		
LD50	Rat	4.7 mg/kg
MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)		
<u>Acute</u>		
Dermal		
LD50	Rabbit	> 2000 mg/kg
Oral		
LD50	Rat	> 2000 mg/kg

Components	Species	Test Results
POLYVINYLPIRROLIDONE (CAS 9003-39-8)		
Acute		
Oral		
LD50	Rat	> 5000 mg/kg
* Estimates for product may be based on additional component data not shown.		
Skin corrosion/irritation	Health injuries are not known or expected under normal use.	
Irritation Corrosion - Skin: P.I.I. value		
MAGNESIUM STEARATE		0
Serious eye damage/eye irritation	Health injuries are not known or expected under normal use. Direct contact with eyes may cause temporary irritation.	
Eye / Kay and Calandra class - Intact		
MAGNESIUM STEARATE		4 Recovery Period: 2 days
Respiratory or skin sensitization		
Respiratory sensitization	Under normal conditions of intended use, this material is not expected to be an inhalation hazard.	
Skin sensitization	Health injuries are not known or expected under normal use.	
Sensitization		
MELPHALAN		Clinical use Result: Positive SAR Result: Positive
Germ cell mutagenicity	Not expected to be genotoxic under occupational exposure conditions. Contains components that produced genotoxicity in laboratory tests.	
Mutagenicity		
MELPHALAN		Ames Assay (GLP) Result: Positive Chromosomal Aberration Assay In Vitro Result: Positive GreenScreen mammalian cell mutation assay Result: Positive Rat micronucleus assay (GLP) Result: Positive SAR Result: Alerts for Chromosomal damage or Mutagenicity. Syrian Hamster Embryo (SHE) cell transformation assay Result: Positive bacterial mutation test (SOS/umu) Result: Positive
Carcinogenicity	Contains a material classified as a carcinogen by external agencies. Carcinogenic effects are not expected as a result of occupational exposure.	
MELPHALAN		Intraperitoneal Result: Positive Species: Mouse Intraperitoneal Result: Positive Species: Rat SAR Result: Positive
IARC Monographs. Overall Evaluation of Carcinogenicity		
MELPHALAN (CAS 148-82-3)		1 Carcinogenic to humans.
POLYVINYLPIRROLIDONE (CAS 9003-39-8)		3 Not classifiable as to carcinogenicity to humans.
SILICA, AMORPHOUS, FUMED (CAS 112945-52-5)		3 Not classifiable as to carcinogenicity to humans.
OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)		
Not listed.		
US. National Toxicology Program (NTP) Report on Carcinogens		
MELPHALAN (CAS 148-82-3)		Known To Be Human Carcinogen.
Reproductive toxicity	Health injuries are not known or expected under normal use. Components in this product have been shown to cause birth defects and reproductive disorders in laboratory animals.	

Reproductivity
MELPHALAN

Fertility and Early Embryonic Development
Result: Positive
Species: Rat
Literature search
Result: Reduced fertility in Humans based on similar compounds.
Species: Human

Specific target organ toxicity - single exposure Not assigned.

Specific target organ toxicity - repeated exposure May cause damage to organs through prolonged or repeated exposure.
MELPHALAN

Clinical use
Result: Bone marrow and blood cells, rapidly dividing cells and the gastrointestinal tract.

Aspiration hazard Not likely, due to the form of the product.

Chronic effects May cause damage to organs through prolonged or repeated exposure. Prolonged inhalation may be harmful. Prolonged exposure may cause chronic effects.

Further information Caution - Potent pharmaceutical agent. Occupational exposure to the substance or mixture may cause adverse effects.

12. Ecological information

Ecotoxicity Not expected to be harmful to aquatic organisms.

Components		Species	Test Results
MAGNESIUM STEARATE (CAS 557-04-0)			
Aquatic			
<i>Acute</i>			
Fish	EC50	Orange-red killfish (Adult Oryzias latipes)	130 mg/l, 96 hours
MELPHALAN (CAS 148-82-3)			
Aquatic			
<i>Acute</i>			
Activated Sludge Respiration	IC50	Residential sludge	> 100 mg/l, 3 hours
Crustacea	EC50	Water flea (Daphnia magna)	> 10 mg/l, 48 hours
POLYVINYLPIRROLIDONE (CAS 9003-39-8)			
<i>Acute</i>			
	IC50	Activated sludge	> 1000 mg/l, 3 hours Static test
Aquatic			
<i>Acute</i>			
Crustacea	EC50	Water flea (Daphnia magna)	84 mg/l, 48 hours Static test
	NOEC	Water flea (Daphnia magna)	32 mg/l, 48 hours Static test

