

Gilotrif® Tablets

Version 1.0 Revision Date: 05/28/2015 MSDS Number: 000000027061 Date of last issue: -
Date of first issue: 05/28/2015

SECTION 1. IDENTIFICATION

Product name : Gilotrif® Tablets

Synonyms : Active ingredient: Afatinib > 15%
Gilotrif® 20 mg film-coated tablets, Gilotrif® 30 mg film-coated tablets, Gilotrif® 40 mg film-coated tablets and Gilotrif® 50 mg film-coated tablets (Bulk)

Product code : 000000027061

Manufacturer or supplier's details

Company name of supplier : Boehringer-Ingelheim Pharmaceuticals, Incorporated

Address : 900 Ridgebury Road
Ridgefield, Connecticut
06877-0368

Emergency telephone number : +1-800-424-9300 CHEMTREC Emergency Phone Number
CHEMTREC – 24 Hours

Routine Contact Number : (203) 778-7759

Recommended use of the chemical and restrictions on use

Recommended use : Mixture for production of finished medicinal products.

Prepared by : Corp. Div. EHS & Sustainability / Global EHS Services
EHS-service@boehringer-ingelheim.com

SECTION 2. HAZARDS IDENTIFICATION**GHS Classification (Hazard Communication Standard (HCS) 29 CFR 1910.1200)**

Acute toxicity (Oral) : Category 4

Eye irritation : Category 2

Reproductive toxicity : Category 2

Specific target organ toxicity - repeated exposure : Category 1 (Skin, Gastro-intestinal system)

GHS Label element (Hazard Communication Standard (HCS) 29 CFR 1910.1200)

Hazard pictograms :  

Signal word : Danger

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Hazard statements : H302 Harmful if swallowed.
H319 Causes serious eye irritation.
H361 Suspected of damaging fertility or the unborn child.
H362 May cause harm to breast-fed children.
H372 Causes damage to organs (Skin, Gastro-intestinal system) through prolonged or repeated exposure.

Precautionary statements : **Prevention:**
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust/ fume/ gas/ mist/ vapours/ spray.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P280 Wear eye protection/ face protection.
P281 Use personal protective equipment as required.
Response:
P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER or doctor/ physician if you feel unwell. Rinse mouth.
P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
P337 + P313 If eye irritation persists: Get medical advice/ attention.
Storage:
P405 Store locked up.
Disposal:
P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards

None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Hazardous components

Chemical Name	CAS-No.	Concentration (%)
Afatinib dimaleate	850140-73-7	>= 15 - <= 99

SECTION 4. FIRST AID MEASURES

General advice : Remove from exposure, lie down.
Take off immediately all contaminated clothing.
Victim to lie down in the recovery position, cover and keep him warm.
First Aid responders should pay attention to self-protection and use the recommended protective clothing

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| If inhaled | : | Move to fresh air.
Call a physician immediately. |
| In case of skin contact | : | Wash off immediately with plenty of water.
Cover wound with sterile dressing.
Call a physician immediately. |
| In case of eye contact | : | Rinse immediately with plenty of water for at least 15 minutes.
Keep eye wide open while rinsing.
Call a physician immediately. |
| If swallowed | : | Rinse mouth.
Drink plenty of water.
Call a physician immediately. |
| Most important symptoms and effects, both acute and delayed | : | Harmful if swallowed.
Causes serious eye irritation.
Suspected of damaging fertility or the unborn child.
Causes damage to organs through prolonged or repeated exposure. |
| Notes to physician | : | Observe the summary of product characteristics of proprietary medicinal products |
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SECTION 5. FIREFIGHTING MEASURES

