MATERIAL SAFETY DATA SHEET

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

Pfizer Inc
Pfizer Pharmaceuticals Group
235 East 42nd Street
New York, New York 10017
1-212-573-2222

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
Contact E-Mail: pfizer-MSDS@pfizer.com

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161
Emergency telephone number:
International CHEMTREC (24 hours): +1-703-527-3887

Material Name: Crizotinib Oral Solution

Trade Name: XALKORI
Chemical Family: Anaplastic Lymphoma Kinase Inhibitor
Intended Use: Pharmaceutical product for the treatment of lung cancer

2. HAZARDS IDENTIFICATION

Appearance: Clear colorless to yellow solution
Signal Word: WARNING

Statement of Hazard: May cause allergic skin reaction.
Suspected of causing genetic defects.

Additional Hazard Information:
Short Term: May cause eye irritation (based on components) .
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, cardiovascular system, respiratory system may occur.

EU Classification
EU Indication of danger: Mutagenic: Category 3
Irritant

EU Hazard Symbols:

EU Risk Phrases:
R43 - May cause sensitization by skin contact.
R68 - Possible risk of irreversible effects.

Australian Hazard Classification (NOHSC): Hazardous Substance. Non-Dangerous Goods.

2. HAZARDS IDENTIFICATION

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings 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	%
Crizotinib	877399-52-5	Not Listed	Xi;R41 Xi;R43 Muta. Cat.3;R68 N,R50	2.43
Hydrochloric Acid	7647-01-0	231-595-7	C;R35 T;R23	**
Sodium hydroxide	1310-73-2	215-185-5	C;R35	**
Phosphoric acid	7664-38-2	231-633-2	C;R34	<5.0
Sodium chloride	7647-14-5	231-598-3	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Water, purified	7732-18-5	231-791-2	Not Listed	*
Flavor	NOT ASSIGNED	Not Listed	Not Listed	*
Pullulan	9057-02-7	232-945-1	Not Listed	*
Sodium benzoate	532-32-1	208-534-8	Not Listed	*
Sucralose	56038-13-2	259-952-2	Not Listed	*

Additional Information: * Proprietary
** to adjust pH
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

For the full text of the R phrases mentioned in this Section, see Section 16

4. 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.

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.

5. FIRE FIGHTING MEASURES

Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.

Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire.

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

Fire / Explosion Hazards: Fine particles (such as dust and mists) may fuel fires/explosions.

6. ACCIDENTAL RELEASE MEASURES

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

Measures for Cleaning / Collecting: Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.

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

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

General Handling: Minimize generating airborne mists and vapors. Avoid breathing vapor or mist. 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.

Storage Conditions: Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

Crizotinib

Pfizer OEL TWA-8 Hr:	15µg/m^3, Sensitizer, Severe Eye Irritant

Hydrochloric Acid

ACGIH Ceiling Threshold Limit:	2 ppm
Australia PEAK	5 ppm 7.5 mg/m^3
Austria OEL - MAKs	5 ppm 8 mg/m^3
Belgium OEL - TWA	5 ppm 8 mg/m^3
Bulgaria OEL - TWA	8.0 mg/m^3
Cyprus OEL - TWA	5 ppm 8 mg/m^3

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Czech Republic OEL - TWA	8 mg/m^3
Estonia OEL - TWA	5 ppm 8 mg/m^3
Germany - TRGS 900 - TWAs	2 ppm 3 mg/m^3
Germany (DFG) - MAK	2 ppm 3.0 mg/m^3
Greece OEL - TWA	5 ppm 7 mg/m^3
Hungary OEL - TWA	8 mg/m^3
Ireland OEL - TWAs	5 ppm 8 mg/m^3
Italy OEL - TWA	5 ppm 8 mg/m^3
Japan - OELs - Ceilings	5 ppm 7.5 mg/m^3
Latvia OEL - TWA	5 ppm 8 mg/m^3
Lithuania OEL - TWA	5 ppm 8 mg/m^3
Luxembourg OEL - TWA	5 ppm 8 mg/m^3
Malta OEL - TWA	5 ppm 8 mg/m^3
Netherlands OEL - TWA	8 mg/m^3
Poland OEL - TWA	5 mg/m^3
Romania OEL - TWA	5 ppm 8 mg/m^3
Slovakia OEL - TWA	5 ppm 8.0 mg/m^3
Slovenia OEL - TWA	5 ppm 8 mg/m^3
Spain OEL - TWA	5 ppm 7.6 mg/m^3

