



# SAFETY DATA SHEET

Revision date: 02-Apr-2015

Version: 3.0

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## 1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND THE COMPANY/UNDERTAKING

### Product Identifier

**Material Name:** Axitinib Film Coated Tablets

**Trade Name:** INLYTA  
**Chemical Family:** Not determined

### Relevant Identified Uses of the Substance or Mixture and Uses Advised Against

**Intended Use:** Pharmaceutical product used as antineoplastic

### Details of the Supplier of the Safety Data Sheet

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## 2. HAZARDS IDENTIFICATION

### Classification of the Substance or Mixture

#### GHS - Classification

Germ Cell Mutagenicity: Category 2  
Reproductive Toxicity: Category 2  
Specific target organ systemic toxicity (repeated exposure): Category 2

#### EU Classification:

EU Indication of danger: Xn - Harmful  
Mutagenic: Category 3  
Toxic to Reproduction: Category 3

#### EU Risk Phrases:

R62 - Possible risk of impaired fertility.  
R63 - Possible risk of harm to the unborn child.  
R68 - Possible risk of irreversible effects.  
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.

### Label Elements

**Signal Word:** Warning  
**Hazard Statements:** H373 - May cause damage to organs through prolonged or repeated exposure H341 - Suspected of causing genetic defects  
H361fd - Suspected of damaging fertility. Suspected of damaging the unborn child.

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**Precautionary Statements:** P260 - Do not breathe dust/fume/gas/mist/vapors/spray  
P314 - Get medical attention/advice if you feel unwell  
P202 - Do not handle until all safety precautions have been read and understood  
P281 - Use personal protective equipment as required  
P308 + P313 - IF exposed or concerned: Get medical attention/advice  
P405 - Store locked up



**Other Hazards**  
**Australian Hazard Classification (NOHSC):**

No data available  
Hazardous Substance. Non-Dangerous Goods.

**Note:** This document has been prepared in accordance with standards for workplace safety, which requires the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warning included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

### 3. COMPOSITION / INFORMATION ON INGREDIENTS

**Hazardous**

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	GHS Classification	%
Axitinib	319460-85-0	Not Listed	Muta. Cat.3;R68 Repr. Cat.3;R62 Repr. Cat.3;R63 Xn;R48-22 N;R50	Muta. 2 (H341) Repr. 2 (H361fd) STOT RE 2 (H373) Aquatic Acute 1 (H400) Aquatic Chronic 1 (H410)	<5
Magnesium Stearate	557-04-0	209-150-3	Not Listed	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	GHS Classification	%
Cellulose microcrystalline	9004-34-4	Not Listed	Not Listed	Not Listed	*
Croscarmellose sodium	74811-65-7	Not Listed	Not Listed	Not Listed	*
Lactose NF, monohydrate	64044-51-5	Not Listed	Not Listed	Not Listed	*
Opadry II Red	Not Assigned	Not Listed	Not Listed	Not Listed	*
Water, purified	7732-18-5	231-791-2	Not Listed	Not Listed	*

**Additional Information:** \* Proprietary  
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety. In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

**For the full text of the R phrases and CLP/GHS abbreviations mentioned in this Section, see Section 16**

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### 4. FIRST AID MEASURES

#### Description of First Aid Measures

- Eye Contact:** Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.
- Skin Contact:** Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.
- Ingestion:** Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.
- Inhalation:** Remove to fresh air and keep patient at rest. Seek medical attention immediately.

#### Most Important Symptoms and Effects, Both Acute and Delayed

- Symptoms and Effects of Exposure:** For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.
- Medical Conditions Aggravated by Exposure:** None known

#### Indication of the Immediate Medical Attention and Special Treatment Needed

- Notes to Physician:** None

### 5. FIRE FIGHTING MEASURES

**Extinguishing Media:** Extinguish fires with CO2, extinguishing powder, foam, or water.

#### Special Hazards Arising from the Substance or Mixture

- Hazardous Combustion Products:** Formation of toxic gases is possible during heating or fire.
- Fire / Explosion Hazards:** Fine particles (such as dust and mists) may fuel fires/explosions.

#### Advice for Fire-Fighters

During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

### 6. ACCIDENTAL RELEASE MEASURES

#### Personal Precautions, Protective Equipment and Emergency Procedures

Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

#### Environmental Precautions

Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

#### Methods and Material for Containment and Cleaning Up

- Measures for Cleaning / Collecting:** Contain the source of spill if it is safe to do so. Collect spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.
- Additional Consideration for Large Spills:** Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

### 7. HANDLING AND STORAGE

#### Precautions for Safe Handling

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### 7. HANDLING AND STORAGE

Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls. Refer to Section 12 - Ecological Information, for information on potential effects on the environment.

#### Conditions for Safe Storage, Including any Incompatibilities

**Storage Conditions:** Store as directed by product packaging.  
**Specific end use(s):** Pharmaceutical product used as antineoplastic

### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

#### Control Parameters

Refer to available public information for specific member state Occupational Exposure Limits.

