

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

1.1. Product identifier

Trade name or designation of the mixture DARAPRIM TABLETS

Registration number -

Synonyms DARAPRIM TABLETS 25 MG * DARAPRIM COMPRIMES * DARAPRIM COMPRIMIDOS * DARAPRIM TABLETAS * DARAPRIM TABLETKI * DARAPRIM TABLETTEN * NDC NO 0173-0201-55 * PYRIMETHAMINE, FORMULATED PRODUCT

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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.

2.3. Other hazards Caution - Potent 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
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PYRIMETHAMINE	< = 20	58-14-0 200-364-2	-	-	
Classification:	DSD:	Muta. Cat. 2;R46, Repr. Cat. 2;R60-61, Xn;R22, N;R51/53			
	CLP:	Acute Tox. 4;H302, Muta. 1B;H340, Repr. 1B;H360, STOT RE 1;H372, Aquatic Chronic 2;H411			

Starch	< 15	9005-25-8 232-679-6	-	-	
Classification:	DSD:	-			
	CLP:	-			

MAGNESIUM STEARATE	< 1	557-04-0 209-150-3	-	-	
Classification:	DSD:	-			
	CLP:	-			

Other components below reportable levels > 68

List of abbreviations and symbols that may be used above

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 In the case of accident or if you feel unwell, seek medical advice immediately (show the label where possible). Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.

4.1. Description of 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 centre immediately. Do not induce vomiting without advice from poison control center.

4.2. Most important symptoms and effects, both acute and delayed Accidental exposure or contact might produce: symptoms of hypersensitivity (such as skin rash, hives, itching) gastrointestinal distress, nausea, vomiting, convulsions, respiratory depression, decrease in blood pressure.

4.3. Indication of any 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 centre.

SECTION 5: Firefighting measures

General fire hazards No unusual fire or explosion hazards noted.

5.1. Extinguishing media

Suitable extinguishing media Water. Foam. Dry chemical powder. Carbon dioxide (CO2).

Unsuitable extinguishing media None known.

5.2. Special hazards arising from the substance or mixture During fire, gases hazardous to health 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	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.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

For non-emergency personnel	Keep unnecessary personnel away. Wear appropriate protective equipment and clothing during clean-up. Avoid inhalation of dust from the spilled material. Wear a dust mask if dust is generated above exposure limits. For personal protection, see section 8.
For emergency responders	Keep unnecessary personnel away. Use personal protection recommended in Section 8 of the SDS.

6.2. Environmental precautions Avoid discharge into drains, water courses or onto the ground.

6.3. Methods and material for containment and cleaning up If sweeping of a contaminated area is necessary use a dust suppressant agent which does not react with the product. Collect dust using a vacuum cleaner equipped with HEPA filter. Minimise dust generation and accumulation. 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 of the SDS.

SECTION 7: Handling and storage

7.1. Precautions for safe handling Provide appropriate exhaust ventilation at places where dust is formed. Minimise dust generation and accumulation. Avoid breathing dust. Avoid contact with eyes. Practice good housekeeping.

7.2. Conditions for safe storage, including any incompatibilities Store in original tightly closed container. Store in a well-ventilated place. Store away from incompatible materials (see Section 10 of the SDS).

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
PYRIMETHAMINE (CAS 58-14-0)	8 HR TWA	7 mcg/m3	
	OHC	4	Reproductive hazard
Ireland. Occupational Exposure Limits Components	Type	Value	Form
MAGNESIUM STEARATE (CAS 557-04-0)	TWA	10 mg/m3	
Starch (CAS 9005-25-8)	TWA	4 mg/m3 10 mg/m3	Respirable dust. Total inhalable dust.

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.

Exposure guidelines

8.2. Exposure controls

Appropriate engineering controls General ventilation normally adequate. 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.

