SAFETY DATA SHEET

1. Identification

Product identifier **VOLIBRIS TABLETS**

Other means of identification

Synonyms VOLIBRIS 5 MG TABLETS * VOLIBRIS 10 MG TABLETS * AMBRISENTAN, 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	< 25
AMBRISENTAN	(S)-2-(4,6-DIMETHYL-PYRIMIDIN-2-YLOXY) -3-METHOXY-3,3- DIPHENYLPROPANOIC ACID * BSF 208075 * GSK1325760	177036-94-1	3.4 - < 7
MAGNESIUM STEARATE	STEARIC ACID, MAGNESIUM SALT * MAGNESIUM DISTEARATE * DIBASIC MAGNESIUM STEARATE * MAGNESIUM DISTEARATE, PURE	557-04-0	< 1
TALC	TALCUM, NON-ASBESTOS FORM * TALC * HYDROUS MAGNESIUM SILICATE	14807-96-6	< 1

Chemical name	Common name and synonyms	CAS number	%
TITANIUM DIOXIDE	TITANIUM OXIDE * TITANIUM(IV) OXIDE * TITANIUM PEROXIDE (TiO2) * PIGMENT WHITE 6	13463-67-7	< 1
Other components below reportable levels			60 - < 70

*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
None known.
The following adverse effects have been noted with therapeutic use of this material: headache; flushing; dizziness.

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
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.

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. Keep out of low areas. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. For personal protection, see section 8 of the SDS.

Methods and materials for containment and cleaning up
Stop the flow of material, if this is without risk. Prevent entry into waterways, sewer, basements or confined areas. Following product recovery, flush area with water. For waste disposal, see section 13 of the SDS.

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

7. Handling and storage

Precautions for safe handling
Avoid prolonged exposure. Observe good industrial hygiene practices.

Conditions for safe storage, including any incompatibilities
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
AMBRISENTAN (CAS 177036-94-1)	8 HR TWA	20 mcg/m3	
	OHC	3	REPRODUCTIVE HAZARD
MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)	OHC	1	

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/m3	Respirable fraction.
		15 mg/m3	Total dust.
TITANIUM DIOXIDE (CAS 13463-67-7)	PEL	15 mg/m3	Total dust.

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

Components	Type	Value	Form
TALC (CAS 14807-96-6)	TWA	0.3 mg/m3	Total dust.
		0.1 mg/m3	Respirable.
		20 mppcf	
		2.4 mppcf	Respirable.

US. ACGIH Threshold Limit Values

Components	Type	Value	Form
MAGNESIUM STEARATE (CAS 557-04-0)	TWA	10 mg/m3	
MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)	TWA	10 mg/m3	
TALC (CAS 14807-96-6)	TWA	2 mg/m3	Respirable fraction.
TITANIUM DIOXIDE (CAS 13463-67-7)	TWA	10 mg/m3	

US. NIOSH: Pocket Guide to Chemical Hazards

Components	Type	Value	Form
MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)	TWA	5 mg/m3	Respirable.
		10 mg/m3	Total
TALC (CAS 14807-96-6)	TWA	2 mg/m3	Respirable.

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

Exposure guidelines

Appropriate engineering controls General ventilation normally adequate.

Individual protection measures, such as personal protective equipment

Eye/face protection If contact is likely, safety glasses with side shields are recommended.

Skin protection

Hand protection For prolonged or repeated skin contact use suitable protective gloves.

Other Wear suitable protective clothing as protection against splashing or contamination.

Respiratory protection No personal respiratory protective equipment normally required. Use a NIOSH/MSHA approved respirator if there is a risk of exposure to dust/fume at levels exceeding the exposure limits.

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. 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. 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.
Ingestion	Health injuries are not known or expected under normal use. May be harmful if swallowed. However, ingestion is not likely to be a primary route of occupational exposure.
Symptoms related to the physical, chemical and toxicological characteristics	None known. The following adverse effects have been noted with therapeutic use of this material: headache; flushing; dizziness.

Information on toxicological effects

Acute toxicity Health injuries are not known or expected under normal use. May be harmful if swallowed.