#### Axitinib

Pfizer OEL TWA-8 Hr: 10µg/m<sup>3</sup>

#### Magnesium Stearate

ACGIH Threshold Limit Value (TWA) 10 mg/m<sup>3</sup>  
Lithuania OEL - TWA 5 mg/m<sup>3</sup>  
Sweden OEL - TWAs 5 mg/m<sup>3</sup>

#### Exposure Controls

**Engineering Controls:** Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

**Personal Protective Equipment:** Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

**Hands:** Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.

**Eyes:** Wear safety glasses or goggles if eye contact is possible.

**Skin:** Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.

**Respiratory protection:** If the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL.

### 9. PHYSICAL AND CHEMICAL PROPERTIES

<b>Physical State:</b>	Tablets	<b>Color:</b>	Red
<b>Odor:</b>	No data available.	<b>Odor Threshold:</b>	No data available.
<b>Molecular Formula:</b>	Mixture	<b>Molecular Weight:</b>	Mixture

**Solvent Solubility:** No data available  
**Water Solubility:** No data available  
**pH:** No data available.  
**Melting/Freezing Point (°C):** No data available  
**Boiling Point (°C):** No data available.  
**Partition Coefficient: (Method, pH, Endpoint, Value)**

#### Axitinib

Predicted 7.4 Log D 3.83

#### Cellulose microcrystalline

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### 9. PHYSICAL AND CHEMICAL PROPERTIES

No data available

**Croscarmellose sodium**

No data available

**Lactose NF, monohydrate**

No data available

**Opadry II Red**

No data available

**Magnesium Stearate**

No data available

**Water, purified**

No data available

**Decomposition Temperature (°C):** No data available.

**Evaporation Rate (Gram/s):** No data available

**Vapor Pressure (kPa):** No data available

**Vapor Density (g/ml):** No data available

**Relative Density:** No data available

**Viscosity:** No data available

**Flammability:**

**Autoignition Temperature (Solid) (°C):** No data available

**Flammability (Solids):** No data available

**Flash Point (Liquid) (°C):** No data available

**Upper Explosive Limits (Liquid) (% by Vol.):** No data available

**Lower Explosive Limits (Liquid) (% by Vol.):** No data available

### 10. STABILITY AND REACTIVITY

**Reactivity:** No data available

**Chemical Stability:** Stable under normal conditions of use.

**Possibility of Hazardous Reactions**

**Oxidizing Properties:** No data available

**Conditions to Avoid:** Fine particles (such as dust and mists) may fuel fires/explosions.

**Incompatible Materials:** As a precautionary measure, keep away from strong oxidizers

**Hazardous Decomposition Products:** No data available

### 11. TOXICOLOGICAL INFORMATION

**Information on Toxicological Effects**

**General Information:** The information included in this section describes the potential hazards of the individual ingredients.

**Known Clinical Effects:** Based on clinical trials in humans, possible adverse effects following exposure to this compound may include: increase in blood pressure (hypertension), diarrhea, fatigue lack of appetite, nausea, vomiting, constipation, inflammation of the mouth (stomatitis), hand-foot syndrome.

**Acute Toxicity: (Species, Route, End Point, Dose)**

**Axitinib**

Mouse Oral NOAEL 2000 mg/kg

Dog Oral NOAEL > 2000mg/kg

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### 11. TOXICOLOGICAL INFORMATION

#### Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

##### **Axitinib**

28 Day(s)	Mouse	Oral	10 mg/kg/day	NOAEL	Blood, Male reproductive system, Female reproductive system
28 Day(s)	Dog	Oral	10 mg/kg/day	LOAEL	Bone Marrow, Gastrointestinal system, Lymphatic system, Reproductive system
26 Week(s)	Mouse	Oral	10 mg/kg/day	LOAEL	Blood, Bone, Gastrointestinal system, Lymphatic system, Reproductive system
26 Week(s)	Dog	Oral	6 mg/kg/day	NOAEL	Gastrointestinal system, Lymphatic system
39 Week(s)	Dog	Oral	(F) 6 mg/kg/day (3 mg/kg BID)	NOAEL	None identified
39 Week(s)	Dog	Oral	(M) 3 mg/kg/day (1.5 mg/kg BID)	LOAEL	Male reproductive system

##### **Magnesium Stearate**

13 Week(s)	Rat	Oral	1092 g/kg	LOAEL	Liver
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#### Reproduction & Development Toxicity: (Duration, Species, Route, Dose, End Point, Effect(s))

##### **Axitinib**

Embryo / Fetal Development	Mouse	Oral	3 mg/kg/day (1.5 mg/kg BID)	NOAEL	Maternal toxicity
Embryo / Fetal Development	Mouse	Oral	1 mg/kg/day (0.5 mg/kg BID)	NOAEL	Developmental toxicity, Teratogenic
Fertility & Early Embryonic Development - Males	Mouse	Oral	100 mg/kg/day (50 mg/kg BID)	NOAEL	Paternal toxicity
Fertility & Early Embryonic Development - Males	Mouse	Oral	10 mg/kg/day (5 mg/kg BID)	NOAEL	Reproductive toxicity
Fertility & Early Embryonic Development-Females	Mouse	Oral	250 mg/kg/day (125 mg/kg BID)	NOAEL	Maternal Toxicity
Fertility & Embryonic Development-Females	Mouse	Oral	< 30 mg/kg/day (15 mg/kg BID)	NOAEL	Reproductive toxicity

#### Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

##### **Axitinib**

Bacterial Mutagenicity (Ames)	<i>Salmonella</i> , <i>E. coli</i>	Negative
<i>In Vitro</i> Cytogenetics	Human Lymphocytes	Negative
<i>In Vivo</i> Micronucleus	Mouse Bone Marrow	Positive

#### Carcinogen Status:

None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

### 12. ECOLOGICAL INFORMATION

#### **Environmental Overview:**

This formulation has not been tested as a whole, the following apply to component substance(s):

#### **Toxicity:**

#### Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

##### **Axitinib**

<i>Skeletonema costatum</i> (Marine Diatom)	OECD	EbC50	72 Hours	> 0.043 mg/L
<i>Mysidopsis bahia</i> (Mysid Shrimp)	OPPTS	LC50	96 Hours	> 0.063 mg/L
<i>Cyprinodon variegatus</i> (Sheepshead Minnow)	OPPTS	LC50	96 Hours	> 0.055 mg/L
<i>Pseudokirchneriella subcapitata</i> (Green Alga)	OECD	EC50	72 Hours	0.9 mg/L

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### Bacterial Inhibition: (Inoculum, Method, End Point, Result)

#### **Axitinib**

Activated sludge OECD EC50 > 1000 mg/L

### Chronic Aquatic Toxicity: (Species, Method, Duration, Endpoint, Result, Adverse Endpoint)

#### **Axitinib**

*Daphnia magna* (Water Flea) OECD 21 Day(s) NOEC 0.088 mg/L

*Pimephales promelas* (Fathead Minnow) OECD 32 Day(s) NOEC 0.0035 mg/L

**Persistence and Degradability:** No data available

#### **Bio-accumulative Potential:**

##### **Partition Coefficient: (Method, pH, Endpoint, Value)**

#### **Axitinib**

Predicted 7.4 Log D 3.83

**Mobility in Soil:** No data available

## **13. DISPOSAL CONSIDERATIONS**

#### **Waste Treatment Methods:**

Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

## **14. TRANSPORT INFORMATION**

The following refers to all modes of transportation unless specified below.

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

## **15. REGULATORY INFORMATION**

**Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture**

#### **Canada - WHMIS: Classifications**

##### **WHMIS hazard class:**

D2b toxic materials

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**15. REGULATORY INFORMATION**



<b>Axitinib</b>	
CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4
EU EINECS/ELINCS List	Not Listed
<b>Cellulose microcrystalline</b>	
CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
EU EINECS/ELINCS List	Not Listed
<b>Croscarmellose sodium</b>	
CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Australia (AICS):	Present
EU EINECS/ELINCS List	Not Listed
<b>Lactose NF, monohydrate</b>	
CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Australia (AICS):	Present
REACH - Annex IV - Exemptions from the obligations of Register:	Present
EU EINECS/ELINCS List	Not Listed
<b>Opadry II Red</b>	
CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
EU EINECS/ELINCS List	Not Listed
<b>Magnesium Stearate</b>	
CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	209-150-3
<b>Water, purified</b>	
CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
REACH - Annex IV - Exemptions from the obligations of Register:	Present
EU EINECS/ELINCS List	231-791-2



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### 16. OTHER INFORMATION

#### Text of R phrases and GHS Classification abbreviations mentioned in Section 3

Germ cell mutagenicity-Cat.2; H341 - Suspected of causing genetic defects  
Reproductive toxicity-Cat.2; H361fd - Suspected of damaging fertility. Suspected of damaging the unborn child.  
Specific target organ toxicity, repeated exposure-Cat.2; H373 - May cause damage to organs through prolonged or repeated exposure  
Hazardous to the aquatic environment, acute toxicity-Cat.1; H400 - Very toxic to aquatic life  
Hazardous to the aquatic environment, chronic toxicity-Cat.1; H410 - Very toxic to aquatic life with long lasting effects

Mutagenic: Category 3  
Toxic to Reproduction: Category 3  
Xn - Harmful  
N - Dangerous for the environment

R62 - Possible risk of impaired fertility.  
R63 - Possible risk of harm to the unborn child.  
R68 - Possible risks of irreversible effects.  
R50 - Very toxic to aquatic organisms.  
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.

**Data Sources:** Pfizer proprietary drug development information. Publicly available toxicity information.

**Reasons for Revision:** Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking.  
Updated Section 12 - Ecological Information. Updated Section 11 - Toxicology Information.  
Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients.

**Revision date:** 02-Apr-2015

Product Stewardship Hazard Communication

**Prepared by:** Pfizer Global Environment, Health, and Safety Operations

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

**End of Safety Data Sheet**