Sodium hydroxide

ACGIH Ceiling Threshold Limit:	2 mg/m^3
Australia PEAK	2 mg/m^3
Austria OEL - MAKs	2 mg/m^3
Bulgaria OEL - TWA	2.0 mg/m^3
Czech Republic OEL - TWA	1 mg/m^3
Estonia OEL - TWA	1 mg/m^3
France OEL - TWA	2 mg/m^3
Greece OEL - TWA	2 mg/m^3
Hungary OEL - TWA	2 mg/m^3
Japan - OELs - Ceilings	2 mg/m^3
Latvia OEL - TWA	0.5 mg/m^3
OSHA - Final PELS - TWAs:	2 mg/m^3
Poland OEL - TWA	0.5 mg/m^3
Slovakia OEL - TWA	2 mg/m^3
Slovenia OEL - TWA	2 mg/m^3
Sweden OEL - TWAs	1 mg/m^3

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Phosphoric acid

ACGIH Threshold Limit Value (TWA)	1 mg/m^3
ACGIH Threshold Limit Value (STEL)	3 mg/m^3
Australia STEL	3 mg/m^3
Australia TWA	1 mg/m^3
Austria OEL - MAKs	1 mg/m^3
Belgium OEL - TWA	1 mg/m^3
Bulgaria OEL - TWA	1.0 mg/m^3
Cyprus OEL - TWA	1 mg/m^3
Czech Republic OEL - TWA	1 mg/m^3
Denmark OEL - TWA	1 mg/m^3
Estonia OEL - TWA	1 mg/m^3
Finland OEL - TWA	1 mg/m^3
France OEL - TWA	0.2 ppm 1 mg/m^3
Germany - TRGS 900 - TWAs	2 mg/m^3
Germany (DFG) - MAK	2 mg/m^3 inhalable fraction
Greece OEL - TWA	1 mg/m^3
Hungary OEL - TWA	1 mg/m^3
Ireland OEL - TWAs	1 mg/m^3
Italy OEL - TWA	1 mg/m^3
Latvia OEL - TWA	1 mg/m^3
Lithuania OEL - TWA	1 mg/m^3
Luxembourg OEL - TWA	1 mg/m^3
Malta OEL - TWA	1 mg/m^3
Netherlands OEL - TWA	1 mg/m^3
OSHA - Final PELS - TWAs:	1 mg/m^3
Poland OEL - TWA	1 mg/m^3
Portugal OEL - TWA	1 mg/m^3
Romania OEL - TWA	1 mg/m^3
Slovakia OEL - TWA	1 mg/m^3
Slovenia OEL - TWA	1 mg/m^3
Spain OEL - TWA	1 mg/m^3
Sweden OEL - TWAs	1 mg/m^3

Sodium chloride

Latvia OEL - TWA	5 mg/m^3
Lithuania OEL - TWA	5 mg/m^3

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.

Environmental Exposure Controls: Refer to specific Member State legislation for requirements under Community environmental legislation.

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.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Respiratory protection: If airborne exposures are within or exceed the Occupational Exposure Band (OEB) range, wear an appropriate respirator with a protection factor sufficient to control exposures to the bottom of the OEB range.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Liquid solution	**Color:**	Clear, colorless to yellow
Molecular Formula:	Mixture	**Molecular Weight:**	Mixture

Partition Coefficient (Measured - Log Pow/Log Kow): 1.83 (crizotinib)

10. STABILITY AND REACTIVITY

Chemical Stability: Stable under normal conditions of use.
Conditions to Avoid: Fine particles (such as dusts, mists and vapors) may fuel fires/explosions. Protect from Light .
Incompatible Materials: As a precautionary measure, keep away from strong oxidizers

11. TOXICOLOGICAL INFORMATION

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

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

Sodium benzoate
Rat Oral LD50 4,070 mg/kg
Mouse Oral LD50 1600 mg/kg

Sodium hydroxide
Mouse IP LD50 40 mg/kg

Phosphoric acid
Rat Oral LD50 1530 mg/kg
Rabbit Dermal LD 50 2730 mg/kg

Sodium chloride
Rat Oral LD50 3000 mg/kg
Mouse Oral LD50 4000 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)

