

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

1.1. Product identifier

Trade name or designation of the mixture	RYTHMOL SR EXTENDED RELEASE CAPSULES
Registration number	-
Synonyms	RYTHMOL SR 225 MG EXTENDED RELEASE CAPSULES * RYTHMOL SR 325 MG EXTENDED RELEASE CAPSULES * RYTHMOL SR 425 MG EXTENDED RELEASE CAPSULES * NDC NO. 65726-261-15 * NDC NO. 65726-262-15 * NDC NO. 65726-263-15 * PROPAFENONE HYDROCHLORIDE, FORMULATED PRODUCT
Issue date	06-November-2013
Version number	03
Revision date	06-November-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

The mixture has been assessed and/or tested for its physical, health and environmental hazards and the following classification applies.

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 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
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PROPAFENONE HYDROCHLORIDE	96	34183-22-7 251-867-9	-	-	
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Classification: **DSD:** Xn;R20/22, Xi;R36/37/38

CLP: Acute Tox. 4;H302

HYDROXYPROPYL METHYL CELLULOSE	3 - < 5	9004-65-3 -	-	-	
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Classification: **DSD:** -

CLP: -

MAGNESIUM STEARATE	1 - < 3	557-04-0 209-150-3	-	-	
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Classification: **DSD:** Xi;R36/37/38

CLP: Skin Irrit. 2;H315, Eye Irrit. 2;H319, STOT SE 3;H335

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.

4.1. Description of first aid measures

Inhalation Physical form suggests that risk of inhalation exposure is negligible.

Skin contact Using appropriate personal protective equipment, remove contaminated clothing and flush exposed area with large amounts of water. Obtain medical attention if skin reaction occurs, which may be immediate or delayed.

Eye contact Wash immediately with clean and gently flowing water. Continue for at least 15 minutes. Obtain medical attention.

Ingestion Never attempt to induce vomiting. Do not attempt to give any solid or liquid by mouth if the exposed subject is unconscious or semi-conscious. Wash out the mouth with water. If the exposed subject is fully conscious, give plenty of water to drink. Obtain medical attention.

4.2. Most important symptoms and effects, both acute and delayed The following adverse effects have been noted with therapeutic use of this material: irregular heartbeat; temporary decrease in white blood cell counts; sensation of bitter taste; dizziness; nausea; vomiting; constipation.

4.3. Indication of any immediate medical attention and special treatment needed No specific antidotes are recommended.

SECTION 5: Firefighting measures

General fire hazards No unusual fire or explosion hazards noted.

5.1. Extinguishing media

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

Unsuitable extinguishing media None known.

5.2. Special hazards arising from the substance or mixture Toxic, corrosive or flammable thermal decomposition products are expected when the product is exposed to fire.

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. For single units (packages): No special requirements needed.
For larger amounts (multiple packages/pallets) of product: Since toxic, corrosive or flammable vapours might be evolved from fires involving this product and associated packaging, self contained breathing apparatus and full protective equipment are recommended for firefighters. If possible, contain and collect firefighting water for later disposal.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

For non-emergency personnel Keep unnecessary personnel away. Wear protective clothing and equipment consistent with the degree of hazard. 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 For large spills, take precautions to prevent entry into waterways, sewers, or surface drainage systems.

6.3. Methods and material for containment and cleaning up Collect and place it in a suitable, properly labelled container for recovery or disposal. Stop the flow of material, if this is without risk. Following product recovery, flush area with water. No specific decontamination or detoxification procedures have been identified for this product.

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 Avoid prolonged exposure. Avoid breaking or crushing capsules.

7.2. Conditions for safe storage, including any incompatibilities Store in original tightly closed container. Store away from incompatible materials (see Section 10 of the MSDS). No storage requirements necessary for occupational hazards. Follow product information storage instructions to maintain efficacy.

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
HYDROXYPROPYL METHYL CELLULOSE (CAS 9004-65-3)	OHC	1	
MAGNESIUM STEARATE (CAS 557-04-0)	OHC	1	
PROPAFENONE HYDROCHLORIDE (CAS 34183-22-7)	OHC	2	>100 - <=1000 mcg/m3

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 Ensure adequate ventilation, especially in confined areas. 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. (eg. EN 166)

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. Select suitable chemical resistant protective gloves (EN 374) with a protective index 6 (>480min permeation time).

- Other Not normally needed.

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.
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	Solid. Capsule.
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)	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 Not 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	This product is expected to be stable.
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	Irritating and/or toxic fumes and gases may be emitted upon the products decomposition.

SECTION 11: Toxicological information

General information	Caution - Pharmaceutical agent. Occupational exposure to the substance or mixture may cause adverse effects.
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Information on likely routes of exposure

Ingestion	Health injuries are not known or expected under normal use. May be harmful if swallowed.
Inhalation	Health injuries are not known or expected under normal use. Inhalation of dusts may cause respiratory irritation.
Skin contact	Health injuries are not known or expected under normal use. Dust or powder may irritate the skin.
Eye contact	Health injuries are not known or expected under normal use. Dust or powder may irritate eye tissue.

Symptoms The following adverse effects have been noted with therapeutic use of this material: irregular heartbeat; temporary decrease in white blood cell count; sensation of bitter taste; dizziness; nausea; vomiting; constipation.

11.1. Information on toxicological effects

Acute toxicity May be harmful if swallowed.

