

Safety Data Sheet

Bezafibrato



Safety Data Sheet dated 3/14/2011, version 2



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

1.1. Product identifier

Identification of the substance

Trade name: Bezafibrato

Trade code: SOLD0062

Chemical name: acid, 2-[4-[2-[(4-chlorobenzoyl)amino]ethyl]phenoxy]-2-methyl-

Molecular formula: C₁₉H₂₀ClN₂O₄

Molecular weight: 361.85

CAS number: 41859-67-0

EC number: 255-567-9

The transition time according to REACH Regulation, Article 23 is still not expired.

1.2 Relevant identified uses of the substance/mixture and uses advised against: See paragraph 3

1.3 Details of the supplier of the safety data sheet

Company:

OLON SPA

Strada Rivoltana, km 6/7

20090 Rodano (MI) Italy

Competent person responsible for the safety data sheet:

msds@olonspa.it

1.4. Emergency telephone number telephone number: +39 0382 8250.1
available Monday through Friday from 9:00 am to 18:00

SECTION 2: Hazards identification

2.1. Classification of the substance or mixture

Directive criteria, 67/548/CE, 99/45/EC and following amendments thereof:

Properties / Symbols:

Toxic for reproduction category 3

Xn Harmful

R Phrases:

R22 Harmful if swallowed.

R52 Harmful to aquatic organisms.

R63 Possible risk of harm to the unborn child

EC regulation criteria 1272/2008 (CLP)

Warning, Acute Tox. 4, Harmful if swallowed.

Warning, Repr. 2, Suspected of damaging the unborn child.

Adverse physicochemical, human health and environmental effects:

No other hazards

2.2. Label elements

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Xn

Symbols:

Xn Harmful

R Phrases:

R22 Harmful if swallowed.

R52 Harmful to aquatic organisms.

R63 Possible risk of harm to the unborn child

S Phrases:

S36/37 Wear suitable protective clothing and gloves.

S60 This material and its container must be disposed of as hazardous waste.

S61 Avoid release to the environment. Refer to special instructions/Safety data sheets.

Symbols:



Warning

Hazard statements:

H302 Harmful if swallowed.

H361d Suspected of damaging the unborn child.

Precautionary statements:

P264 Wash hands thoroughly after handling.

P281 Use personal protective equipment as required.

P301+P312 IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell.

P308+P313 IF exposed or concerned: Get medical advice/attention.

P405 Store locked up.

P501 Dispose of contents/container in accordance with all local/Regional/national/international regulations.

Special Provisions:

Not classified

2.3. Other hazards

The product can support combustion. The ignition of dust in certain conditions can cause an explosion. Dust may be sensitive to electrostatic ignition sources. In case of fire, may emit toxic fumes (oxides of nitrogen, carbon).

vPvB Substances: - PBT Substances: Not classified

Other Hazards:

No other hazards

SECTION 3: Composition/information on ingredients

3.1. Substances

Identification of the substance

Chemical characterization: Bezafibrato

Trade code: SOLDO062

SOLDO062/2

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Product type and use: active pharmaceutical ingredient
CAS number: 41859-67-0
EC number: 255-567-9

100 % Propanoic acid, 2-[4-[2-[(4-chlorobenzoyl)amino]ethyl]phenoxy]-2-methyl-
CAS: 41859-67-0 EC: 255-567-9

Repr. Cat. 3,Xn; R22-63-52

 3.1/4/Oral Acute Tox. 4 H302

 3.7/2 Repr. 2 H361d

3.2. Mixtures
N.A.

SECTION 4: First aid measures

4.1. Description of first aid measures

In case of skin contact:

Immediately take off all contaminated clothing.

Areas of the body that have - or are only even suspected of having - come into contact with the product must be rinsed immediately with plenty of running water and possibly with soap.

Wash thoroughly the body (shower or bath).

In case of eyes contact:

In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

In case of Ingestion:

Give nothing to eat or drink.

