SAFETY DATA SHEET

Section 1: IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

1.1. Product identifier

Product Name LGX818

Product Code(s) PF00014
Synonyms LGX818-NXA, encorafenib
Trade Name: Not established
Compound Number PF-07263896; VC-001215214
Chemical Family: Not determined

LGX818 (encorafenib)
CAS No 1269440-17-6

1.2. Relevant identified uses of the substance or mixture and uses advised against

Recommended Use Pharmaceutical active

1.3. Details of the supplier of the safety data sheet

Pfizer Inc
235 East 42nd Street
New York, New York 10017
1-800-879-3477

Pfizer Ireland Pharmaceuticals
OSG Building
Ringaskiddy, Co. Cork.
Ireland
+353 21 4378701

1.4. Emergency telephone number

Emergency Telephone Chemtrec 1-800-424-9300 International Chemtrec (24 hours):+1-703-527-3887
E-mail address pfizer-MSDS@pfizer.com

Section 2: HAZARDS IDENTIFICATION

2.1. Classification of the substance or mixture

Carcinogenicity Category 2
Reproductive toxicity Category 1B
Specific target organ toxicity (repeated exposure) Category 2
Acute aquatic toxicity Category 2

OSHA Classification
Physical Hazard Combustible Dust

2.2. Label elements

Signal word Danger

Hazard statements
H351 - Suspected of causing cancer
H360FD - May damage fertility. May damage the unborn child
May form combustible dust concentrations in air
H373 - May cause damage to organs through prolonged or repeated exposure
H401 - Toxic to aquatic life

Precautionary Statements

P201+P202 - Obtain special instructions before use. 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
P273 - Avoid release to the environment
P280 - Wear protective gloves and protective clothing
P308 + P313 - IF exposed or concerned: Get medical advice/attention
P405 - Store locked up
P501 - Dispose of contents/container in accordance with all local and national regulations

Supplemental Hazard

Strong dust explosion characteristic. Very high sensitivity to ignition. Compound, not fully tested, additional hazards may exist.

2.3. Other hazards

Other hazards

An Occupational Exposure Value has been established for this substance (see Section 8).

Note:

This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the product or its ingredients 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.

Section 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

Hazardous

Chemical name	Weight-%	REACH Registration Number	EC No	Classification according to Regulation (EC) No. 1272/2008 [CLP]	Specific concentration limit (SCL)	M-Factor	M-Factor (long-term)
LGX818 (encorafenib) 1269440-17-6	100		Not Listed	Carc.2(H351) Repr.1B(H360FD) STOT RE 2(H373) Aquatic Acute 2 (H401)	Not Listed	No data available	No data available

Full text of H- and EUH-phrases: see section 16

Acute Toxicity Estimate
No information available

Additional information

Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

Section 4: FIRST AID MEASURES

4.1. Description of first aid measures

Inhalation Remove to fresh air. Seek immediate medical attention/advice.

Eye contact Rinse thoroughly with plenty of water for at least 15 minutes, lifting lower and upper eyelids. Consult a physician.

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.

4.2. Most important symptoms and effects, both acute and delayed

Most important symptoms and effects For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

4.3. Indication of any immediate medical attention and special treatment needed

Note to physicians None.

Section 5: FIRE-FIGHTING MEASURES

5.1. Extinguishing media

Suitable Extinguishing Media Dry chemical, CO2, alcohol-resistant foam or water spray.

5.2. Special hazards arising from the substance or mixture

Specific hazards arising from the chemical Strong dust explosion characteristic. Very high sensitivity of a dust cloud to ignition, based on minimum ignition energy.

Hazardous combustion products Carbon monoxide, carbon dioxide, oxides of nitrogen, sulfur oxides, hydrogen chloride and other chlorine-, florine-, and sulfur-containing compounds

5.3. Advice for firefighters

Special protective equipment for fire-fighters Firefighters should wear self-contained breathing apparatus and full firefighting turnout gear. Use personal protection equipment.

Section 6: ACCIDENTAL RELEASE MEASURES

6.1. Personal precautions, protective equipment and emergency procedures

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

For emergency responders Use personal protection recommended in Section 8.

6.2. Environmental precautions

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

6.3. Methods and material for containment and cleaning up

Methods for containment Prevent further leakage or spillage if safe to do so.

Methods for cleaning up Eliminate possible ignition sources (e.g., heat, sparks, flame, impact, friction, electricity), and follow appropriate grounding procedures. Collect spilled material by a method that controls dust generation. Avoid use of a filtered vacuum to clean spills of dry solids, due to the potential for electrostatic discharge and the strong dust explosion potential and very high sensitivity to ignition. Clean spill area thoroughly.

Prevention of secondary hazards Clean contaminated objects and areas thoroughly observing environmental regulations.

6.4. Reference to other sections

Reference to other sections See section 8 for more information. See section 13 for more information.