Components	Species	Test results
HYDROXYPROPYL METHYL CELLULOSE (CAS 9004-65-3)		
Acute		
<i>Oral</i>		
LD50	Rat	> 2000 mg/kg
MAGNESIUM STEARATE (CAS 557-04-0)		
Acute		
<i>Oral</i>		
LD50	Rat	> 2000 mg/kg
PROPAFENONE HYDROCHLORIDE (CAS 34183-22-7)		
Acute		
<i>Oral</i>		
	Rat	700 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. Dust or powder may irritate eye tissue.

Respiratory sensitisation Not available.

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

Maximisation assay (Magnusson and Kligman)

HYDROXYPROPYL METHYL CELLULOSE Result: negative
Species: Guinea pig

Germ cell mutagenicity No data available to indicate product or any components present at greater than 0.1% are mutagenic or genotoxic.

Germ cell mutagenicity**Mutagenicity**

PROPAFENONE HYDROCHLORIDE Ames Assay, Literature data
Result: negative
Chromosomal Aberration Assay In Vitro, human lymphocytes, Literature data
Result: negative
Chromosomal Aberration Assay In Vivo, bone marrow, Literature data
Result: negative
Species: Hamster
Chromosomal Aberration Assay In Vivo, bone marrow, Literature data
Result: negative
Species: Rat
Chromosomal Aberration Assay In Vivo; germ cells, Literature data
Result: negative
Species: Hamster
Dominant lethal assay, Literature data
Result: negative
Species: Mouse

Mutagenicity

PROPAFENONE HYDROCHLORIDE

Micronucleus Assay, Literature data

Result: negative

Species: Hamster

Micronucleus Assay, Literature data

Result: negative

Species: Rat

Carcinogenicity

Health injuries are not known or expected under normal use.

PROPAFENONE HYDROCHLORIDE

2 year bioassay, Literature data

Result: negative

Species: Mouse

2 year bioassay, Literature data

Result: negative

Species: Rat

Reproductive toxicity

Components in this product have been shown to cause birth defects and reproductive disorders in laboratory animals. This product is not expected to cause reproductive or developmental effects.

Reproductive toxicity**Reproductivity**

PROPAFENONE HYDROCHLORIDE

Embryo-foetal development - Oral, Literature data

Result: LOAEL (foetal effects) = 15 mg/kg/day (increased post-implantation loss, no maternal effect)

Species: Rabbit

Embryo-foetal development - Oral, Literature data

Result: Maternal and foetal toxicity (no evidence of malformations) with dose of 150 mg/kg/day

Species: Rabbit

Embryo-foetal development - Oral, Literature data

Result: Maternal and foetal toxicity (no evidence of malformations) with doses of 600 mg/kg/day

Species: Rat

Embryo-foetal development - Oral, Literature data

Result: NOAEL (maternal and foetal) = 270 mg/kg/day

Species: Rat

Fertility, Literature data

Result: NOAEL (oral) / fertility = 270 mg/kg/day (maximum dose; 3X equivalent of recommended maximum human therapeutic dose)

Species: Rat

Specific target organ toxicity - single exposure None known.**Specific target organ toxicity - repeated exposure** None known.

PROPAFENONE HYDROCHLORIDE

Repeat dose non-clinical studies

Result: NOAEL = 90 mg/kg/day (equivalent to maximum recommended human dose); with doses of 180 mg/kg/day or more for 6 months adverse, but reversible, changes were observed in kidney; with doses of 270 mg/kg/day fatty degeneration of liver was observed

Species: Rat

Organ: kidney, liver

Aspiration hazard

Not likely, due to the form of the product.

Mixture versus substance information

No information available.

Other information

Caution - Pharmaceutical agent.

SECTION 12: Ecological information**12.1. Toxicity**

No information is available about the potential of this product to produce adverse environmental effects.

Components**Species****Test results**

HYDROXYPROPYL METHYL CELLULOSE (CAS 9004-65-3)

Aquatic*Acute*

Fish

EC50

Fish

> 100 mg/l, 96 hours

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
Microtox	EC50	Microtox 12.5 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-atmospheric)

MAGNESIUM STEARATE 17 Hours Estimated

UV/visible spectrum wavelength

MAGNESIUM STEARATE 210 nm

Biodegradability

Percent degradation (Aerobic biodegradation-inherent)

MAGNESIUM STEARATE 77 %, 28 days BOD

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)

HYDROXYPROPYL METHYL CELLULOSE -5

Bioconcentration factor (BCF)

HYDROXYPROPYL METHYL CELLULOSE 3.2 Estimated

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

HYDROXYPROPYL METHYL CELLULOSE 0 atm m³/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. Observe all local and national regulations when disposing of this product. Collect for recycling or recovery if possible. The disposal method for rejected products/returned goods must ensure that they cannot be re-sold or re-used.
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(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.

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	<p>R20/22 Harmful by inhalation and if swallowed.</p> <p>R36/37/38 Irritating to eyes, respiratory system and skin.</p> <p>H302 Harmful if swallowed.</p> <p>H315 Causes skin irritation.</p> <p>H319 Causes serious eye irritation.</p> <p>H335 May cause respiratory irritation.</p>
Revision information	<p>Product and Company Identification: Product and Company Identification</p> <p>Composition / Information on Ingredients: Ingredients</p> <p>Transport Information: Agency Name and Packaging Type/Transport Mode Selection</p> <p>Regulatory Information: United States</p> <p>GHS: Classification</p>
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.