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

11. TOXICOLOGICAL INFORMATION

Sodium hydroxide
Eye Irritation Rabbit Severe
Skin Irritation Rabbit Severe

Phosphoric acid
Eye Irritation Rabbit Severe
Skin Irritation Rabbit Severe

Sodium chloride
Eye Irritation Rabbit Moderate
Skin Irritation Rabbit Mild

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
3 Month(s) Rat Oral (M) 100 / (F) 250 mg/kg/day LOAEL Male reproductive system, Bone Marrow, Liver, Gastrointestinal system, Pituitary

Sodium benzoate
10 Day(s) Rat Oral 27370 mg/kg LOAEL Liver, Blood
10 Day(s) Mouse Oral 45 g/kg LOAEL Liver, Kidney, Blood, Ureter, Bladder

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

Crizotinib
Embryo / Fetal Development Rat Oral 200 mg/kg/day LOAEL Maternal toxicity, Developmental toxicity
Embryo / Fetal Development Rabbit Oral 60 mg/kg/day NOAEL Maternal Toxicity
Embryo / Fetal Development Rabbit Oral 60 mg/kg/day LOAEL Developmental toxicity

Sodium benzoate
Embryo / Fetal Development Rat Oral 44 g/kg LOEL Developmental toxicity

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

Crizotinib
Bacterial Mutagenicity (Ames) *Salmonella* , *E. coli* Negative
In Vitro Micronucleus Chinese Hamster Ovary (CHO) cells Positive without activation
In Vitro Chromosome Aberration Human Lymphocytes Positive
In Vivo Micronucleus Rat Bone Marrow Positive

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

Hydrochloric Acid
IARC: Group 3 (Not Classifiable)

12. ECOLOGICAL INFORMATION

Environmental Overview: This mixture contains material that is toxic to aquatic life. Releases to the environment should be avoided.

Partition Coefficient (Measured - Log Pow/Log Kow): 1.83 (crizotinib)

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

Crizotinib
Cyprinodon variegatus (Sheepshead Minnow) OECD LC50 96 Hours > 5.2 mg/L
Skeletonema costatum (Marine Diatom) OECD EC50 72 Hours < 0.10-0.19 mg/L
Tisbe battagliai (Marine Copepod) OECD EC50 48 Hours 0.66 mg/L

Phosphoric acid
Gambusia affinis (Mosquitofish) LC50 96 Hours 3-3.5 mg/L
Daphnia magna (Water Flea) EC-50 12 Hours 4.6 mg/L

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

Crizotinib
Activated sludge OECD EC50 > 1000 mg/L

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

EU Symbol: Xn , Xi
EU Indication of danger: Mutagenic: Category 3
Irritant

EU Risk Phrases:
R43 - May cause sensitization by skin contact.
R68 - Possible risk of irreversible effects.

EU Safety Phrases:
S22 - Do not breathe dust.

15. REGULATORY INFORMATION

S24/25 - Avoid contact with skin and eyes.
S36/37/39 - Wear suitable protective clothing, gloves and eye/face protection.

OSHA Label:
WARNING
May cause allergic skin reaction.
Suspected of causing genetic defects.

Canada - WHMIS: Classifications

WHMIS hazard class:
D2b toxic materials

Hydrochloric Acid

CERCLA/SARA 313 Emission reporting	1.0 %
CERCLA/SARA Hazardous Substances and their Reportable Quantities:	5000 lb 2270 kg
CERCLA/SARA - Section 302 Extremely Hazardous TPQs	500 lb
CERCLA/SARA - Section 302 Extremely Hazardous Substances EPCRA RQs	5000 lb
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 5 Schedule 6
EU EINECS/ELINCS List	231-595-7

Sodium hydroxide

CERCLA/SARA Hazardous Substances and their Reportable Quantities:	1000 lb 454 kg
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 5 Schedule 6
EU EINECS/ELINCS List	215-185-5

Water, purified

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

Pullulan

Inventory - United States TSCA - Sect. 8(b)	Present

15. REGULATORY INFORMATION

Australia (AICS):	Present
EU EINECS/ELINCS List	232-945-1

Phosphoric acid

CERCLA/SARA Hazardous Substances and their Reportable Quantities:	5000 lb 2270 kg
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 5 Schedule 6
EU EINECS/ELINCS List	231-633-2

Sodium chloride

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	231-598-3

Sodium benzoate

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	208-534-8

Sucralose

Australia (AICS):	Present
EU EINECS/ELINCS List	259-952-2

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R23 - Toxic by inhalation.
R34 - Causes burns.
R35 - Causes severe burns.
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 2 - Hazard Identification.

Prepared by: Product Stewardship Hazard Communication
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