Section 7: HANDLING AND STORAGE

7.1. Precautions for safe handling

Advice on safe handling

Ground and bond all bulk transfer equipment. Avoid open handling. Minimize dust generation. All conductive elements of the system that contact the dry substance should be properly bonded and grounded and equipped with proper explosion relief or suppression systems. This material should not be flowed through nonconductive ducts or pipes because of the potential for electrostatic discharge ignition. Restricting the use of high resistivity materials, such as plastics, should be considered. Use local exhaust ventilation or perform work under fume hood/fume cupboard. Avoid inhalation and contact with skin, eye, and clothing. Wash hands and any exposed skin after removal of PPE. 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. When handling, use appropriate personal protective equipment (see Section 8).

General hygiene considerations Handle in accordance with good industrial hygiene and safety practice.

7.2. Conditions for safe storage, including any incompatibilities

Storage Conditions Store at room temperature in properly labeled containers. Keep away from heat, sparks and flames.

7.3. Specific end use(s)

Specific use(s) Pharmaceutical active.

Section 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control parameters

LGX818 (encorafenib)

Pfizer OEL TWA-8 Hr: 40 µg/m^3

8.2. Exposure controls

Engineering controls Engineering controls should be used as the primary means to control exposures. Use process containment, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits.

Environmental exposure controls No information available.

Personal protective equipment Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE). Contact your safety and health professional or safety equipment supplier for assistance in selecting the correct protective clothing/equipment based on an assessment of the workplace conditions, other chemicals used or present in the workplace and specific operational processes.

Eye/face protection Wear safety glasses as minimum protection (goggles recommended). (Eye protection

must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.).

Hand protection Wear impervious gloves (e.g. Nitrile, etc.) as minimum protection. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.).

Skin and body protection Wear impervious protective clothing when handling this compound. (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.).

Respiratory protection Under normal conditions of use, 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 (e.g. particulate respirator with a full mask, P3 filter). (Respirators must meet the standards in accordance with EN136, EN143, ASTM F2704-10 or international equivalent.).

General hygiene considerations Handle in accordance with good industrial hygiene and safety practice.

Section 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Physical state	Powder
Color	white
Odor	No information available.
Odor threshold	No information available
Molecular formula	C22 H27 Cl F N7 O4 S
Molecular weight	540.0173

Property	**Values**
pH	No data available
Melting point / freezing point	185 °C
Boiling point / boiling range	
Flash point	No information available
Evaporation rate	No data available
Flammability (solid, gas)	No data available
Flammability Limit in Air	
Upper flammability limit:	No data available
Lower flammability limit:	No data available
Vapor pressure	<0.84 uPa@20C
Vapor density	No data available
Relative density	No data available
Water solubility	(0.01 g/l)
Solubility(ies)	No data available
Partition coefficient	2.81
Autoignition temperature	450 °C
Decomposition temperature	>150
Kinematic viscosity	No data available
Dynamic viscosity	No data available
Particle characteristics	
Particle Size	4-43 um
Particle Size Distribution	No information available
Explosive properties	No information available

Partition Coefficient: (Method, pH, Endpoint, Value)
LGX818 (encorafenib)
Measured 7 Log P 2.6

9.2. Other information

pKa:	4.53 - 6.97

9.2.1. Information with regard to physical hazard classes

Flammable solids	Not readily combustible. Not a Division 4.1 material

9.2.2. Other safety characteristics

Sensitivity to Mechanical Impact	Not sensitive
Dust Explosivity:	This material may present a dust explosivity hazard
Minimum Oxygen Concentration (%)	10-11
Maximum Pressure Rise (bar)	8.7
Maximum Rate of Pressure Rise (bar/sec)	861
K_{st} (bar.m/s)	234
Minimum Ignition Energy (mJ)	5
Minimum Ignition Temperature (°C)	**610-620**
Minimum Explosive Conc. (g/m^3)	90-100
Charge Relaxation Time:	
Ambient Humidity:	2.3 Hours
Low Humidity:	2.8 Hours
Resistivity (ohm-m):	
Powder:	Ambient: >10^14 Low: >10^14

Section 10: STABILITY AND REACTIVITY

10.1. Reactivity
Reactivity No data available.
10.2. Chemical stability
Stability Stable under normal conditions.
Explosion data
Sensitivity to Mechanical Impact Not sensitive.
Sensitivity to Static Discharge No data available.

10.3. Possibility of hazardous reactions
Possibility of hazardous reactions No information available.
10.4. Conditions to avoid
Conditions to avoid Fine particles (such as dust and mists) may fuel fires/explosions.

10.5. Incompatible materials
Incompatible materials As a precautionary measure, keep away from strong oxidizers.

10.6. Hazardous decomposition products
Hazardous decomposition products No data available.

Section 11: TOXICOLOGICAL INFORMATION

11.1. Information on hazard classes as defined in Regulation (EC) No 1272/2008

Long Term: Animal studies have shown a potential to cause adverse effects on the fetus.
Known Clinical Effects: Adverse effects associated with therapeutic use include decreased red blood cell count (anemia), weight loss, constipation, liver effects, joint pain, abdominal pain, diarrhea, tiredness, nausea, skin rash, vomiting.

