Safety Data Sheet for Drug product

Date of issue: 21-SEP-2016
Replaces version of: 20-OCT-2015
ACLASTA LIVI 5MG 100ML 1X1 US (RECLAST) 704434 (MARS)

1. Identification of the substance/preparation and of the company

Product name	ACLASTA LIVI 5MG 100ML 1X1 US (RECLAST)
Chemical Class	Phosphonic acid derivative
Generic Name	Zoledronic acid
Pharmacological Action	Calcium regulator, Bone metabolism
Usage	Drug product (pharmaceutical bulk, primary packed, finished product, pharmaceutical intermediate)
Company name	Novartis Pharma AG 4002 Basel Switzerland Tel: +41 61 324 11 11, email: sds.support@novartis.com
Emergency phone number	CHEMTEL (International) +1 813 676 1670 (365/24/7)

2. Hazards identification

For side effects, which could also have impact for people working with this substance, please refer to the Patient Information Leaflet.

3. Composition / information on ingredients

For classification of declared components, see section 15, "Regulatory Information"

Chemical Name	Contains:	CAS Number
Zoledronic acid	0.004 - 0.1 %	165800-06-6

Remaining components are inert ingredients.

For TLV values of declared components, see Section 8, Exposure controls / Personal

4. First aid measures

Eye Contact	Immediately rinse eyes thoroughly with running water as long as possible (approx. 15 min). Take injured quickly to factory medical center or call an ambulance (code word: eye accident).
Skin Contact	Remove contaminated clothing. Rinse contaminated skin immediately with plenty of water and soap and seek medical advice.
Inhalation	Remove the victim from danger zone, avoid further exposure.
Ingestion	If swallowed, seek medical advice immediately and show this container or label.
Notes to Physician	General measures to eliminate the substance and to reduce absorption.

5. Fire fighting measures

Suitable Extinguishing Media	Water spray or fog, foam, dry chemical powder, CO2, dry sand
Unsuitable Extinguishing Media	No restrictions
Dangerous Combustion Products	nitrogen oxides, irritating/corrosive gases, phosphorus oxides
Protective equipment for firefighters	Wear self-contained breathing apparatus and fire protective suite.

6. Accidental release measures

Personal precautions	Avoid contact with skin, eyes and clothing.
Environmental	Must not be released into sewers, drains or wells.

precautions

Methods for cleaning Transfer large quantities into a container. Clean up the rest with absorbent material and discharge properly.

7. Handling and storage

No special handling requirements for normal use of this material.
Store in a dry and cool place and observe special instructions from supplier.

8. Exposure controls / Personal protection

Occupational Exposure Limit (OEL)

no data available

TLV values of declared components
Contains:
Zoledronic acid

List type	Value	Unit	
Internal exposure limit	2	µg/m3	HHA Database

Personal protection for open handling

Health care personnel		Safety glasses (EN166) Lab coat Disposable gloves (EN374)

9. Physical and chemical properties

Formulation	Injection solution in ampul
Flash Point	not applicable

10. Stability and reactivity

Under the normal conditions of use, the product is stable.

11. Toxicological information

Acute Toxicity

Data of Zoledronic acid
LD50: 200 - 2000 mg/kg
Route: oral
Species: rat, Sex: both sexes
Duration: 14 days
Method: 96/54/EC, B.1 tris (ATC Method)

Irritation, Corrosion

Data of Zoledronic acid
Eyes (Species: rabbit) severe irritant
Evaluation based on the skin irritation test.

Data of Zoledronic acid
Skin (Species: rabbit) irritant
Method: Draize test

Sensitisation

Data of Zoledronic acid
Skin (Species: guinea pig) not sensitizing
Method: OECD Guideline 406 (Skin Sensitisation)

Mutagenicity

Data of Zoledronic acid
Negative with and without metabolic activation (AMES-Test (reverse mutation assay))
in vitroCell: Strains of Salmonella typhimurium and Escherichia coli.
Method: OECD Guideline 471 (Bacterial Reverse Mutation Assay)