- | | | |
|---|---|--|
| Suitable extinguishing media | : | Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Water
Dry chemical
Foam
Carbon dioxide (CO ₂) |
| Specific hazards during fire-fighting | : | In case of fire and/or explosion do not breathe fumes.
Can be released in case of fire:
Nitrogen oxides (NO _x)
Hydrogen chloride gas
Hydrogen fluoride
Carbon oxides |
| Further information | : | Collect contaminated fire extinguishing water separately. This must not be discharged into drains.
Fire residues and contaminated fire extinguishing water must be disposed of in accordance with local regulations.
Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. |
| Special protective equipment for firefighters | : | Self-contained breathing apparatus (EN 133)
complete suit protecting against chemicals |
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SECTION 6. ACCIDENTAL RELEASE MEASURES

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| Personal precautions, protec- | : | Wear personal protective equipment. |
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tive equipment and emergency procedures	Ensure adequate ventilation. Never return spills in original containers for re-use.
Environmental precautions	: Do not flush into surface water or sanitary sewer system.
Methods and materials for containment and cleaning up	: Wear personal protective equipment. Clean-up methods - large spillage Dampen, pick up mechanically and dispose of. Clean-up methods - small spillage Use approved industrial vacuum cleaner for removal. Keep in suitable, closed containers for disposal.

SECTION 7. HANDLING AND STORAGE

Advice on protection against fire and explosion	: No special protective measures against fire required.
Advice on safe handling	: Provide sufficient air exchange and/or exhaust in work rooms. Routine housekeeping should be instituted to ensure that dusts do not accumulate on surfaces. Minimize dust generation and accumulation. Dry powders can build static electricity charges when subjected to the friction of transfer and mixing operations. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres. Breathing must be protected when large quantities are decanted without local exhaust ventilation. Keep container closed when not in use.
Conditions for safe storage	: Store in original container. Protect from heat and direct sunlight. Jointless smooth floor Keep container tightly closed.
Materials to avoid	: Keep away from food, drink and animal feedingstuffs. Advice on Segregation

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION**Components with workplace control parameters**

Components	Basis	Factor	Cateryory	Values	Remark
(E)-4-Dimethylamino-but-2-enoic acid (4-(3-chloro-4-fluorophenylamino)-7-(tetrahydro-furan-3-yloxy)-quinazolin-6-yl)-amide Dimaleat 850140-73-7	ECL		3A	15 µg/m3	
	BIPC		1b		
ECL (BIPI Exposure Control Limit)					

Contains no substances with occupational exposure limit values.

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Engineering measures : Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment). Use only appropriately classified electrical equipment and powered industrial trucks.

Personal protective equipment

Respiratory protection : Respirator must be worn if exposed to dust.
Protecting mask (EN 136)
particle filter P3 (EN 143)

Hand protection Material : Nitrile rubber
Break through time : 480 min
Glove thickness : 0.43 mm
Directive : Protective gloves against chemicals and micro-organisms
Protective index : Class 6

Eye protection : Safety glasses with side-shields
(Not necessary when using full face mask)

Skin and body protection : Laboratory: laboratory coat; factory: disposable Overall.

Protective measures : Handle in accordance with good industrial hygiene and safety practice.
Do not breathe dust.
Avoid contact with skin, eyes and clothing.
Only use protective equipment in accordance with national/international regulations. Follow the national regulations about wearing personal protective equipment and the warranty given by the manufacturer for the safe function.

Hygiene measures : General industrial hygiene practice.
Wash hands and face before breaks and immediately after handling the product.
Keep working clothes separately.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance	: solid
Colour	: white
Odour	: No data available
Odour Threshold	: No data available
pH	: No data available
Melting point/range	: No data available

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Boiling point/boiling range	: Not applicable
Flash point	: Not applicable
Evaporation rate	: Not applicable
Flammability (solid, gas)	: No data available
Upper explosion limit	: No data available
Lower explosion limit	: No data available
Vapour pressure	: Not applicable
Relative vapour density	: Not applicable
Relative density	: No data available
Solubility(ies) Water solubility	: No data available
Partition coefficient: n- octanol/water	: No data available
Auto-ignition temperature	: No data available
Decomposition temperature	: No data available
Viscosity Viscosity, dynamic	: Not applicable
Explosive properties	: No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity	: No dangerous reaction known under conditions of normal use.
Chemical stability	: No decomposition if stored and applied as directed.
Possibility of hazardous reac- tions	: Dust may form explosive mixture in air.
Conditions to avoid	: Avoid moisture.
Incompatible materials	: No data available
Hazardous decomposition products	: No data available

SECTION 11. TOXICOLOGICAL INFORMATION**Acute toxicity**

Harmful if swallowed.