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

LGX818 (encorafenib)
Rat Oral 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)
LGX818 (encorafenib)
Skin irritation Rabbit Non-irritating
Skin Sensitization - LLNA Mouse Negative

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)
LGX818 (encorafenib)
13 Week(s) Rat Oral <= 20 mg/kg/day NOAEL Gastrointestinal System, Male reproductive system
13 Week(s) Monkey Oral 20 mg/kg/day NOAEL Eyes
28 Day(s) Rat Oral 20 mg/kg/day NOAEL Skin, Gastrointestinal system, Male reproductive system

Reproduction & Development Toxicity: (Duration, Species, Route, Dose, End Point, Effect(s))
LGX818 (encorafenib)
Embryo / Fetal Development Rat Oral 5 mg/kg NOAEL Maternal toxicity, Embryotoxicity
Embryo / Fetal Development Rat Oral 5 mg/kg/day NOEL Embryotoxicity
Embryo / Fetal Development Rabbit Oral 25 mg/kg Embryotoxicity, Maternal Toxicity, Fertility

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)
LGX818 (encorafenib)
Bacterial Mutagenicity (Ames) *Salmonella* Negative
Chromosome Aberration Human Lymphocytes Negative
In Vivo Micronucleus Rat Bone marrow Negative

Carcinogenicity Not listed as a carcinogen by IARC, NTP or US OSHA.

11.2. Information on other hazards

11.2.1. Endocrine disrupting properties

Endocrine disrupting properties No information available.

11.2.2. Other information

Other adverse effects No information available.

Section 12: ECOLOGICAL INFORMATION

Environmental Overview: Releases to the environment should be avoided.

12.1. Toxicity

Aquatic Toxicity: (Species, Method, End Point, Duration, Result)
LGX818 (encorafenib)
Fish LC50 96 Hours > 14 mg/L
Daphnia magna (Water Flea) EC50 48 Hours > 15 mg/L
Pseudokirchneriella subcapitata (Green Alga) ErC50 72 Hours 8.2 mg/L

Aquatic Toxicity Comments: A greater than symbol (>) indicates that aquatic toxicity was not observed at the maximum dose tested.

Bacterial Inhibition: (Inoculum, Method, End Point, Result)
LGX818 (encorafenib)
Activated sludge EC50 > 1000 mg/L

Chronic Aquatic Toxicity: (Species, Method, Duration, Endpoint, Result, Adverse Endpoint)
LGX818 (encorafenib)
Pseudokirchneriella subcapitata (Green Alga) N/A 3 Day(s) NOEC 2 mg/L Growth

12.2. Persistence and degradability

Persistence and degradability Not readily biodegradable.

Biodegradation: (Method, Inoculum, Biodeg Study, Result, Endpoint, Duration, Classification)
LGX818 (encorafenib)
Activated sludge Ready 0-2 % After 28 Day(s) Not readily biodegradable

12.3. Bioaccumulative potential

Bioaccumulation None known.

Partition Coefficient: (Method, pH, Endpoint, Value)
LGX818 (encorafenib)
Measured 7 Log P 2.6

12.4. Mobility in soil

Mobility in soil No information available.

12.5. Results of PBT and vPvB assessment

PBT and vPvB assessment No information available.

12.6. Endocrine disrupting properties

Endocrine disrupting properties No information available.

12.7. Other adverse effects
No information available.

Section 13: DISPOSAL CONSIDERATIONS

13.1. 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 wastewater 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.

Section 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.

Section 15: REGULATORY INFORMATION

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

LGX818 (encorafenib)

CERCLA/SARA Section 313 de minimus %	Not Listed
California Proposition 65	Not Listed
EINECS	Not Listed
Standard for Uniform Scheduling of Medicines and Poisons (SUSMP)	Schedule 4

European Union

Take note of Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work

Authorizations and/or restrictions on use:

This product does not contain substances subject to authorization (Regulation (EC) No. 1907/2006 (REACH), Annex XIV) This product does not contain substances subject to restriction (Regulation (EC) No. 1907/2006 (REACH), Annex XVII)

Persistent Organic Pollutants

Not applicable

Ozone-depleting substances (ODS) regulation (EC) 1005/2009

Not applicable

Legend:

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
EINECS/ELINCS - European Inventory of Existing Chemical Substances/European List of Notified Chemical Substances
AICS - Australian Inventory of Chemical Substances

15.2. Chemical safety assessment

Chemical Safety Report No information available

Section 16: OTHER INFORMATION

Key or legend to abbreviations and acronyms used in the safety data sheet

Full text of H-Statements referred to under section 3

Carcinogenicity-Cat.2; H351 - Suspected of causing cancer Reproductive toxicity-Cat.1B; H360FD - May damage fertility. May damage the unborn child Specific target organ toxicity, repeated exposure-Cat.1; H372 - Causes damage to organs through prolonged or repeated exposure H401 - Toxic to aquatic life Hazardous to the aquatic environment, chronic toxicity-Cat.1;

Data Sources:	Pfizer proprietary drug development information.
Reason for revision	Updated Section 9 - Physical and Chemical Properties. Updated Section 12 - Ecological Information.
Revision date	06-Dec-2021
Prepared By	Pfizer Global Environment, Health, and Safety

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