Do not under any circumstances induce vomiting. OBTAIN A MEDICAL EXAMINATION IMMEDIATELY.

In case of Inhalation:

After contact with skin, wash immediately with soap and plenty of water.

4.2. Most important symptoms and effects, both acute and delayed

None

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

In case of accident or unwellness, seek medical advice immediately (show directions for use or safety data sheet if possible).

Treatment:

None

SECTION 5: Firefighting measures

5.1. Extinguishing media

Suitable extinguishing media:

Water.

Carbon dioxide (CO₂).

Extinguishing media which must not be used for safety reasons:

avoid water jets to disperse the product.

5.2. Special hazards arising from the substance or mixture

Do not inhale explosion and combustion gases.

Burning produces heavy smoke.

Substance that can sustain combustion when exposed to heat and ignition sources. Thermal decomposition produces toxic fumes of oxides of nitrogen and carbon. In the absence of oxygen may generate other toxic gases. Like most organic powders, may cause an explosion if the powder is dispersed into the air and set off.

5.3. Advice for firefighters

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Use suitable breathing apparatus .

Wear respirator, gloves, protective footwear. CAUTION: Pressurized containers may explode when exposed to fire. And 'recommended the use of breathing apparatus and full protection for fire fighting, since the combustion of this substance may generate toxic fumes, corrosive and flammable. If possible contain water used for fire fighting and collect for later disposal Collect contaminated fire extinguishing water separately. This must not be discharged into drains.

Move undamaged containers from immediate hazard area if it can be done safely.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

Wear personal protection equipment.

Remove persons to safety.

See protective measures under point 7 and 8.

6.2. Environmental precautions

Circumscribe the area of the spill and prevent the staff will come into contact if not properly protected. Avoid flames, sparks and prevent static buildup. Avoid generation of dust.

Do not allow to enter into soil/subsoil. Do not allow to enter into surface water or drains.

Retain contaminated washing water and dispose it.

In case of gas escape or of entry into waterways, soil or drains, inform the responsible authorities.

Suitable material for taking up: absorbing material, organic, sand

6.3. Methods and material for containment and cleaning up

Wash with plenty of water.

6.4. Reference to other sections

See also section 8 and 13

SECTION 7: Handling and storage

7.1. Precautions for safe handling

Avoid contact with skin and eyes, inhalation of vapours and mists.

Don't use empty container before they have been cleaned.

Before making transfer operations, assure that there aren't any incompatible material residuals in the containers.

Contaminated clothing should be changed before entering eating areas.

Do not eat or drink while working.

See also section 8 for recommended protective equipment.

7.2. Conditions for safe storage, including any incompatibilities

Always keep the containers tightly closed.

Keep away from food, drink and feed.

Incompatible materials:

None in particular.

Instructions as regards storage premises:

Adequately ventilated premises.

7.3. Specific end use(s)

None in particular

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Propanoic acid, 2-[4-[2-[(4-chlorobenzoyl)amino]ethyl]phenoxy]-2-methyl- - Index: NA, CAS: 41859-67-0, EC No: 255-567-9

TLV TWA - TLV STEL- OEL 8h- OEL short: None.

8.2. Exposure controls

Eye protection:

Safety glasses with side protection or estate or visor. Must be available eye wash station.

Work, however, according to good working practices.

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Protection for skin:

Use clothing that provides comprehensive protection to the skin, e.g. cotton, rubber, PVC or viton.

Protection for hands:

Use protective gloves that provides comprehensive protection, e.g. P.V.C., neoprene or rubber.

Respiratory protection:

Not needed for normal use.

Provide exhaust systems in the workplace. Avoid inhalation of vapors and dust. Adequate ventilation to the premises where the product is stored and / or manipulated, however, avoid excessive ventilation and dust dispersed generation. Change clothes at the end of shift.

Use respiratory protection where ventilation is insufficient or exposure is prolonged.