Individual protection measures, such as personal protective equipment

General information	Personal protection equipment should be chosen according to the CEN standards and in discussion with the supplier of the personal protective equipment. Follow all local regulations if personal protective equipment (PPE) is used in the workplace.
Eye/face protection	If contact is likely, safety glasses with side shields are recommended. (e.g. EN 166). Not normally needed.
Skin protection	
- Hand protection	For prolonged or repeated skin contact use suitable protective gloves. Select suitable chemical resistant protective gloves (EN 374) with a protective index 6 (>480min permeation time). Not normally needed.

- Other	Wear suitable protective clothing as protection against splashing or contamination. (EN 14605 for splashes, EN ISO 13982 for dust). Not normally needed.
Respiratory protection	When workers are facing concentrations above the exposure limit they must use appropriate certified respirators. Where breathable aerosols/dust are formed, use suitable combination filter for gases/vapours of organic, inorganic, acid inorganic, alkaline compounds and toxic particles (eg. EN 14387). No personal respiratory protective equipment normally required.
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.
Hygiene measures	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.
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	Tablet.
Colour	Not available.
Odour	Not available.
Odour 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.
Vapour pressure	Not available.
Vapour density	Not available.
Relative density	Not available.
Solubility(ies)	
Solubility (water)	Not available.
Solubility (other)	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. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
10.5. Incompatible materials	Acids. Peroxides. Phenols.

10.6. Hazardous decomposition products

None known. Irritating and/or toxic fumes and gases may be emitted upon the product's decomposition.

SECTION 11: Toxicological information

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

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 Accidental exposure or contact might produce: symptoms of hypersensitivity (such as skin rash, hives, itching) gastrointestinal distress, nausea, vomiting, convulsions, respiratory depression, decrease in blood pressure.

11.1. Information on toxicological effects

Acute toxicity May be harmful if swallowed.

Components	Species	Test results
MAGNESIUM STEARATE (CAS 557-04-0)		
Acute		
<i>Oral</i>		
LD50	Rat	> 2000 mg/kg
PYRIMETHAMINE (CAS 58-14-0)		
Acute		
<i>Oral</i>		
LD50	Rat	440 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

PYRIMETHAMINE

Acute dermal irritation; OECD 404
Result: Minimal irritant

Irritation Corrosion - Skin: P.I.I. value

MAGNESIUM STEARATE

0

Serious eye damage/eye irritation Direct contact with eyes may cause temporary irritation. Health injuries are not known or expected under normal use.

Eye

PYRIMETHAMINE

Acute ocular irritation; OECD 405
Result: Mild
IRE Assay
Result: Negative; not likely to be a severe irritant

Eye / Kay and Calandra class - Intact

MAGNESIUM STEARATE

4
Recovery Period: 2 days

Respiratory sensitisation No studies have been conducted.

Skin sensitisation Knowledge about sensitisation hazard is incomplete.

Germ cell mutagenicity Health injuries are not known or expected under normal use. May cause genetic defects.

Mutagenicity

PYRIMETHAMINE

Ames Assay, GLP assay
Result: negative
Chromosomal Aberration Assay In Vitro
Result: positive
GreenScreen Assay
Result: positive
In vivo Micronucleus
Result: positive
Mouse Lymphoma Cell (L5178Y) Mutation Assay, GLP assay
Result: positive
SAR, DEREK, Lhasa, UK
Result: Plausible structural alert identified
Sister Chromatid Exchange
Result: positive

Carcinogenicity Carcinogenic effects are not expected as a result of occupational exposure.

Carcinogenicity
PYRIMETHAMINE

18 month bioassay
Result: negative
Species: Mouse
18 month bioassay
Result: negative
Species: Rat
25 mg/kg Intraperitoneal
Result: positive
Species: Mouse

IARC Monographs. Overall Evaluation of Carcinogenicity

PYRIMETHAMINE (CAS 58-14-0)

3 Not classifiable as to carcinogenicity to humans.

Reproductive toxicity

Components in this product have been shown to cause birth defects and reproductive disorders in laboratory animals. Possible risk of harm to the unborn child. May cause harm to breastfed babies.

