SAFETY DATA SHEET

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

Product Identifier

Material Name: Palbociclib Capsules

Trade Name: IBRANCE
Chemical Family: Kinase inhibitor

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

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

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

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

Germ Cell Mutagenicity: Category 2
Specific target organ systemic toxicity (repeated exposure): Category 2
Chronic aquatic toxicity: Category 2

Label Elements

Signal Word: Warning

Hazard Statements:
H341 - Suspected of causing genetic defects
H373 - May cause damage to organs through prolonged or repeated exposure: testes, bone marrow
H411 - Toxic to aquatic life with long lasting effects

Precautionary Statements:
P201 - Obtain special instructions before use
P260 - Do not breathe dust/fume/gas/mist/vapors/spray
P273 - Avoid release to the environment
P281 - Use personal protective equipment as required
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P314 - Get medical attention/advice if you feel unwell
P391 - Collect spillage
P405 - Store locked up
P501 - Dispose of contents/container in accordance with all local and national regulations

Other Hazards An Occupational Exposure Value has been established for one or more of the ingredients (see Section 8).

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	GHS Classification	%
Palbociclib (PD 0332991)	571190-30-2	Not Listed	Muta 2 (H341) STOT RE. 2 (H373) Aquatic Chronic 2 (H411)	20 - 30

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Cellulose microcrystalline	9004-34-4	Not Listed	Not Listed	*
Colloidal silicon dioxide	7631-86-9	231-545-4	Not Listed	*
Magnesium Stearate	557-04-0	209-150-3	Not Listed	*
Lactose Monohydrate	64044-51-5	Not Listed	Not Listed	*
Sodium starch glycolate	9063-38-1	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 CLP/GHS abbreviations mentioned in this Section, see Section 16

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.

Conditions for Safe Storage, Including any Incompatibilities

Storage Conditions: Store as directed by product packaging.

Specific end use(s): Pharmaceutical product

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

Palbociclib (PD 0332991)

Pfizer OEL TWA-8 Hr:	1µg/m^3

Colloidal silicon dioxide

Australia TWA	2 mg/m^3
Austria OEL - MAKs	4 mg/m^3
Czech Republic OEL - TWA	0.1 mg/m^3 4.0 mg/m^3
Estonia OEL - TWA	2 mg/m^3
Finland OEL - TWA	5 mg/m^3
Germany - TRGS 900 - TWAs	4 mg/m^3
Germany (DFG) - MAK	4 mg/m^3
Ireland OEL - TWAs	6 mg/m^3 2.4 mg/m^3
Latvia OEL - TWA	1 mg/m^3
OSHA - Final PELs - Table Z-3 Mineral D:	20 mppcf Listed
Slovakia OEL - TWA	4.0 mg/m^3
Slovenia OEL - TWA	0.3 mg/m^3
Switzerland OEL -TWAs	4 mg/m^3

Magnesium Stearate

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

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). 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.
Hands:	Impervious disposable gloves (e.g. Nitrile, etc.) (double recommended) if skin contact with drug product is possible and for bulk processing operations. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.)
Eyes:	Wear safety glasses or goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)
Skin:	Impervious disposable protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations. (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.)

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Capsule	**Color:**	Yellow
Odor:	No data available.	**Odor Threshold:**	No data available.
Molecular Formula:	Mixture	**Molecular Weight:**	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)
PD 0332991-0054
No data available
Palbociclib (PD 0332991)
Measured 7 Log D 1.11
Cellulose microcrystalline
No data available
Colloidal silicon dioxide
No data available
Sodium starch glycolate
No data available
Magnesium Stearate
No data available
Lactose Monohydrate
No data available
PD 0332991-0002
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

Flammablity:
- **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. As a precautionary measure, keep away from heat sources and electrostatic discharge.
- **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 various forms of the active ingredient. The remaining information 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: decreased white blood cells (leukopenia), neutropenia, decreased red blood cell count (anemia), fatigue, and nausea.

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

PD 0332991-0054
Rat Oral Maximally Tolerated Dose 500 mg/kg

Palbociclib (PD 0332991)
Rat (M) Oral Minimum Lethal Dose >/= 1000 mg/kg

Lactose Monohydrate
Rat Oral LD 50 29700 mg/kg

PD 0332991-0002
Dog Oral Maximum Asymptomatic Dose 10 mg/kg

Safety Pharmacology: **PD 0332991-0054:** Neurofunctional not significant Pulmonary decreased respiratory rate (5.0 mg/kg)
PD 0332991-0002 *In vitro* Cardiovascular and *In vivo* Cardiovascular increased QT interval

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

Palbociclib (PD 0332991)
Eye Irritation (*In vitro* , BCOP) Not applicable Negative
Eye Irritation Rabbit Mild
Skin Irritation Rabbit Non-irritating
Skin Sensitization - LLNA Mouse Negative

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

PD 0332991-0054
3 Week(s) Rat Oral 50 mg/kg/day LOAEL Blood, Bone marrow, Lymphoid tissue, Male reproductive system
3 Week(s) Dog Oral 0.2 mg/kg/day NOAEL Blood, Bone Marrow, Lymphoid tissue, Male reproductive system