Product:

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Acute oral toxicity : Acute toxicity estimate: 505.05 mg/kg
Method: Calculation method

Components:**Afatinib dimaleate:**

Acute oral toxicity : Acute toxicity estimate (Rat): > 300 - < 600 mg/kg
Acute toxicity estimate (Mouse): > 1,200 mg/kg

Acute inhalation toxicity : Remarks: No data available

Acute dermal toxicity : Remarks: No data available

Skin corrosion/irritation

Not classified based on available information.

Components:**Afatinib dimaleate:**

Species: Rabbit
Result: No skin irritation

Serious eye damage/eye irritation

Causes serious eye irritation.

Components:**Afatinib dimaleate:**

Species: Rabbit
Result: Risk of serious damage to eyes.
Method: OECD Test Guideline 405

Respiratory or skin sensitisation

Skin sensitisation: Not classified based on available information.
Respiratory sensitisation: Not classified based on available information.

Components:**Afatinib dimaleate:**

Method: DEREK
Result: Alert for skin sensitization

Germ cell mutagenicity

Not classified based on available information.

Components:**Afatinib dimaleate:**

Genotoxicity in vitro : Test Type: Ames test
Species: Salmonella typhimurium
Result: positive
: Test Type: Chromosomal aberration test
Species: Human lymphocytes
Result: negative
Genotoxicity in vivo : Test Type: Micronucleus test

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Species: Rat
Result: negative

Test Type: Micronucleus test
Species: Mouse
Result: negative

Test Type: Comet assay
Species: Rat
Result: negative

Carcinogenicity

Not classified based on available information.

Components:**Afatinib dimaleate:**

Remarks: No data available

IARC

No component of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA

No component of this product present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by OSHA.

NTP

No component of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity

Suspected of damaging fertility or the unborn child.

Components:**Afatinib dimaleate:**

Reproductive toxicity - Assessment : Suspected of damaging the unborn child., Effects on or via lactation

STOT - single exposure

Not classified based on available information.

STOT - repeated exposure

Causes damage to organs (Skin, Gastro-intestinal system) through prolonged or repeated exposure.

Components:**Afatinib dimaleate:**

Target Organs: Skin, Gastro-intestinal system
Assessment: The substance or mixture is classified as specific target organ toxicant, repeated exposure, category 1.

Repeated dose toxicity**Components:****Afatinib dimaleate:**

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Species: Rat
NOAEL: 4 mg/kg
Exposure time: 28-day

Species: Rat
NOAEL: 1.5 mg/kg
Exposure time: 26 weeks

Species: miniature swine
NOAEL: 0.5 mg/kg
Exposure time: 13 weeks

Species: miniature swine
NOAEL: 0.5 mg/kg
Exposure time: 52 weeks

Aspiration toxicity

Not classified based on available information.

Components:**Afatinib dimaleate:**

No data available

Further information**Components:****Afatinib dimaleate:**

Remarks: May (possibly) cause phototoxic reactions.

SECTION 12. ECOLOGICAL INFORMATION**Ecotoxicity****Components:****Afatinib dimaleate:**

Toxicity to fish : Remarks: No data available

Toxicity to daphnia and other aquatic invertebrates : Remarks: No data available

Toxicity to algae : Remarks: No data available

Toxicity to fish (Chronic toxicity) : Remarks: No data available

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity) : Remarks: No data available

Toxicity to bacteria : EC50 (activated sludge): = 143 mg/l
Exposure time: 3 h
Method: Activated Sludge, Respiration Inhibition Test.