Thermal Hazards:

None

Environmental exposure controls:

None

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Appearance and colour: white crystalline powder

Odour: odourless

Odour threshold: N.D.

pH: N.D.

Melting point / freezing point: 186 °C (1)

Initial boiling point and boiling range: N.D.

Solid/gas flammability: N.D.

Upper/lower flammability or explosive limits: N.D.

Vapour density: N.D.

Flash point: N.D.

Evaporation rate: N.D.

Vapour pressure: 8.39×10^{-12} a 25°C (2)

Relative density: 1.260±0.06 g/cm³ (2)

Solubility in water: 0.15 g/l a 25°C (2)

Lipid solubility: N.D.

Partition coefficient (n-octanol/water): Log Pow 2.504±0.419 a 25°C (2)

Auto-ignition temperature: N.D.

Decomposition temperature: N.D.

Viscosity: N.D.

Explosive properties: N.D.

Oxidizing properties: N.D.

9.2 Other information

Miscibility: N.D.

Fat Solubility: N.D.

Conductivity: N.D.

(1) Ref.: Ref.: -SRC PhysProp Database -Habibi-Yangjeh Aziz; Bulletin of the Korean Chemical Society. 2008, 29(4), 833-841

(2) Ref.: Ref.: Calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02 (© 1994-2010 ACD/Labs)

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SECTION 10: Stability and reactivity

- 10.1. Reactivity
Stable under normal conditions
- 10.2. Chemical stability
Stable under normal conditions
- 10.3. Possibility of hazardous reactions
N.D.
- 10.4. Conditions to avoid
Stable under normal conditions.
- 10.5. Incompatible materials
N.D.
- 10.6. Hazardous decomposition products
None.

SECTION 11: Toxicological information

11.1. Information on toxicological effects

Bezafibrato - Index: N.A., CAS: 41859-67-0, EC No: 255-567-9

ACUTE TOXICITY:

Acute toxicity: oral

F12-J25-K60 orl-rat LD50 mg/kg 1082

F05-F12-J25 orl-mus LD50 mg/kg 723

Ref.: Kiso to Rinsho. Clinical Report. 1988, 22, 4293, (KSRNAM)

GENETIC TOXICITY:

in vitro:

Chromosome aberration test using Chinese hamster cells

Not mutagenic

Unscheduled DNA synthesis (UDS) test in primary rat hepatocytes
mutagenic

Not

in vivo

DNA synthesis inhibition tests in male mice Not mutagenic

Micronuclei test in mice and rats Not mutagenic

Cytogenetic (bone marrow) test in the rat and Chinese hamster Not mutagenic

Spermatogonia test in the mouse Not mutagenic

Ref.: BEZALIP® SR PRODUCT MONO-GRAPH. ACTAVIS Group PTC ehf. May 26, 2008, p 24.

CARCINOGENICITY: Res: NEGATIVE

oral: Effect level

A 33-month chronic oral (diet) carcinogenicity study of bezafibrate [3000 ppm (122-142 mg/kg/day, or 6000 ppm (256-306 mg/kg/day))] was conducted in the CawHoe-Wiga strain of Sprague Dawley rats (100 animals/sex/dose). The impact of treatment on body weight was significant.

There was no generalized tumorigenic response to bezafibrate. The total number of tumors and the number of malignant, metastasizing, and multiple site tumors were comparable between groups. However, the treated groups revealed a slight decrease in the incidence of tumor bearers. When tumors were analyzed by affected sites, the only organ displaying a clear relationship between increased tumor incidence and bezafibrate treatment was the testis.

Ref.: BEZALIP® SR PRODUCT MONO-GRAPH. ACTAVIS Group PTC ehf. May 26, 2008, p 27.

TOXICITY TO REPRODUCTION / DEVELOPMENT: Res. NEGATIVE

Reproductive toxicity

the male rats were treated with doses of 70 or 363 mg / kg / day for 15 weeks and then were mated with untreated females. There were no adverse effects on fertility.