Components	Species	Test Results
AMBRISENTAN (CAS 177036-94-1)		
Acute		
Oral		
LD50	Rat	>= 3160 mg/kg
MAGNESIUM STEARATE (CAS 557-04-0)		
Acute		
Oral		
LD50	Rat	> 2000 mg/kg
MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)		
Acute		
Dermal		
LD50	Rabbit	> 2000 mg/kg
Oral		
LD50	Rat	> 2000 mg/kg
TITANIUM DIOXIDE (CAS 13463-67-7)		
Acute		
Inhalation		
LC50	Rat	6820 mcg/m3
Oral		
LD50	Rat	> 24 g/kg
Chronic		
Inhalation		
LOEC	Rat	8.6 mg/m3, 1 years TiO2 accumulated in interstitial macrophages, aggregated interstitial cells and particle laden macrophrages in lymphoid tissue.
NOAEC	Rat	250 mg/m3, 2 years Highest dose 5 mg/m3, 24 months
Subacute		
Inhalation		
LOEL	Rat	0.1 - 35 mg/m3, 4 weeks Mild macrophage hyperplasia, no change in bronchio-alveolar lavage fluid.
NOAEC	Guinea pig	26 mg/m3, 3 weeks No evidence of significant inflammation in respiratory tract.
Oral		
NOAEL	Rat	100000 ppm, 14 Day Dietary study, highest dose tested.
Subchronic		
Inhalation		
LOEC	Rat	3.2 - 20 mg/m3, 8 min Accumulation of TiO2 in macrophages and evidence of pulmonary inflammation.

* 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. Prolonged skin contact may cause temporary irritation.

Irritation Corrosion - Skin

TITANIUM DIOXIDE	0, Literature data Result: Non-irritant Species: Guinea pig 0, Literature data Result: Non-irritant Species: Human Acute dermal irritation; OECD 404, Literature data Result: Non-irritant Species: Rabbit
AMBRISENTAN	Reconstituted Human Epidermis (RHE) Result: Negative - Not likely to be a significant irritant.

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.

Eye

TITANIUM DIOXIDE	OECD 405, Literature data Result: Mild irritant Species: Rabbit
AMBRISENTAN	Reconstituted Human Corneal Epithelium (HCE) Result: Negative; not likely to be a severe irritant

Eye / Kay and Calandra class - Intact

MAGNESIUM STEARATE	4 Recovery Period: 2 days

Respiratory or skin sensitization

Respiratory sensitization Not available.

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

Sensitization

TITANIUM DIOXIDE	5 % Optimisation Test, Literature data - Vehicle: petrolatum Result: Negative Species: Guinea pig Test Duration: 48 hour exposure
AMBRISENTAN	OECD 429 / Local Lymph Node Assay, Maximum concentration = 50%; vehicle = DMF Result: Negative Species: Mouse
TITANIUM DIOXIDE	Patch test, Literature data Result: Negative Species: Human

Germ cell mutagenicity Health injuries are not known or expected under normal use. No data available to indicate product or any components present at greater than 0.1% are mutagenic or genotoxic.

Mutagenicity

AMBRISENTAN	Ames Assay, GLP assay Result: Negative
TITANIUM DIOXIDE	Ames, Literature data Result: Negative
AMBRISENTAN	Chromosomal Aberration Assay In Vitro Result: Positive
TITANIUM DIOXIDE	Micronucleus Assay in vitro, CHO cells, Literature data Result: Negative Micronucleus Assay in vitro, cultured human peripheral lymphocytes, Literature data Result: Positive
AMBRISENTAN	Micronucleus Assay, GLP assay Result: Negative Species: Rat
TITANIUM DIOXIDE	Syrian Hamster Embryo (SHE) cell transformation assay Result: Negative
AMBRISENTAN	Unscheduled DNA Synthesis in vivo Result: Negative Species: Rat

Mutagenicity

TITANIUM DIOXIDE	WIL2-NS HPRT/ t-Thioguanidine - Human B-Cell lymphoblastoid, Literature data Result: Positive

Carcinogenicity Health injuries are not known or expected under normal use. Contains a material (titanium dioxide) classified as a carcinogen by external agencies. 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.

