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

Product Identifier

Material Name: Crizotinib Capsules
Trade Name: XALKORI, CRIZALK
Chemical Family: Anaplastic Lymphoma Kinase Inhibitor

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

Intended Use: Pharmaceutical product for the treatment of lung cancer

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

- Serious Eye Damage/Eye Irritation: Category 1
- Skin Sensitization: Category 1
- Germ Cell Mutagenicity: Category 2
- Acute aquatic toxicity: Category 1

EU Classification:

- EU Indication of danger: Mutagenic: Category 3
- Xi - Irritant
- Dangerous for the Environment

EU Risk Phrases:

- R41 - Risk of serious damage to eyes.
- R43 - May cause sensitization by skin contact.
- R68 - Possible risk of irreversible effects.
- R50 - Very toxic to aquatic organisms.

Label Elements

Signal Word: Danger
Hazard Statements:

- H318 - Causes serious eye damage
- H317 - May cause an allergic skin reaction
- H341 - Suspected of causing genetic defects
- H400 - Very toxic to aquatic life
Precautionary Statements:

- P280 - Wear protective gloves/protective clothing/eye protection/face protection
- P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
- P310 - Immediately call a POISON CENTRE or doctor/physician
- P261 - Avoid breathing dust/fume/gas/mist/vapors/spray
- P272 - Contaminated work clothing should not be allowed out of the workplace
- P302+ P352 - IF ON SKIN: Wash with plenty of soap and water
- P333 + P313 - If skin irritation or rash occurs: Get medical advice/attention
- P321 - Specific treatment (see supplemental instructions on the administration of antidotes on this label)
- P363 - Wash contaminated clothing before reuse
- P202 - Do not handle until all safety precautions have been read and understood
- P308 + P313 - IF exposed or concerned: Get medical attention/advice
- P405 - Store locked up
- P273 - Avoid release to the environment
- P391 - Collect spillage
- P501 - Dispose of contents/container in accordance with all local and national regulations

Other Hazards
Australian Hazard Classification (NOHSC):

No data available
Hazardous Substance. 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

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crizotinib</td>
<td>877399-52-5</td>
<td>Not Listed</td>
<td>Xi;R41</td>
<td>Eye Dam.1 (H318) Skin Sens.1 (H317)</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Xi;R43</td>
<td>Muta. 2 (H341) Aquatic Acute 1 (H400)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Muta. Cat.3;R68</td>
<td>N,R50</td>
<td></td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>9004-34-6</td>
<td>232-674-9</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Dicalcium Phosphate</td>
<td>7757-93-9</td>
<td>231-826-1</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>209-150-3</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Silicium dioxide</td>
<td>Not Assigned</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

PZ01417
SAFETY DATA SHEET

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
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 drug product

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

Crizotinib
Pfizer OEL TWA-8 Hr: 15µg/m³, Sensitizer, Severe Eye Irritant

Microcrystalline cellulose
ACGIH Threshold Limit Value (TWA) 10 mg/m³
Australia TWA 10 mg/m³
Belgium OEL - TWA 10 mg/m³
Estonia OEL - TWA 10 mg/m³
France OEL - TWA 10 mg/m³
Ireland OEL - TWAs 10 mg/m³
Latvia OEL - TWA 2 mg/m³
OSHA - Final PELS - TWAs: 15 mg/m³
Portugal OEL - TWA 10 mg/m³
Romania OEL - TWA 10 mg/m³
Russia OEL - TWA 6 mg/m³
Spain OEL - TWA 10 mg/m³
Switzerland OEL - TWAs 3 mg/m³
Vietnam OEL - TWAs 10 mg/m³

Dicalcium Phosphate
Latvia OEL - TWA 10 mg/m³

Magnesium stearate
ACGIH Threshold Limit Value (TWA) 10 mg/m³
Lithuania OEL - TWA 5 mg/m³
Sweden OEL - TWAs 5 mg/m³

Exposure Controls

PZ01417
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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 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

Physical State:
Capsule

Color:
White / Pink and Pink / Pink

Odor:
No data available.

Molecular Formula:
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)

Silicium dioxide
No data available

Sodium starch glycolate
No data available

Magnesium stearate
No data available

Microcrystalline cellulose
No data available

Dicalcium Phosphate
No data available

Hard gelatin capsules
No data available

Crizotinib
Predicted 7.4 Log D 2.07

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: diarrhea, nausea, vomiting, fatigue, visual disturbances, and headache. Additionally, effects on liver, respiratory system, cardiovascular system may occur.

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

Magnesium stearate
Rat Oral LD50 > 2000 mg/kg
Rat Inhalation LC50 > 2000 mg/m³

Microcrystalline cellulose
Rat Oral LD50 > 5000 mg/kg
Rabbit Dermal LD50 > 2000 mg/kg

Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

Microcrystalline cellulose
Skin Irritation Rabbit Non-irritating
Eye Irritation Rabbit Non-irritating

Crizotinib
Skin Corrosivity (In vitro, RHE) Not applicable Negative
Eye Irritation (In vitro, BCOP) Not applicable Negative
Eye Irritation Rabbit Severe
Skin Sensitization - LLNA Mouse Positive

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

Crizotinib
7 Day(s) Rat Oral 150 mg/kg/day NOAEL None identified
28 Day(s) Mouse Oral 200 mg/kg/day NOAEL None identified
1 Month(s) Rat Oral 10 mg/kg/day NOAEL Bone Marrow, Kidney, Male reproductive system
1 Month(s) Dog Oral 20 mg/kg/day NOAEL None identified
11. TOXICOLOGICAL INFORMATION