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During the female fertility in female rats were given 150 or 700 mg / kg / day for two weeks and were then mated with untreated males. Assay with bezafibrate continued during pregnancy and the postnatal day 12. Some letters were delivered by Caesarian section on day 13 of pregnancy and examined. A low fetal weight of pups was observed at the highest dose. Among the dams, the number of births has been reduced in high dose and survival was compromised. The puppies there was evidence of bruising on the skull, spine, limbs and a tendency to easy bleeding.

Ref: SR PRODUCT BEZALIP® MONO-GRAPH. Actavis Group PTC ehf. May 26, 2008, p 24.

Developmental toxicity / teratogenicity

NOT TERATOGEN/EQUIVOCAL

Female rats were dosed from the 7th to 16th day of pregnancy with 150, 300 or 600 mg/kg/day bezafibrate. Ninety-six (96) mated animals produced 84 pregnancies resulting in 1050 live and dead offspring. Aside from a dose-dependent and treatment related increase in mean placental weight in the mid and high dose group, there were no findings of treatment related fetocidal, embryocidal or teratogenic actions.

Toxicity to reproduction: other studies

Female rats were dosed from day 16 of the pre-natal period through day 21 of lactation with 4, 40 and 400 mg/kg/day bezafibrate. At the highest dose, which was near the toxic level for rats, there was a significant reduction in the number of live offspring as well as an increase in pups lost during lactation. The high dose group offspring had lower birth weights and showed a re-tardation of neuromuscular coordination. Liver weights of offspring from the high dose treatment group were increased relative to control.

Ref.: BEZALIP® SR PRODUCT MONO-GRAPH. ACTAVIS Group PTC ehf. May 26, 2008, p 25.

Possible risk of harm to the unborn child

Toxic for reproduction category 3

SECTION 12: Ecological information

12.1. Toxicity

Adopt good working practices, so that the product is not released into the environment.

BIODEGRADATION:

screening tests: Biodegradation in water a 28 g > 75 %

Ref.: EDQM European Directorate for the Quality of Medicines & Healthcare. BEZAFIBRATE CRS SAFETY DATA SHEET, 27/11/2009.

BIOACCUMULATION:

aquatic / sediment: BCF (aquatic species) 46.87 a pH 1 31.07 a pH 3
1.0 a pH 5-10

Ref.: Calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02 (© 1994-2010 ACD/Labs)
unspecified species

TRANSPORT AND DISTRIBUTION:

Adsorption / desorption: Koc at 20°C 545.76 a pH 1

89.09 a pH 4 1.0 a pH 7-10 a 25 °C

Ref.: Calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02 (© 1994-2010 ACD/Labs)

AQUATIC TOXICITY:

Short-term toxicity to fish: LC50 for freshwater fish LC50/96h mg/l >
100

Short-term toxicity to aquatic invertebrates: EC50 / LC50 for freshwater invertebrates

Daphnia magna EC50/48h mg/l 30.3

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Toxicity to aquatic algae and cyanobacteria: EC50 / LC50 for freshwater algae
IC50/72h mg/l > 100

Ref.: EDQM European Directorate for the Quality of Medicines & Healthcare. BEZAFIBRATE
CRS SAFETY DATA SHEET, 27/11/2009
Harmful to aquatic organisms.

12.2. Persistence and degradability

None

12.3. Bioaccumulative potential

Bioaccumulative: See above

12.4. Mobility in soil

See above

12.5. Results of PBT and vPvB assessment

List of substances dangerous for the environment and corresponding classification:

100% - 100% Propanoic acid, 2-[4-[2-[(4-chlorobenzoyl)amino]ethyl]phenoxy]-2-methyl-

CAS: 41859-67-0 EC: 255-567-9

R52 Harmful to aquatic organisms.

vPvB Substances: - PBT Substances: Not classified

12.6. Other adverse effects

None

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Recover, if possible. Send to authorised disposal plants or for incineration under controlled conditions. In so doing, comply with the local and national regulations currently in force.

