SAFETY DATA SHEET

1. Identification

Product identifier **ULTIVA INJECTION**

Other means of identification Not available.

Synonym(s) ULTIVA INJECTION 1 MG * ULTIVA INJECTION 2 MG * ULTIVA INJECTION 5 MG * ARCOD INJECTION 1 MG * ARCOD INJECTION 2 MG * ARCOD INJECTION 5 MG * REMIFENTANIL HYDROCHLORIDE, 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

Hazardous components

Chemical name	Common name and synonyms	CAS number	%
GLYCINE	AMINOACETIC ACID 2-AMINOACETIC ACID AMINOETHANOIC ACID GLYCOCOLL GLYCOSTHENE	56-40-6	80 - < 90
REMIFENTANIL HYDROCHLORIDE	3-(4-METHOXYCARBONYL-4-((1-OXOPROI ACID, METHYL ESTER, HYDROCHLORIDE GI 87084B 913 (GW ACN)	132539-07-2	6.7 - < 26.8

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

4. First-aid measures

Inhalation In case of accident by inhalation: remove casualty to fresh air and keep at rest. If breathing is difficult, trained personnel should give oxygen. If not breathing, give artificial respiration. Get medical attention if symptoms occur.

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	Immediately flush eyes with plenty of water for at least 15 minutes. Get medical attention if irritation develops and persists.
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.
Most important symptoms/effects, acute and delayed	The following adverse effects have been noted with therapeutic use of this material: interference with control of muscle contraction; changes in heart rate or pulse; changes in blood pressure; respiratory depression; cessation of breathing; nausea; vomiting; itching; shivering.
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 centre.
General information	Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves. 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.

5. Fire-fighting measures

Suitable extinguishing media	Water fog. Foam. Dry chemical powder.
Unsuitable extinguishing media	Carbon dioxide (CO2).
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	In the event of fire, cool tanks with water spray.
Specific methods	Cool containers exposed to flames with water until well after the fire is out.

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. Use a NIOSH/MSHA approved respirator if there is a risk of exposure to dust/fume at levels exceeding the exposure limits. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Avoid inhalation of dust from the spilled material. For personal protection, see section 8 of the MSDS.
Methods and materials for containment and cleaning up	Minimize dust generation and accumulation. If sweeping of a contaminated area is necessary use a dust suppressant agent which does not react with the product. Sweep up or vacuum up spillage and collect in suitable container for disposal. Collect dust using a vacuum cleaner equipped with HEPA filter. Prevent entry into waterways, sewer, basements or confined areas. Following product recovery, flush area with water. For waste disposal, see section 13 of the MSDS.
Environmental precautions	Avoid discharge into drains, water courses or onto the ground.

7. Handling and storage

Precautions for safe handling	Minimize dust generation and accumulation. Provide appropriate exhaust ventilation at places where dust is formed. Avoid breathing dust. Avoid contact with skin and eyes. Avoid prolonged exposure. In case of insufficient ventilation, wear suitable respiratory equipment. Practice good housekeeping.
Conditions for safe storage, including any incompatibilities	Store in original tightly closed container. Store in a well-ventilated place. Guard against dust accumulation of this material. Store away from incompatible materials (see Section 10 of the MSDS).

8. Exposure controls/personal protection

Occupational exposure limits

GSK Components	Type	Value	Note
GLYCINE (CAS 56-40-6)	8 HR TWA	5000 mcg/m3	
	OHC	1	
REMIFENTANIL HYDROCHLORIDE (CAS 132539-07-2)	15 MIN STEL	1 mcg/m3	
	OHC	5	SKIN

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

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. Good general ventilation (typically 10 air changes per hour) should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels to an acceptable level. Ventilation should be sufficient to effectively remove and prevent buildup of any dusts or fumes that may be generated during handling or thermal processing. If engineering measures are not sufficient to maintain concentrations of dust particulates below the Occupational Exposure Limit (OEL), suitable respiratory protection must be worn.

Individual protection measures, such as personal protective equipment

Eye/face protection	If contact is likely, safety glasses with side shields are recommended.
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.
Other	Not normally needed.
Respiratory protection	Respiratory protective equipment (RPE) is not required for normal handling of this product.
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.
General hygiene considerations	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. Keep away from food and drink. 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.

9. Physical and chemical properties

Appearance

Physical state	Solid.
Form	Powder.
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)	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. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
Incompatible materials	Strong oxidizing agents.
Hazardous decomposition products	Irritating and/or toxic fumes and gases may be emitted upon the products decomposition.