Reproduction & Development Toxicity: (Duration, Species, Route, Dose, End Point, Effect(s))

<table>
<thead>
<tr>
<th>Substance</th>
<th>Duration</th>
<th>Species</th>
<th>Route</th>
<th>Dose</th>
<th>End Point</th>
<th>Effect(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crizotinib</td>
<td>3 Month(s)</td>
<td>Rat</td>
<td>Oral</td>
<td>(M) 100 / (F) 250 mg/kg/day</td>
<td>LOAEL</td>
<td>Maternal toxicity, Developmental toxicity</td>
</tr>
<tr>
<td>Crizotinib</td>
<td>3 Month(s)</td>
<td>Dog</td>
<td>Oral</td>
<td>25 mg/kg/day</td>
<td>NOAEL</td>
<td>Blood</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Substance</th>
<th>Study Type</th>
<th>Cell Type/Organism</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crizotinib</td>
<td>In Vitro</td>
<td>Micronucleus</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>In Vitro</td>
<td>Chromosome Aberration</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>In Vivo</td>
<td>Micronucleus</td>
<td>Positive</td>
</tr>
</tbody>
</table>

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

12. ECOLOGICAL INFORMATION

Environmental Overview: Very toxic to aquatic organisms. Releases to the environment should be avoided.

Toxicity:

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

<table>
<thead>
<tr>
<th>Substance</th>
<th>Method</th>
<th>Species</th>
<th>End Point</th>
<th>Duration</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crizotinib</td>
<td>OECD</td>
<td>Cyprinodon variegatus (Sheepshead Minnow)</td>
<td>LC50 96 Hours</td>
<td>&gt; 5.2 mg/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OECD</td>
<td>Skeletonema costatum (Marine Diatom)</td>
<td>EC50 72 Hours</td>
<td>&lt; 0.10-0.19 mg/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OECD</td>
<td>Tisbe battagliai (Marine Copepod)</td>
<td>EC50 48 Hours</td>
<td>0.66 mg/L</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Substance</th>
<th>Inoculum</th>
<th>Method</th>
<th>End Point</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crizotinib</td>
<td>Activated sludge</td>
<td>OECD EC50</td>
<td>&gt; 1000 mg/L</td>
<td></td>
</tr>
</tbody>
</table>

Persistence and Degradability: No data available

Bio-accumulative Potential:

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

<table>
<thead>
<tr>
<th>Substance</th>
<th>Method</th>
<th>pH</th>
<th>Endpoint</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crizotinib</td>
<td>Predicted</td>
<td>7.4</td>
<td>Log D</td>
<td>2.07</td>
</tr>
</tbody>
</table>

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.

This material is regulated for transportation as a hazardous material/dangerous good.

UN number: UN 3077
UN proper shipping name: Environmentally Hazardous Substance, Solid, n.o.s (crizotinib)
Transport hazard class(es): 9
Packing group: III

5 kg/5L Exception:
Effective January 1, 2015, UN3082 and UN3077 materials contained in good quality packaging in the quantities listed below are not regulated as dangerous goods for transport by any mode:
  * Single packagings containing a net quantity of 5 liters or less for liquids or a net mass of 5 kg or less for solids.
  * Combination packagings containing a net quantity per inner packaging of 5 liters or less for liquids or a net mass of 5 kg or less for solids.

15. REGULATORY INFORMATION

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

Canada - WHMIS: Classifications
WHMIS hazard class: D2b toxic materials

Crizotinib
  CERCLA/SARA 313 Emission reporting Not Listed
  California Proposition 65 Not Listed
  EU EINECS/ELINCS List Not Listed

Silicium dioxide
  CERCLA/SARA 313 Emission reporting Not Listed
  California Proposition 65 Not Listed
15. REGULATORY INFORMATION

<table>
<thead>
<tr>
<th>Material</th>
<th>CERCLA/SARA 313 Emission reporting</th>
<th>California Proposition 65</th>
<th>Inventory - United States TSCA - Sect. 8(b)</th>
<th>Australia (AICS)</th>
<th>EU EINECS/ELINCS List</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium starch glycolate</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Present</td>
<td>Present</td>
<td>Not Listed</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Present</td>
<td>Present</td>
<td>Not Listed</td>
</tr>
<tr>
<td>Dicalcium Phosphate</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Present</td>
<td>Present</td>
<td>232-674-9</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Present</td>
<td>Present</td>
<td>209-150-3</td>
</tr>
<tr>
<td>Hard gelatin capsules</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

16. OTHER INFORMATION

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

- Serious eye damage/eye irritation-Cat.1; H318 - Causes serious eye damage
- Sensitization, skin-Cat.1; H317 - May cause an allergic skin reaction
- Germ cell mutagenicity-Cat.2; H341 - Suspected of causing genetic defects
- Hazardous to the aquatic environment, acute toxicity-Cat.1; H400 - Very toxic to aquatic life

Xn - Harmful
Xi - Irritant
N - Dangerous for the environment
R41 - Risk of serious damage to eyes.
R43 - May cause sensitization by skin contact.
R68 - Possible risks of irreversible effects.
R50 - Very toxic to aquatic organisms.

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

**Reasons for Revision:** Updated Section 7 - Handling and Storage. Updated Section 14 - Transport Information.

**Revision date:** 09-Mar-2015

**Prepared by:** Product Stewardship Hazard Communication

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*