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NOEC (activated sludge): = 9 mg/l
Exposure time: 3 h
Method: Activated Sludge, Respiration Inhibition Test.

Persistence and degradability

No data available

Bioaccumulative potential**Components:****Afatinib dimaleate:**

Partition coefficient: n-octanol/water : Remarks: No data available

Mobility in soil

No data available

Other adverse effects**Product:**

Ozone-Depletion Potential : Regulation: 40 CFR Protection of Environment; Part 82 Protection of Stratospheric Ozone - CAA Section 602 Class I Substances
Remarks: This product neither contains, nor was manufactured with a Class I or Class II ODS as defined by the U.S. Clean Air Act Section 602 (40 CFR 82, Subpt. A, App.A + B).

SECTION 13. DISPOSAL CONSIDERATIONS**Disposal methods**

Waste from residues : Dispose of in accordance with local regulations.
Contaminated packaging : Packs that cannot be cleaned should be disposed of in the same manner as the contents.
Uncontaminated packaging can be recycled.

SECTION 14. TRANSPORT INFORMATION**International Regulation****Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code**

Not applicable for product as supplied.

National Regulations**SECTION 15. REGULATORY INFORMATION****EPCRA - Emergency Planning and Community Right-to-Know Act**

SARA 311/312 Hazards : Acute Health Hazard
Chronic Health Hazard

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SARA 302 : No chemicals in this material are subject to the reporting requirements of SARA Title III, Section 302.

SARA 313 : This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

Clean Air Act

This product neither contains, nor was manufactured with a Class I or Class II ODS as defined by the U.S. Clean Air Act Section 602 (40 CFR 82, Subpt. A, App.A + B).

This product does not contain any hazardous air pollutants (HAP), as defined by the U.S. Clean Air Act Section 12 (40 CFR 61).

This product does not contain any chemicals listed under the U.S. Clean Air Act Section 112(r) for Accidental Release Prevention (40 CFR 68.130, Subpart F).

This product does not contain any chemicals listed under the U.S. Clean Air Act Section 111 SOCM I Intermediate or Final VOC's (40 CFR 60.489).

Clean Water Act

This product does not contain any Hazardous Substances listed under the U.S. CleanWater Act, Section 311, Table 116.4A.

This product does not contain any Hazardous Chemicals listed under the U.S. CleanWater Act, Section 311, Table 117.3.

This product does not contain any toxic pollutants listed under the U.S. Clean Water Act Section 307

Massachusetts Right To Know

No components are subject to the Massachusetts Right to Know Act.

Pennsylvania Right To Know

Afatinib dimaleate	850140-73-7	90 - 100 %
Non-hazardous galenic excipients	Not Assigned	70 - 90 %

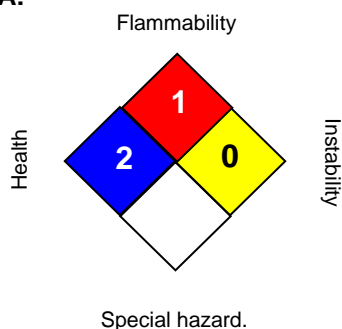
New Jersey Right To Know

Afatinib dimaleate	850140-73-7	90 - 100 %
Non-hazardous galenic excipients	Not Assigned	70 - 90 %

California Prop 65 : This product does not contain any chemicals known to State of California to cause cancer, birth defects, or any other reproductive harm.

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SECTION 16. OTHER INFORMATION**Further information****NFPA:****HMIS III:**

HEALTH	2*
FLAMMABILITY	1
PHYSICAL HAZARD	0

0 = not significant, 1 = Slight,
2 = Moderate, 3 = High
4 = Extreme, * = Chronic

Vertical lines in the left hand margin indicate an amendment from the previous version. Refer to NFPA 654, Standard for the Prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids, for safe handling. Sources of key data used to compile the Safety Data Sheet : The specifications are based on own tests and/or literature data.

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The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.