Material Safety Data Sheet

BONIVA(R) F. C. Tablets (100 mg)

1. Product and Company Identification

Product name	BONIVA(R) F. C. Tablets (100 mg)
Product code	03 4628 4
Company information	Enquiries: Local representation: Hoffmann-La Roche Inc. 340 Kingsland Street USA-Nutley, N.J. 07110-1199 United States of America Phone 001-973/235 50 00 US Emergency phone: (800)-827-6243 US Chemtrec phone: (800)-424-9300
Characterization	final product

2. Composition/Information on ingredients

Ingredients	**Concentration**
Ibandronate CAS: 138926-19-9	~ 38 %
Microcrystalline cellulose CAS: 9004-34-6	~ 13 %
Stearic acid purified fine grade CAS: 57-11-4	~ 2 %
Silicon dioxide colloidal (Aerosil 200, silica) CAS: 7631-86-9	~ 1 %

3. Hazards identification

Emergency Overview

Form		solid
Color		white
Hazard Overview	-	May cause gastrointestinal effects.

Potential Health Effects	- Exposure: Ingestion - Target Organs: gastrointestinal system
	- Acute Effects: May cause gastrointestinal effects., Signs and symptoms may include nausea, vomiting, diarrhea, constipation, cramps, and loss of appetite.
	- Chronic Effects: No adverse effects known
	- Carcinogenicity: formulation not listed by NTP, IARC or OSHA - Carcinogenicity: IARC Gr3 not classifiable *1
Additional Health Information	- Conditions Aggravated: Hypersensitivity to this material and other materials in its chemical class. Uncorrected hypocalcemia. Severe renal impairment.
*1 referring to:	Silicon dioxide colloidal (Aerosil 200, silica)

4. First-aid measures

Eye contact	- in case of contact with eyes rinse thoroughly with plenty of water and get medical advice
Skin contact	- remove immediately contaminated clothes, wash affected skin with plenty of water
Inhalation	- in case of inhalation remove to fresh air and seek medical aid
Ingestion	- consult physician

5. Fire-fighting measures

Suitable extinguishing media	- water spray jet, dry powder, foam, carbon dioxide
Flash point (liquid)	not applicable
Specific hazards	- Toxic emissions may be given off in a fire
Protection of fire-fighters	- use self-contained breathing apparatus
Special method of fire-fighting	- cool endangered containers with water spray

6. Accidental release measures

Personal precautions	- ensure adequate ventilation
Environmental protection	- avoid release to the environment
Methods for cleaning up	- Scoop or shovel spilled material into a suitable labeled open head drum - Secure the drum cover and move the container to a safe holding area - Clean spill area thoroughly - Collect wash with a noncombustible absorbent material and transfer to labeled container for treatment and disposal. - Check area for residual material and repeat clean up if detected

7. Handling and storage

Handling

Technical measures	- local exhaust ventilation necessary - avoid dust formation; consider dust explosion hazard

Storage

Storage conditions	- keep containers tightly closed - room temperature - store in a dry place

8. Exposure controls/Personal protection

Engineering Measures	- see 7.	
Threshold value (USA) air	- ACGIH-TLV: 3 mg/m3 (respirable fraction)	*1
	- ACGIH-TLV: 10 mg/m3 (inhalable fraction)	*1
	- OSHA-PEL: 6 mg/m3	*1
	- NIOSH-REL: 6 mg/m3	*1
	- ACGIH-TLV: 10 mg/m3	*2
	- OSHA-PEL: 5 mg/m3 (respirable dust fraction)	*2
	- OSHA-PEL: 15 mg/m3 (total dust)	*2
	- NIOSH-REL: 5 mg/m3 (respirable dust fraction)	*2
	- NIOSH-REL: 10 mg/m3 (total dust)	*2
Threshold value (Roche) air	- IOEL: 0.002 mg/m3	*3

Personal protective equipment

Respiratory protection	- Respiratory protection is recommended as a precaution to minimze exposure. Effective engineering controls are considered to be the primary means to control worker exposure. Respiratory protection should not substitute for feasible engineering controls. - respiratory protection not necessary
Hand protection	- protective gloves

Eye protection	-	safety glasses
Body protection	-	protective clothing

*1	referring to:	Silicon dioxide colloidal (Aerosil 200, silica)
*2	referring to:	Microcrystalline cellulose
*3	referring to:	Ibandronate

9. Physical and chemical properties

Color	white
Form	solid

10. Stability and reactivity

Stability	-	stable under normal conditions
Conditions to avoid	-	None known
Materials to avoid	-	None known