TITANIUM DIOXIDE	0.5 mg/m3, Literature data Result: Negative Species: Rat Test Duration: 24 months 0.72 - 14.8 mg/m3, Literature data Result: Negative Species: Mouse 10 - 250 mg/m3, Dietary study - Literature data. Result: Inflammation at all doses with alveolar/bronchiolar adenoma at the highest concentration. Species: Rat Test Duration: 24 months 25000 - 50000 ppm, Dietary study Result: Negative Species: Mouse 25000 - 50000 ppm, Dietary study - Literature data. Result: Negative Species: Rat 7.2 - 14.8 mg/m3, Literature data Result: Lung tumour Species: Rat Test Duration: 24 months

IARC Monographs. Overall Evaluation of Carcinogenicity

TITANIUM DIOXIDE (CAS 13463-67-7)	2B Possibly carcinogenic to humans.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not listed.

Reproductive toxicity Suspected of damaging fertility or the unborn child.

Reproductivity

AMBRISENTAN	Embryo-foetal development Result: Foetal toxicity, malformations in multiple species; endothelin receptor antagonist class effect Fertility, Male Result: Testicular toxicity, reduced fertility in mice and rats

Specific target organ toxicity - single exposure None known.

Specific target organ toxicity - repeated exposure None known.

Aspiration hazard Not available.

Chronic effects Prolonged exposure may cause chronic effects.

Further information Caution - 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
AMBRISENTAN (CAS 177036-94-1)			
Aquatic			
Acute			
Algae	EC50	Algae	10 - 100 mg/l, 96 hours QSAR Estimate
Crustacea	EC50	Daphnia	10 - 100 mg/l, 48 hours QSAR Estimate
Fish	EC50	Fish	10 - 100 mg/l, 96 hours QSAR Estimate

Components		Species	Test Results
MAGNESIUM STEARATE (CAS 557-04-0)			
Aquatic			
Acute			
Fish	EC50	Orange-red killfish (Adult Oryzias latipes)	130 mg/l, 96 hours
TALC (CAS 14807-96-6)			
Aquatic			
Acute			
Fish	EC50	Zebra fish (Adult Brachydanio rerio)	> 100 g/l, 24 hours Static renewal test
TITANIUM DIOXIDE (CAS 13463-67-7)			
Aquatic			
Acute			
Crustacea	EC50	Water flea (Daphnia magna)	> 1000 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

Biodegradability

Percent degradation (Aerobic biodegradation-inherent)

MAGNESIUM STEARATE 77 %, 28 days BOD

Percent degradation (Aerobic biodegradation-soil)

MAGNESIUM STEARATE 50 %, 13 days

Bioaccumulative potential

Partition coefficient n-octanol / water (log Kow)

AMBRISENTAN 1.2 (Measured).

Bioconcentration factor (BCF)

MAGNESIUM STEARATE > 9999 Estimated

Mobility in soil

Adsorption

Soil/sediment sorption - log Koc

MAGNESIUM STEARATE 5.86 Estimated

Mobility in general Not available.

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 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.

14. Transport information

DOT

Not regulated as a dangerous good.

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)

Not 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

MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)
TALC (CAS 14807-96-6)
TITANIUM DIOXIDE (CAS 13463-67-7)

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

MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)
TALC (CAS 14807-96-6)
TITANIUM DIOXIDE (CAS 13463-67-7)

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

MICROCRYSTALLINE CELLULOSE (CAS 9004-34-6)
TALC (CAS 14807-96-6)
TITANIUM DIOXIDE (CAS 13463-67-7)

US. Rhode Island RTK

Not regulated.

US. California Proposition 65

WARNING: This product contains a chemical known to the State of California to cause cancer.

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

TITANIUM DIOXIDE (CAS 13463-67-7) Listed: September 2, 2011

International Inventories

Country(s) or region	Inventory name	On inventory (yes/no)*
Australia	Australian Inventory of Chemical Substances (AICS)	No
Canada	Domestic Substances List (DSL)	No
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
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 11-05-2014

Revision date 11-05-2014

Version # 02

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: Business Units
Composition / Information on Ingredients: Ingredients
Exposure Controls / Personal Protection:
Physical & Chemical Properties:
Regulatory Information: United States
GHS: Classification