

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

1.1. Product identifier

Trade name or designation of the mixture	RETIGABINE IR TABLET
Registration number	-
Synonyms	POTIGA * TROBALT * POTIGA TABLETS (50 MG, 100 MG, 200 MG, 300 MG , 400 MG) * TROBALT TABLETS (50 MG, 100 MG, 200 MG, 300 MG , 400 MG) * EZOGABINE IMMEDIATE RELEASE TABLETS * RETIGABINE IMMEDIATE RELEASE TABLETS
Issue date	02-August-2010
Version number	05
Revision date	30-April-2012
Supersedes date	20-April-2012

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 (by country / geographic region):
Africa / EU / Israel / Middle East
(English / European languages): +44 (0) 1235 239 670
Asia Pacific (except China): +65 3158 1074
China: +86 10 5100 3039
Middle East / Africa (Arabic-speaking countries): +44 (0) 1235 239 671
United States: +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.
Not expected to be a significant health hazard unless product is crushed or broken.
Toxic by ingestion.
Health effects information is based on hazards of components.
This product contains an ingredient(s) that is very toxic to aquatic organisms; and may cause long-term adverse effects in the aquatic environment.

SECTION 3: Composition/information on ingredients

3.1. Mixtures

General information

Chemical name	%	CAS-No. / EC No.	REACH Registration No.	INDEX No.	Notes
RETIGABINE	60.0 - 63.0	150812-12-7	-	-	
Classification:	DSD: T;R23/25, N;R50/53				
	CLP: Acute Tox. 3;H301, Acute Tox. 3;H331, Aquatic Acute 1;H400, Aquatic Chronic 1;H410				
Titanium dioxide	0.6 - 1.2	13463-67-7 236-675-5	-	-	
Classification:	DSD: -				
	CLP: -				

>35.0

SECTION 4: First aid measures

General information

Pre-placement and periodic health surveillance is not usually indicated. The final determination of the need for health surveillance should be determined by local risk assessment.

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

Accidental exposure or contact might produce: tingling lips
Additional effects of overexposure may occur. The possible symptoms of overexposure include: dizziness; somnolence; fatigue; weakness; memory effects; headache; dyspeptic symptoms; nausea; diarrhoea; constipation; abnormal nervous system sensations; blurred vision; vertigo; tremor; incoordination; mental impairment; anxiety; malaise; hallucinations; anaemia; nervousness; weight gain; changes in clinical chemistry parameters; urine retention; swelling; irregular heartbeat.

4.3. Indication of any immediate medical attention and special treatment needed

No specific antidotes are recommended.

SECTION 5: Firefighting measures

General fire hazards

Expected to be non-combustible.

5.1. Extinguishing media

Suitable extinguishing media

Water or foam extinguishers are recommended.

Unsuitable extinguishing media

Carbon dioxide or dry powder extinguishers may be ineffective.

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

Since toxic, corrosive or flammable vapours might be evolved from fires involving this material, self contained breathing apparatus and full protective equipment are recommended for firefighters.

Special fire fighting procedures

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 Wear protective clothing and equipment consistent with the degree of hazard.

For emergency responders 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. 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 breaking or crushing tablets.

7.2. Conditions for safe storage, including any incompatibilities 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	Form
RETIGABINE (150812-12-7)	8 HR TWA	2000 mcg/m ³	Skin
	OHC Short Term Excursion	1 5000 mcg/m ³	
United Kingdom Components	Type	Value	Form
Titanium dioxide (13463-67-7)	TWA	4 mg/m ³	Respirable.
		10 mg/m ³	Inhalable

Biological limit values

EU

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

United Kingdom

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

Recommended monitoring procedures Not available.

Derived No Effect Level (DNEL) Not available.

Predicted no effect concentrations (PNECs) Not available.

8.2. Exposure controls

Appropriate engineering controls Not available.

Individual protection measures, such as personal protective equipment

General information An eye wash station should be available.

Eye/face protection Wear approved safety glasses with side shields if eye contact is possible.

Skin protection

- **Hand protection** None required for the normal handling of this material.

- **Other** Not available.

Respiratory protection If respiratory protective equipment (RPE) is used, the type of RPE will depend upon air concentrations present, required protection factor as well as hazards, physical properties and warning properties of substances present. Follow local regulations for respirator use in the workplace.

Thermal hazards Not available.

Hygiene measures Wear appropriate clothing to avoid skin contact. Wash hands and arms thoroughly after handling.

Environmental exposure controls

Hazard guidance and control recommendations Not available.

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 applicable.

Melting point/freezing point Not available.

Initial boiling point and boiling range Not available.

Flash point Not applicable.

Evaporation rate Not applicable.

Flammability (solid, gas) Not applicable.

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.

Vapour pressure Not applicable.

Vapour density Not applicable.

Relative density Not available.

Solubility(ies) Not available.

Partition coefficient (n-octanol/water) Not available.

Decomposition temperature Not available.

Viscosity Not applicable.

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 Not available.