Palbociclib (PD 0332991)
15 Week(s) Rat Oral (M) 10 / (F) 200 mg/kg/day NOAEL Male reproductive system
15 Week(s) Dog Oral (M) 0.2 / (F) 2.0 mg/kg/day NOAEL Male reproductive system
27 Week(s) Rat Oral (M) <10 / (F) <50 mg/kg/day NOAEL Bone Marrow, Lymphoid tissue, Male reproductive system
39 Week(s) Dog Oral (M) <0.2 / (F) <3.0 mg/kg/day NOAEL Bone Marrow, Male reproductive system, Lymphoid tissue

Magnesium Stearate
13 Week(s) Rat Oral 1092 g/kg LOAEL Liver

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

11. TOXICOLOGICAL INFORMATION

Palbociclib (PD 0332991)

Embryo / Fetal Development	Rabbit	Oral	10 mg/kg/day	NOAEL	Maternal toxicity, Developmental toxicity
Embryo / Fetal Development	Rat	Oral	100 mg/kg/day	NOAEL	Maternal Toxicity, Developmental toxicity
Fertility & Early Embryonic Development-Females	Rat	Oral	300 mg/kg/day	NOAEL	Reproductive toxicity
Fertility & Early Embryonic Development - Males	Rat	Oral	10 mg/kg/day	NOAEL	Negative
Embryo / Fetal Development	Rat	Oral	100 mg/kg/day	NOAEL	Maternal Toxicity, Developmental toxicity, Not Teratogenic
Embryo / Fetal Development	Rabbit	Oral	10 mg/kg/day	NOAEL	Maternal Toxicity, Developmental toxicity
Prenatal & Postnatal Development	Rat	Oral	100 mg/kg/day	NOAEL	Maternal Toxicity
Prenatal & Postnatal Development	Rat	Oral	300 mg/kg/day	NOAEL	No effects at maximum dose

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

PD 0332991-0054

Bacterial Mutagenicity (Ames)	*Salmonella* , *E. coli*	Negative
In Vitro Cytogenetics	Human Lymphocytes	Negative
In Vivo Micronucleus	Rat Bone Marrow	Positive

Palbociclib (PD 0332991)

Bacterial Mutagenicity (Ames)	*Salmonella* , *E. coli*	Negative
In Vitro Chromosome Aberration	Rat Bone Marrow	Positive
In Vitro Kinetochore Analysis	Chinese Hamster Ovary (CHO) cells	Positive
In Vivo Micronucleus	Rat Bone Marrow	Positive

Lactose Monohydrate

In Vitro Bacterial Mutagenicity (Ames)	*Salmonella* , *E. coli*	Negative

PD 0332991-0002

In Vitro Micronucleus	Chinese Hamster Ovary (CHO) cells	Positive without activation
Bacterial Mutagenicity (Biolum Ames)	*Salmonella*	Negative

Genetic Toxicity Comments: **PD 0332991-0002** The above genetic toxicity studies (*In vitro* Micronucleus and Biolum Ames) were preliminary assays.
PD 0332991-0054: Investigation into the mechanism of the positive response in the *in vivo* micronucleus assay suggests an aneugenic rather than clastogenic mechanism.

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

Colloidal silicon dioxide

IARC: Group 3 (Not Classifiable)
NTP: Reasonably Anticipated To Be A Human Carcinogen

12. ECOLOGICAL INFORMATION

Environmental Overview: Releases to the environment should be avoided. Environmental properties have not been thoroughly investigated.

Toxicity:

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

Palbociclib (PD 0332991)
Activated sludge OECD EC50 > 1400

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

Palbociclib (PD 0332991)
Daphnia magna (Water Flea) OECD 21 Day(s) NOEC 0.27 mg/L

Persistence and Degradability:
Biodegradation: (Method, Inoculum, Biodeg Study, Result, Endpoint, Duration, Classification)
Palbociclib (PD 0332991)
OECD Activated sludge Ultimate (CO2 Evolution) 2% After 28 Day(s) Not Ready

Bio-accumulative Potential:
Partition Coefficient: (Method, pH, Endpoint, Value)
Palbociclib (PD 0332991)
Measured 7 Log D 1.11

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
Technical Shipping Name: (palbociclib)
Transport hazard class(es): 9
Packing group: III
Environmental Hazard(s): Marine Pollutant

5 kg/5L Exception:
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.

DOT

DOT Proper shipping name: Not regulated

15. REGULATORY INFORMATION

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

Caution - Substance not fully tested (VIIA)

Palbociclib (PD 0332991)

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

Cellulose microcrystalline

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

Colloidal silicon dioxide

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	231-545-4

Magnesium Stearate

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

Lactose Monohydrate

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Australia (AICS):	Present
EU EINECS/ELINCS List	Not Listed

Sodium starch glycolate

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	Not Listed

16. OTHER INFORMATION

Text of CLP/GHS Classification abbreviations mentioned in Section 3

Specific target organ toxicity, repeated exposure-Cat.2; H373 - May cause damage to organs through prolonged or repeated exposure
Germ cell mutagenicity-Cat.2; H341 - Suspected of causing genetic defects
Hazardous to the aquatic environment, chronic toxicity-Cat.2; H411 - Toxic to aquatic life with long lasting effects

Data Sources:	Pfizer proprietary drug development information.
Reasons for Revision:	Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 11 - Toxicology Information.
Revision date:	14-Jul-2017
	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