SECTION 14: Transport information

14.1. UN number

Not classified as dangerous in the meaning of transport regulations.

14.2 UN proper shipping name:

N.A.

14.3 Transport hazard class(es):

N.A.

14.4 Packing Group:

N.A.

14.5 Environmental hazards

N.A.

14.6 Special Precautions for User

N.A.

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

Environmental Pollutant:

No

SECTION 15: Regulatory information

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture
Dir. 67/548/EEC (Classification, packaging and labelling of dangerous substances). Dir. 99/45/EEC (Classification, packaging and labelling of dangerous preparations). Dir. 98/24/EC (Risks related to chemical agents at work). Dir. 2000/39/EC (Occupational exposure limit values); Dir. 2006/8/CE. Regulation (CE) n. 1907/2006 (REACH), Regulation (CE) n. 1272/2008 (CLP), Regulation (CE) n. 790/2009 (1st ATP CLP), Regulation (EU) n. 453/2010 (Annex I).

Where applicable, refer to the following regulatory provisions :

Directive 2003/105/CE ('Activities linked to risks of serious accidents') and subsequent amendments.

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Regulation (EC) nr 648/2004 (detergents).
1999/13/EC (VOC directive)
15.2 Chemical Safety Assessment
No

SECTION 16: Other information

Full text of phrases referred to in Section 3:

R22 Harmful if swallowed.
R52 Harmful to aquatic organisms.
R63 Possible risk of harm to the unborn child

H302 Harmful if swallowed.
H361d Suspected of damaging the unborn child.

This document was prepared by a competent person who has received appropriate training.

Main bibliographic sources: Abbreviations and Acronyms:

ADR:	European Agreement concerning the International Carriage of Dangerous Goods by Road.
CAS:	Chemical Abstracts Service (division of the American Chemical Society).
CLP:	Classification, Labeling, Packaging.
DNEL:	Derived No Effect Level.
EINECS:	European Inventory of Existing Commercial Chemical Substances.
GefStoffVO:	Ordinance on Hazardous Substances, Germany.
GHS:	Globally Harmonized System of Classification and Labeling of Chemicals.
IATA:	International Air Transport Association.
IATA-DGR:	Dangerous Goods Regulation by the "International Air Transport Association" (IATA).
ICAO:	International Civil Aviation Organization.
ICAO-TI:	Technical Instructions by the "International Civil Aviation Organization" (ICAO).
IMDG:	International Maritime Code for Dangerous Goods.
INCI:	International Nomenclature of Cosmetic Ingredients.
KSt:	Explosion coefficient.
LC50:	Lethal concentration, for 50 percent of test population.
LD50:	Lethal dose, for 50 percent of test population.
PNEC:	Predicted No Effect Concentration.
RID:	Regulation Concerning the International Transport of Dangerous Goods by Rail.
STEL:	Short Term Exposure limit.
STOT:	Specific Target Organ Toxicity.
TLV:	Threshold Limiting Value.
TWATLV:	Threshold Limit Value for the Time Weighted Average 8 hour day. (ACGIH Standard).
WGK:	German Water Hazard Class.
N.D. / N.A.:	non disponibile / not available

SOURCES CONSULTED:

ECDIN - Environmental Chemicals Data and Information Network - Joint Research Centre, Commission of the European Communities
SAX's DANGEROUS PROPERTIES OF INDUSTRIAL MATERIALS - Eight Edition - Van Nostrand Reinold
CCNL - Appendix 1

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Insert further consulted bibliography

The information contained in this document are based on knowledge available at the time of completion, the requirements relating to proper use of the product.

They only refer to the product indicated and constitutes no guarantee, express or implied.

The user must verify the suitability and completeness of such information in relation to the specific use intended.

This sheet supersedes all previous editions.