11. Toxicological information

Acute toxicity	-	LD_{50}	811	mg/kg	(oral, rat)	*3
	-	LD_{50}	30	mg/kg	(i.v., rat)	*3
Subacute toxicity	-	NOAEL	0.09	mg/kg/d	(i.v., dog, 28 d); higher doses cause kidney damage	*3
Local effects	-	skin: moderately irritating (rabbit)				*4
	-	skin, eyes, mucous membranes: corrosive				*3
Sensitization	-	non-sensitizing (guinea pig)				*3
Chronic toxicity	-	NOAEL 0.15 mg/kg/w (i.v., several species; 26 weeks); higher doses cause kidney damage				*3
Mutagenicity	-	not mutagenic (various in vivo and in vitro test systems)				*3
Carcinogenicity	-	not carcinogenic (oral, several species)				*3
Reproduction toxicity	-	not teratogenic, not embryotoxic (i.v., several species)				*3
	-	does not lower parental fertility (i.v., several species)				*3
Note	-	dosage (oral): 2.5 to 50 mg/d				*3
	-	dosage (i.v.): 0.5 mg/3 months to 2.5 mg/day				*3
	-	high doses cause: liver damages, kidney damages				*3
	-	decrease in serum calcium level possible				*3
	-	inhibits mechanisms reducing bone mass by long-term binding to bone tissue				*3

*3	referring to:	Ibandronate
*4	referring to:	Stearic acid purified fine grade

12. Ecological information

Ready biodegradability	- not readily biodegradable ≤ 3 %, 28 d (CO_2 Evolution Test, Modified Sturm Test, OECD No. 301B)	*3
	- not readily biodegradable 0 %, 28 d (Manometric Respirometry Test, OECD No. 301 F)	*3
Inherent biodegradability	- not inherently biodegradable < 10 %, 1 d < 10 %, 15 d < 10 %, 28 d (Zahn-Wellens test, OECD No. 302 B)	*3
	- not inherently biodegradable < 10 %, 28 d (Zahn-Wellens test, OECD No. 302 B)	*3
Abiotic degradation	- stable in water, no photodegradation (200 mg/l, water) < 2 %, 14 d, ~ 22 °C, under illumination	*3
Ecotoxicity	- Oncorhynchus kisutch LC_{50} (96 d) 12 mg/l	*4
	- no adverse influence on substrate biodegradation (activated sludge) concentration (28 d) 41.5 mg/l (OECD No. 301B, Modified Sturm Test)	*3
	- barely toxic for planktonic crustaceans (Daphnia magna) NOEC (48 h) 100 mg/l EC_{50} (48 h) > 180 mg/l (OECD No. 202)	*3
	- barely toxic for fish (carp) LC_{50} (96 h) 200 mg/l LC_0 (96 h) 86 mg/l (OECD No. 203)	*3
	- strongly toxic for algae (Selenastrum capricornutum) EbC_{50} (72 h) 1.4 mg/l ErC_{50} (72 h) 4.7 mg/l NOEC (72 h) 0.22 mg/l (OECD No. 201)	*3
	- barely inhibitory on aerobic bacterial reproduction (activated sludge) NOEC (5 h) 1300 mg/l (growth test)	*3
	- highly toxic for algae (Scenedesmus subspicatus) EbC_{50} (72 h) 0.218 mg/l (nominal concentration) ErC_{50} (72 h) 0.390 mg/l (nominal concentration) NOEC (72 h) < 0.1 mg/l (nominal concentration) (OECD No. 201)	*3
	- highly toxic for algae (Scenedesmus subspicatus) EC_{50} (14 d) 0.5 mg/l (nominal concentration) NOEC (14 d) 0.1 mg/l (nominal concentration) (OECD No. 201)	*3
	- no adverse influence on substrate biodegradation concentration (28 d) 100 mg/l (Manometric Respirometry Test, OECD No. 301 F)	*3

Mobility	-	no significant adsorption (, 28 d, ~22 °C) K_d = 1210 l/kg (activated sludge) (Adsorption to activated sludge in biodegradability test) *3
Note	-	after the regular 28 days in the Zahn-Wellens test, without significant degradation and still 400 mg DOC/l, 200 mg DOC/l benzoate was added as a well degradable substrate; after 5 days, only 150 mg DOC/l was left, showing some cometabolic degradation *3

*3 referring to: Ibandronate
*4 referring to: Stearic acid purified fine grade

13. Disposal considerations

Waste from residues	-	incinerate in qualified installation with flue gas scrubbing - observe local/national regulations regarding waste disposal
Contaminated packaging	-	Empty containers must be triple rinsed prior to disposal, recycling or reuse.
RCRA waste	-	not regulated under RCRA

14. Transport information

Note	-	not classified by transport regulations, proper shipping name non-regulated

15. Regulatory information

TSCA Status	-	FDA Exemption - not on inventory
Reporting Requirements	-	The United States Environmental Protection Agency (USEPA) has not established a Reportable Quantity (RQ) for releases of this material. - In New Jersey, report all releases which are likely to endanger the public health, harm the environment or cause a complaint to the NJDEPE Hotline (1-609-292-5560) and to local officials. - State and local regulations vary and may impose additional reporting requirements.

16. Other information

Use	-	Boniva is used in the treatment and prevention of osteoporosis in postmenopausal women.
Edition documentation	-	first edition

The information in this safety data sheet is based on current scientific knowledge. It should not be taken as expressing or implying any warranty concerning product characteristics.