10.2. Chemical stability This product is expected to be stable.

10.3. Possibility of hazardous reactions Not available.

10.4. Conditions to avoid None for normal handling of this product.

10.5. Incompatible materials Not available.

10.6. Hazardous decomposition products Toxic, corrosive or flammable thermal decomposition products are expected when the product is exposed to fire.

SECTION 11: Toxicological information

General information This product contains active ingredient(s) with the following activity: a potassium channel activator

Information on likely routes of exposure

Ingestion Exposure from ingestion may occur.

Inhalation No studies have been conducted.

Skin contact Direct contact may occur.

Eye contact Direct contact may occur.

Symptoms Possible effects of overexposure in the workplace include: weakness; headache; nausea; diarrhoea; somnolence; dizziness; abnormal nervous system sensations; blurred vision; vertigo; tremor; memory effects; fatigue; dyspeptic symptoms; constipation; mental impairment; anxiety; malaise; hallucinations; weight gain; changes in clinical chemistry parameters; urine retention; swelling; irregular heartbeat; incoordination; anaemia; nervousness

11.1. Information on toxicological effects

Acute toxicity Toxicity might occur following ingestion. Toxic effects were associated with repeated ingestion of this material.

Components	Species	Test results
RETIGABINE (150812-12-7)		
Acute		
<i>Oral</i>		
LD	Rat	100 mg/kg
Chronic		
<i>Oral</i>		
NOAEL	Rat	5.1 mg/kg/day, 90-day
Subchronic		
<i>Oral</i>		
NOAEL	Dog	3 mg/kg/day, 13 weeks < 4.64 mg/kg/day, 52 weeks
	Rat	17.8 mg/kg/day, 26 weeks 10 mg/kg/day, 13 weeks
Titanium dioxide (13463-67-7)		
Acute		
<i>Inhalation</i>		
LC50	Rat	6820 mcg/m3
<i>Oral</i>		
LD50	Rat	> 24 g/kg
Skin corrosion/irritation		
Serious eye damage/eye irritation	Not available.	
Respiratory sensitisation	No studies have been conducted.	
Skin sensitisation	Sensitisation (allergic skin reaction) is not expected.	
Germ cell mutagenicity	Not expected to be genotoxic under occupational exposure conditions.	
Mutagenicity		
RETIGABINE		Rat UDS assay Result: negative bacterial mutation assay (Ames) Result: negative human peripheral lymphocyte test (chromosome aberration) Result: positive in vitro UDS assay Result: negative mammalian cell mutation assay (CHO/HGPRT forward mutation assay) Result: negative mouse micronucleus assay Result: negative
Carcinogenicity		
RETIGABINE		Not expected to produce cancer in humans under occupational exposure conditions. Titanium dioxide produced carcinogenic effects in Carcinogenic activity was seen in inhalation studies using laboratory animals. High concentrations or doses administered over an extended period of time were required to produce adverse effects. ICH S1B Result: negative Species: Rat Test Duration: 2 years Neonatal, Dose day 8 and day 15 Result: negative Species: Mouse Observation Period: 1 years

IARC Monographs. Overall Evaluation of Carcinogenicity

Titanium dioxide (CAS 13463-67-7)

2B Possibly carcinogenic to humans.

Reproductive toxicity

This material is not considered to be a hazard to human fertility under occupational exposure conditions. The ingredient retigabine has caused adverse effects on the development of unborn offspring in animal studies. These effects are linked only to high doses of this substance; low doses did not produce this adverse effect. Effects seen at therapeutic or higher doses are likely not relevant to occupational hazard estimation.

Reproductivity

RETIGABINE

4.64 - 46.4 mg/kg/day Fertility and general reproductive performance
Result: negative
Species: Rat

Specific target organ toxicity - single exposure

Adverse effects might occur in the following organ(s) following overexposure: central nervous system.

Specific target organ toxicity - repeated exposure

Repeated exposure to high doses may result in adverse effects in the following organs or tissues: liver; bladder. The nature and/or extent of these effects do not meet the criteria for classification under international labelling regulations.

Aspiration hazard

No studies have been conducted.

Mixture versus substance information

No studies have been conducted.

Other information

Not available.

SECTION 12: Ecological information

12.1. Toxicity

This product contains an ingredient(s) that is very toxic to aquatic organisms; and may cause long-term adverse effects in the aquatic environment. Consult the MSDS of the active ingredient for specific information about potential environmental effects. Appropriate precautions should be taken to limit release of this material to the environment. Local regulations and procedures should be consulted prior to environmental release.