Data of Zoledronic acid

	Negative with and without metabolic activation (Chromosome Aberration Study) in vitroCell: Chinese hamster ovary (CHO) cells
	Data of Zoledronic acid Negative with and without metabolic activation (Gene Mutation Assay in Vitro) in vitroCell: V79 cells (embryonic lung fibroblasts) of the Chinese hamster
	Data of Zoledronic acid Negative (Micronucleus Test) oral, Species: rat, Cell: Bone marrow
Chronic Effects	Data of Zoledronic acid Nephrotoxicity - reversible (Repeated Dose Toxicity) NOAEL: 0.005 mg/kg/d Route: intravenous Species: dog, Organ: Kidneys / Gastrointestinal tract Dosage: 0.1 mg/kg/d, Duration: 52 weeks
	Data of Zoledronic acid Nephrotoxicity - reversible (Repeated Dose Toxicity) NOAEL: 0.001 mg/kg/d Route: subcutaneous Species: rat, Organ: Kidneys Dosage: <= 0.01 mg/kg/d, Duration: 12 months
	Data of Zoledronic acid No evidence for carcinogenicity (Carcinogenesis) Route: oral Species: mouse, Organ: Bone Dosage: <= 1 mg/kg/d, Duration: 104 weeks
	Data of Zoledronic acid No evidence for carcinogenicity (Carcinogenesis) Route: oral Species: rat, Organ: Bone Dosage: <= 2 mg/kg/d, Duration: 104 weeks
Reproduction Toxicity	Data of Zoledronic acid Not teratogenic / not embryotoxic (Embryo-Fetal Development) NOEL: 0.1 mg/kg/d Route: subcutaneous Species: rabbit
	Data of Zoledronic acid Embryotoxicity/fetotoxicity and teratogenicity (Embryo-Fetal Development) NOEL: 0.1 mg/kg/d Route: subcutaneous Species: rat
	Data of Zoledronic acid Reproductive effects at maternally toxic dose (Fertility and early Embryonic Development) LOAEL: 0.01 mg/kg/d Route: subcutaneous Species: rat
	Data of Zoledronic acid Maternal toxicity (Embryo-Fetal Development) LOAEL: 0.01 mg/kg/d Route: subcutaneous Species: rabbit
	Data of Zoledronic acid Increased pre-implantation loss (Fertility and early Embryonic Development) LOAEL: 0.01 mg/kg/d Route: subcutaneous Species: rat

12. Ecological information

Biological Elimination	Data of Zoledronic acid Degradation: 1 % (aerobic: Temperature: 20 - 22 °C CO2) Not readily degradable Initial conc.: 58.1 mg/l, Duration: 28 days Method: 92/69/EC (L383) C.4-C * Carbon dioxide (CO2) evolution
Fish acute toxicity	no data available
Fish chronic toxicity	Data of Zoledronic acid LOEC: 1 mg/l NOEC: NOEC: 0.31 mg/l Species: fathead minnow (pimephales promelas) Exp. time: 32 days Method: OECD 210 * 1992
Aquatic invertebrate acute toxicity	Data of Zoledronic acid EC50: > 18 mg/l Species: daphnia magna (water flea) Exp. time: 48 hours Method: 92/69/EEC (L383) C.2 * Acute toxicity for daphnia
Aquatic invertebrate chronic toxicity	Data of Zoledronic acid LOEC: 1.2 mg/l NOEC: NOEC: 0.38 mg/l Species: daphnia magna (water flea) Exp. time: 21 days Method: OECD 211 * 2008
Algae Toxicity	Data of Zoledronic acid EbC50: 5.1 mg/l ErC50: 15 mg/l NOEC: 2.2 mg/l Species: Pseudokirchneriella subcapitata/Selenastrum capricornutum (Green algae) Exp. time: 72 hours Method: 92/69/EC (L383) C.3
Bacterial Respiration Inhibition	Data of Zoledronic acid EC50: 100 mg/l Species: activated sludge Exp. time: 30 Minutes Method: Inhibition of Oxygen Consumption by activated sludge (87/302/EEC), Part C Inhibitory effects can be excluded.
Ecotoxicity Summary	Data of Zoledronic acid Avoid release into soil, rivers or drains.

13. Disposal considerations

Disposal Requirements Fill into suitable waste receptacles, seal and label them properly. Incineration in an approved, controlled furnace with combustion gas scrubbing and emission gas control. Local regulations should be adhered to.

14. Transport information

Regulation	Class	UN No.	PG	Label	LQ
RID/ADR:	Not restricted	0			N.A.
IMDG-Code:	Not restricted	0			
ICAO/IATA-DGR:	Not restricted	0			

ICAO/IATA-DGR: no dangerous good
Proper shipping name: -

15. Regulatory information

Classifications of components:

Chemical Name	Contains:	CAS Number	Picto	Signal Word	Classification
Zoledronic acid	0.004 - 0.1 %	165800-06-6		D	H302, H315, H318, H361, H335, H372, H402, H411

Remaining components are inert ingredients.

16. Other information

Changes since the previous version in Section
3. Composition / information on ingredients
15. Regulatory information
16. Other information

Abbreviations used

H302: Harmful if swallowed.
H315: Causes skin irritation.
H318: Causes serious eye damage.
H335: May cause respiratory irritation.
H361: Suspected of damaging fertility or the unborn child.
H372: Causes damage to organs through prolonged or repeated exposure.
H402: Harmful to aquatic life.(in EU not leading to classification as hazardous)
H411: Toxic to aquatic life with long lasting effects.

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Product should be stored, handled and used in accordance with good industrial hygiene practices and in conformity with legal regulations. The information contained herein is based on the present state of our knowledge and is intended to describe our products from the point of view of safety requirements. It should therefore not be construed as guaranteeing specific properties.