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

Persistence and degradability

Photolysis

Half-life (Photolysis-atmospheric)

MAGNESIUM STEARATE 17 Hours Estimated

UV/visible spectrum wavelength

MAGNESIUM STEARATE 210 nm

Hydrolysis

Half-life (Hydrolysis-acidic)

MELPHALAN 4.9 Hours, pH 5 Buffer Solution

Half-life (Hydrolysis-basic)

MELPHALAN 3.9 Hours

Half-life (Hydrolysis-neutral)

MELPHALAN 4.9 Hours, pH 7 Buffer Solution

Biodegradability

Percent degradation (Aerobic biodegradation-inherent)

MAGNESIUM STEARATE 77 %, 28 days BOD
POLYVINYLPIRROLIDONE 0 %, 28 days Modified MITI test, Activated sludge

Percent degradation (Aerobic biodegradation-ready)

MAGNESIUM STEARATE 95 %, 22 days Sturm test

Percent degradation (Aerobic biodegradation-soil)

MAGNESIUM STEARATE 50 %, 13 days

Bioaccumulative potential

Partition coefficient n-octanol / water (log Kow)

MELPHALAN -0.52, at pH 7
1

Bioconcentration factor (BCF)

MAGNESIUM STEARATE > 9999 Estimated
MELPHALAN 1 Estimated

Mobility in soil

Adsorption

Soil/sediment sorption - log Koc

MAGNESIUM STEARATE 5.86 Estimated

Mobility in general

Volatility

Henry's law

MELPHALAN 0 atm m³/mol, 25 C Estimated

Distribution

Octanol/water distribution coefficient log DOW

MELPHALAN -0.52, pH 7.4

Other adverse effects Not available.

13. Disposal considerations

Disposal instructions Collect and reclaim or dispose in sealed containers at licensed waste disposal site. Do not discharge into drains, water courses or onto the ground. Dispose in accordance with all applicable 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). Avoid discharge into water courses or onto the ground.

Contaminated packaging Since emptied containers may retain product residue, follow label warnings even after container is emptied. Empty containers should be taken to an approved waste handling site for recycling or disposal.

14. Transport information

DOT

Not regulated as a dangerous good.

Not available.

IATA

Not regulated as dangerous goods.

IMDG

Not regulated as dangerous goods.

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code MARPOL Annex II applies to liquids used in a ship's operation that pose a threat to the marine environment. These materials may not be transported in bulk.

15. Regulatory information

US federal regulations

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

Not regulated.

CERCLA Hazardous Substance List (40 CFR 302.4)

MELPHALAN (CAS 148-82-3) Listed.

SARA 304 Emergency release notification

Not regulated.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not listed.

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

Not listed.

SARA 311/312 Hazardous chemical No**SARA 313 (TRI reporting)**

Not regulated.

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.**US state regulations****US. California Controlled Substances. CA Department of Justice (California Health and Safety Code Section 11100)**

Not listed.

US. Massachusetts RTK - Substance List

MELPHALAN (CAS 148-82-3)
 MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)
 SILICA, AMORPHOUS, FUMED (CAS 112945-52-5)

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

MELPHALAN (CAS 148-82-3)
 MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)

US. Pennsylvania Worker and Community Right-to-Know Law

MELPHALAN (CAS 148-82-3)
 MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)
 SILICA, AMORPHOUS, FUMED (CAS 112945-52-5)

US. Rhode Island RTK

MELPHALAN (CAS 148-82-3)

US. California Proposition 65

WARNING: This product contains a chemical known to the State of California to cause cancer and birth defects or other reproductive harm.

US - California Proposition 65 - CRT: Listed date/Carcinogenic substance

MELPHALAN (CAS 148-82-3) Listed: February 27, 1987

US - California Proposition 65 - CRT: Listed date/Developmental toxin

MELPHALAN (CAS 148-82-3) Listed: July 1, 1990

International Inventories

Country(s) or region	Inventory name	On inventory (yes/no)*
Australia	Australian Inventory of Chemical Substances (AICS)	Yes
Canada	Domestic Substances List (DSL)	Yes
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

Country(s) or region	Inventory name	On inventory (yes/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	09-21-2015
Revision date	09-21-2015
Version #	19
Further information	HMIS® is a registered trade and service mark of the NPCA.
HMIS® ratings	Health: 2* Flammability: 0 Physical hazard: 0
NFPA ratings	Health: 2 Flammability: 0 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	Product and Company Identification: Product and Company Identification Composition / Information on Ingredients: Ingredients Physical & Chemical Properties: Toxicological Information: Ecological Information: Ecotoxicity Transport Information: Regulatory Information: Risk Phrases - Class. GHS: Classification