Components		Species	Test results
RETIGABINE (150812-12-7)			
Aquatic			
<i>Acute</i>			
Activated Sludge Respiration	IC50	Activated sludge	> 100 mg/l, 3 hours
	NOEC	Activated sludge	100 mg/l, 3 hours
Algae	EC50	Green algae (<i>Pseudokirchnerella subcapitata</i>)	0.13 mg/l, 72 hours, Measured
	NOEC	Algae	0.037 mg/l, 72 hours
<i>Chronic</i>			
Crustacea	LOEC	Water flea (<i>Daphnia magna</i>)	3.1 mg/l, 21 days, Measured
	NOEC	<i>Daphnia</i>	0.9 mg/l, 21 days
Fish	Growth test LOEC	Fish	0.1 mg/l, 28 days, Measured
	Growth test NOEC	Fathead minnow (Juvenile <i>Pimephales promelas</i>)	0.032 mg/l, 28 days, Measured
Other	LOEC	Chironomid (<i>Chironomus riparius</i>)	100 mg/l, 28 days, Measured
	NOEC Growth	Chironomid (<i>Chironomus riparius</i>)	32 mg/l, 28 days, Measured

Titanium dioxide (13463-67-7)

Aquatic

Acute

Crustacea

EC50 Water flea (*Daphnia magna*) > 1000 mg/l, 48 hours, Static test

12.2. Persistence and degradability

This material contains an active pharmaceutical ingredient that has been shown to be chemically unstable in water when exposed to light. Aqueous photolysis may be a significant depletion mechanism. This material contains an active ingredient that is not readily biodegradable (as defined by 1993 OECD Testing Guidelines). It may persist in the environment.

Photolysis

UV/visible spectrum wavelength

RETIGABINE

304 nm Measured, pH 1-13

Biodegradability**Percent degradation (Aerobic biodegradation-ready)**

RETIGABINE

< 5 %, 28 days BOD

12.3. Bioaccumulative potential This material contains an active ingredient that will not have a tendency to bioaccumulate in the food chain.

Partition coefficient**n-octanol/water (log Kow)**

RETIGABINE

2.18 (Measured).

12.4. Mobility in soil

This material contains an active ingredient that is not likely to adsorb to soil or sediment if released directly to the environment.

Adsorption**Soil/sediment sorption - log Kd**

RETIGABINE

1.3 - 2.2 Measured

Mobility in general

This material contains an active pharmaceutical ingredient with octanol/water partition coefficient data that suggests that for environmental fate predictions the active pharmaceutical ingredient will not have the tendency to distribute into fats.

Distribution**Octanol/water distribution coefficient log DOW**

RETIGABINE

2.1 Measured., pH 5

2.2 Measured., pH 7

2.2 Measured., pH 9

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 Not available.

Contaminated packaging Not available.

EU waste code Not available.

Disposal methods/information 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.

SECTION 14: Transport information

The SDS should accompany all shipments for reference in the event of spillage or accidental release. Only authorised persons trained and competent in accordance with appropriate national and international regulatory requirements may prepare dangerous goods for transport.

ADR

Not regulated as dangerous goods.

Not subject to ADR, see SP 601.

IATA

14.1. UN number UN3249

14.2. UN proper shipping name Medicine, solid, toxic, n.o.s. (RETIGABINE IMMEDIATE RELEASE TABLETS (CONTAINING 60% - 63% RETIGABINE))

14.3. Transport hazard class(es) 6.1

Subsidiary class(es) -

14.4. Packing group III

14.5. Environmental hazards Not available.

Labels required 6.1

ERG Code 6L

14.6. Special precautions for user Per IATA 7.1.6.3, may require environmentally hazardous substance mark (fish and tree symbol). May be able to ship as an Excepted or Limited Quantity.

IMDG

14.1. UN number UN3249

14.2. UN proper shipping name Medicine, solid, toxic, n.o.s. (RETIGABINE IMMEDIATE RELEASE TABLETS (CONTAINING 60% - 63% RETIGABINE)), Marine pollutant

14.3. Transport hazard class(es) 6.1

Subsidiary class(es) -

14.4. Packing group III

14.5. Environmental hazards

Marine pollutant

Yes

Labels required

6.1

EmS No.

F-A, S-A

14.6. Special precautions for user

Per IMDG 5.2.1.6 may require environmentally hazardous substance mark (fish and tree symbol). May be able to ship as an Excepted or Limited Quantity.

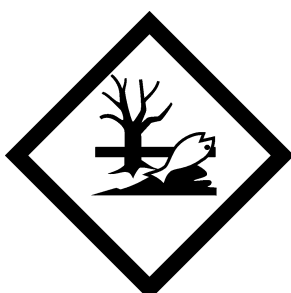
14.7. Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

This substance/mixture is not intended to be transported in bulk.

ADN; IATA; IMDG; RID



Marine pollutant



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. 143/2011 Annex XIV Substances Subject to Authorisation

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.

National regulations Not available.

15.2. Chemical safety assessment Not available.

SECTION 16: Other information

List of abbreviations Not available.

References GSK Hazard Determination

Information on evaluation method leading to the classification of mixture Not available.

Full text of any statements or R-phrases and H-statements under Sections 2 to 15
R23/25 Toxic by inhalation and if swallowed.
R50/53 Very toxic to aquatic organisms, May cause long-term adverse effects in the aquatic environment.

H301 - Toxic if swallowed.

H331 - Toxic if inhaled.

H400 - Very toxic to aquatic life.

H410 - Very toxic to aquatic life with long lasting effects.

Revision information TRANSPORT INFORMATION: Material Transportation Information

Training information Not available.

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.

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