11. Toxicological information

Information on likely routes of exposure

Ingestion	Health injuries are not known or expected under normal use.
Inhalation	Health injuries are not known or expected under normal use. May cause irritation to the respiratory system. Substance likely to cause pharmacologically mediated or other adverse effects upon inhalation.
Skin contact	Health injuries are not known or expected under normal use. Dust or powder may irritate the skin. Pharmacological effects might occur following direct contact with skin.
Eye contact	Health injuries are not known or expected under normal use. Dust or powder may irritate eye tissue. Direct contact with eyes might produce evidence of pharmacological effects.
Symptoms related to the physical, chemical and toxicological characteristics	The following adverse effects have been noted with therapeutic use of this material: interference with control of muscle contraction; changes in heart rate or pulse; changes in blood pressure; respiratory depression; cessation of breathing; nausea; vomiting; itching; shivering. No specific target organ effects have been identified.

Information on toxicological effects

Acute toxicity Health injuries are not known or expected under normal use.

Components	Species	Test Results
GLYCINE (CAS 56-40-6)		
Acute		
Oral		
LD50	Rat	7930 mg/kg
REMIFENTANIL HYDROCHLORIDE (CAS 132539-07-2)		
Acute		
Dermal		
LD50	Rabbit	> 2000 mg/kg, Pharmacological effects evident from dermal absorption.
Oral		
LD50	Rat	> 2000 mg/kg
Subacute		
Other		
NOEL	Dog	< 0.01 mg/kg/day, 32 Day, Pharmacological effects, intravenous dosing.
	Rat	< 0.05 mg/kg/day, 4 weeks, Pharmacological effects, intravenous dosing.
TD	Dog	0.03 mg/kg/day, 32 Day, Intravenous infusion
	Rat	2.5 mg/kg/day, 4 weeks, intravenous

* 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

REMIFENTANIL HYDROCHLORIDE	Acute dermal irritation; OECD 404 Result: Non-irritant Species: Rabbit

Serious eye damage/eye irritation Health injuries are not known or expected under normal use. Dust or powder may irritate eye tissue.

Eye

REMIFENTANIL HYDROCHLORIDE	6 mg/kg Result: Non-lethal, non-irritating. Species: Rabbit

Eye

REMIFENTANIL HYDROCHLORIDE	>= 12.5 mg/kg Result: Lethal Species: Rabbit

Respiratory sensitization Not available.

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

Sensitization

REMIFENTANIL HYDROCHLORIDE	Buehler assay 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.

REMIFENTANIL HYDROCHLORIDE	1.6 - 6.6 mg/kg Micronucleus Test, Intravenous dosing. Result: Negative Species: Rat 1.6 - 6.6 mg/kg Unscheduled DNA Synthesis, in vivo - in vitro, Intravenous dosing. Result: Negative Species: Rat 80 - 120 mg/kg Micronucleus Assay, Intravenous dosing. Result: Negative Species: Mouse Ames, GLP Result: Negative Chromosomal Aberration Assay In Vitro Result: Negative L5178Y mouse lymphoma thymidine kinase locus assay, GLP Result: Negative

Carcinogenicity Health injuries are not known or expected under normal use.

Reproductive toxicity This product is not expected to cause reproductive or developmental effects.

REMIFENTANIL HYDROCHLORIDE	0.1 - 0.5 mg/kg/day Embryofetal Development, Intravenous dosing. Result: Maternal NOAEL Species: Rabbit 0.5 - 1.6 mg/kg/day Fertility/foetal development, Intravenous dosing. Result: Reduced food consumption. Species: Rat 0.5 - 5 mg/kg/day Fertility, Male, Intravenous dosing. Result: Reduced fertility, toxicity, including death at higher doses. Species: Rat 0.8 mg/kg/day Embryofetal Development, Intravenous dosing. Result: Maternal toxicity; Foetal NOAEL 1 - 2 mg/kg/day Embryofetal Development, Intravenous dosing. Result: Maternal toxicity, resorptions, foetal malformations. Species: Rabbit 5 mg/kg/day Fertility/foetal development, Intravenous dosing. Result: Maternal toxicity; Foetal NOAEL Species: Rat

Specific target organ toxicity - single exposure None known.

REMIFENTANIL HYDROCHLORIDE	Clinical studies. Species: Human

Specific target organ toxicity - repeated exposure None known.

Aspiration hazard Not available.

12. Ecological information

Ecotoxicity Not expected to be harmful to aquatic organisms.