Reproductivity

PYRIMETHAMINE

SAR / QSAR, DEREK, Lhasa, UK
Result: Plausible
Teratogenicity, Literature data
Result: Adverse developmental effects; oral doses of 1-2 mg/kg/day
Species: Rat

Specific target organ toxicity - single exposure

Not assigned.

Specific target organ toxicity - repeated exposure

May cause damage to organs.

PYRIMETHAMINE

Clinical use
Organ: bone marrow; blood; central nervous system

Aspiration hazard

Not available.

Mixture versus substance information

No information available.

Other information

Caution - Pharmaceutical agent. Occupational exposure to the substance or mixture may cause adverse effects.

SECTION 12: Ecological information

12.1. Toxicity

Not expected to be harmful to aquatic organisms.

Components

Species

Test results

MAGNESIUM STEARATE (CAS 557-04-0)

Aquatic

Acute

Fish

EC50

Orange-red killifish (Adult Oryzias latipes)

130 mg/l, 96 hours

PYRIMETHAMINE (CAS 58-14-0)

Acute

IC50

Activated sludge

> 3200 mg/l, 3 hours Nominal

NOEC

Activated sludge

10, 3 hours

Aquatic

Acute

Algae

EC50

Green algae (Chlorella pyrenoidosa)

20 mg/l, 48 hours

Crustacea

EC50

Water flea (Daphnia magna)

4.8 mg/l, 48 hours Static test

Fish

EC50

Rainbow trout (Juvenile Oncorhynchus mykiss)

5.9 mg/l, 48 hours Static test

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

12.2. 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-neutral)

PYRIMETHAMINE

6 Months Measured, Deionized Water

Biodegradability

Percent degradation (Aerobic biodegradation-inherent)

MAGNESIUM STEARATE

77 %, 28 days BOD

PYRIMETHAMINE

2 %, 28 days Modified MITI (II) 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

12.3. Bioaccumulative potential

Partition coefficient

n-octanol/water (log Kow)

PYRIMETHAMINE

2.7 (Measured).

Bioconcentration factor (BCF)

MAGNESIUM STEARATE

> 9999 Estimated

12.4. Mobility in soil

Adsorption

Soil/sediment sorption - log Koc

MAGNESIUM STEARATE

5.86 Estimated

Mobility in general

Volatility

Henry's law

PYRIMETHAMINE

0 atm m³/mol, 25 C Estimated

Distribution

Octanol/water distribution coefficient log DOW

PYRIMETHAMINE

2.44, pH 7.4

12.5. Results of PBT

Not available.

and vPvB

assessment

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). Avoid discharge into water courses or onto the ground.

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. Do not discharge into drains, water courses or onto the ground. Dispose in accordance with all applicable regulations.

Special precautions

Dispose in accordance with all applicable regulations.

SECTION 14: Transport information

ADR

Not regulated as dangerous goods.

IATA

Not regulated as dangerous goods.

IMDG

Not regulated as dangerous goods.

14.7. Transport in bulk

according to Annex II of

MARPOL73/78 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.

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(10) 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.

National regulations

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

R22 Harmful if swallowed.
R46 May cause heritable genetic damage.
R51/53 Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
R60 May impair fertility.
R61 May cause harm to the unborn child.
H302 Harmful if swallowed.
H340 May cause genetic defects.
H360 May damage fertility or the unborn child.
H372 Causes damage to organs through prolonged or repeated exposure.
H411 Toxic to aquatic life with long lasting effects.

Revision information

Product and Company Identification: Product and Company Identification
Composition / Information on Ingredients: Undisclosed Ingredient Statement
Physical & Chemical Properties:
Toxicological Information:
Ecological Information: Mobility
Transport information:
Regulatory Information: United States
GHS: Classification

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.