Components		Species	Test Results
GLYCINE (CAS 56-40-6)			
Aquatic			
Acute			
Fish	EC50	Fathead minnow (Adult Pimephales promelas)	> 100 mg/l
REMIFENTANIL HYDROCHLORIDE (CAS 132539-07-2)			
Aquatic			
Acute			
Activated Sludge Respiration	IC50	Residential sludge	> 91.2 mg/l, 3 hours, OECD 209
Crustacea	EC50	Water flea (Daphnia magna)	> 360 mg/l, 48 hours, Static test, OECD 202

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

Persistence and degradability

Photolysis

Half-life (Photolysis-atmospheric)

GLYCINE	4.6 Hours Estimated

UV/visible spectrum wavelength

REMIFENTANIL HYDROCHLORIDE	267 nm Measured, pH 7

Hydrolysis

Half-life (Hydrolysis-acidic)

REMIFENTANIL HYDROCHLORIDE	21.3 Days Measured

Half-life (Hydrolysis-basic)

REMIFENTANIL HYDROCHLORIDE	3.5 Hours Measured

Half-life (Hydrolysis-neutral)

REMIFENTANIL HYDROCHLORIDE	9.5 Hours Measured

Biodegradability

Percent degradation (Aerobic biodegradation-soil)

REMIFENTANIL HYDROCHLORIDE	22.62 - 30.41 %, 64 days

Bioaccumulative potential

Partition coefficient n-octanol / water (log Kow)

GLYCINE	-3.21
REMIFENTANIL HYDROCHLORIDE	1.36

Mobility in soil

Adsorption

Soil/sediment sorption - log Koc

GLYCINE	0 Estimated
REMIFENTANIL HYDROCHLORIDE	1.97 - 2.99, pH 4.5-6.5

Mobility in general

Volatility

Henry's law

GLYCINE	0 atm m^3/mol Estimated
REMIFENTANIL HYDROCHLORIDE	0 atm m^3/mol Calculated

Other adverse effects Not available.

13. Disposal considerations

Disposal instructions Collect and reclaim or dispose in sealed containers at licensed waste disposal site.

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).

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

UN number UN3249

UN proper shipping name	Medicine, solid, toxic, n.o.s. (ULTIVA INJECTION (CONTAINING <27% REMIFENTANIL HYDROCHLORIDE))
Transport hazard class(es)	6.1(PGIII)
Subsidiary class(es)	Not available.
Packing group	III
Special precautions for user	Not available.
Labels required	6.1
Special provisions	T1, TP33
Packaging exceptions	153
Packaging non bulk	213
Packaging bulk	240
Qty limits cargo	200 kg
Qty limits passenger	100 kg

IATA

UN number	UN3249
UN proper shipping name	Medicine, solid, toxic, n.o.s. (ULTIVA INJECTION (CONTAINING <27% REMIFENTANIL HYDROCHLORIDE))
Transport hazard class(es)	6.1(PGIII)
Subsidiary class(es)	-
Packaging group	III
Labels required	6.1
ERG Code	Not available.

IMDG

UN number	UN3249
UN proper shipping name	MEDICINE, SOLID, TOXIC, N.O.S. (ULTIVA INJECTION (CONTAINING <27% REMIFENTANIL HYDROCHLORIDE))
Transport hazard class(es)	6.1(PGIII)
Subsidiary class(es)	-
Packaging group	III
Environmental hazards	
Marine pollutant	No
Labels required	6.1
EmS	F-A, S-A
Special precautions for user	Not available.

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.

DOT

IATA; IMDG

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.

US. OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not listed.

SARA 304 Emergency release notification

Not regulated.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

Hazard categories	Immediate Hazard - Yes Delayed Hazard - No Fire Hazard - Yes Pressure Hazard - No Reactivity Hazard - No
SARA 302 Extremely hazardous substance	No
SARA 311/312 Hazardous chemical	No

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.
Food and Drug Administration (FDA)	Not regulated.

US state regulations

US. Massachusetts RTK - Substance List

Not regulated.

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

Not regulated.

US. Pennsylvania RTK - Hazardous Substances

Not regulated.

US. Rhode Island RTK

Not regulated.

US. California Proposition 65

California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): This material is not known to contain any chemicals currently listed as carcinogens or reproductive toxins.

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	11-01-2013
Revision date	11-01-2013

Version #	10
Further information	Not available.
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 Hazards Identification: US Hazard Categories Composition / Information on Ingredients: Ingredients Physical & Chemical Properties: Transport Information: Proper Shipping Name/Packing Group Regulatory Information: United States GHS: Classification