



SAFETY DATA SHEET

Revision date: 19-Feb-2019

Version: 3.0

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

Product Identifier

Material Name: ZIRABEV (Bevacizumab)

Trade Name: ZIRABEV
Compound Number: PF-06439535
Synonyms: Bevacizumab-Pfizer; Beva-PFE
Chemical Family: Recombinant protein

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

Intended Use: Pharmaceutical product

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

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161

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

Emergency telephone number:
International CHEMTREC (24 hours): +1-703-527-3887

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

Reproductive Toxicity: Category 2

Label Elements

Signal Word: Warning
Hazard Statements: H361fd - Suspected of damaging fertility. Suspected of damaging the unborn child.

Precautionary Statements: P201 - Obtain special instructions before use
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
P501 - Dispose of contents/container in accordance with all local and national regulations

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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	%
EDTA	60-00-4	200-449-4	Eye Irrit. 2A (H319)	<1
SODIUM HYDROXIDE	1310-73-2	215-185-5	Skin Corr. 1A (H314)	###
Bevacizumab	216974-75-3	Not Listed	Repr.2 (H361fd)	1-5

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Succinic acid	110-15-6	203-740-4	Not Listed	*
Sucrose	57-50-1	200-334-9	Not Listed	*
Polysorbate 80	9005-65-6	500-019-9	Not Listed	*
Water for Injection	7732-18-5	231-791-2	Not Listed	###

Additional Information:

* Proprietary
as required
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.

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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 mists) may fuel fires/explosions.

Advice for Fire-Fighters

During all firefighting 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 spill with absorbent material. Clean spill area thoroughly.

Additional Consideration for Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Cleanup operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

Precautions for Safe Handling

Restrict access to work area. Avoid open handling. Minimize generating airborne mists and vapors. Use appropriate engineering controls to maintain exposures below the B-OEB taking all applicable routes of exposure into consideration. A change area to facilitate 'good laboratory/manufacturing' decontamination practices is recommended. Avoid inhalation and contact with skin, eye, and clothing. When handling, use appropriate personal protective equipment (see Section 8). 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.

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

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8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

Sucrose

ACGIH Threshold Limit Value (TWA)	10 mg/m ³
Australia TWA	10 mg/m ³
Belgium OEL - TWA	10 mg/m ³
Bulgaria OEL - TWA	10.0 mg/m ³
Estonia OEL - TWA	10 mg/m ³
France OEL - TWA	10 mg/m ³
Ireland OEL - TWAs	10 mg/m ³
Latvia OEL - TWA	5 mg/m ³
Lithuania OEL - TWA	10 mg/m ³
OSHA - Final PELs - TWAs:	15 mg/m ³
Portugal OEL - TWA	10 mg/m ³
Slovakia OEL - TWA	6 mg/m ³
Spain OEL - TWA	10 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
Switzerland OEL - TWAs	2 mg/m ³

The Biotherapeutic Occupational Exposure Band (B-OEB) is an acceptable daily intake (ADI) range, based on available hazard data with appropriate safety factors applied. Engineering control measures should be utilized to bring exposures into the relevant B-OEB; supplementary administrative controls and personal protective equipment are to be used to achieve exposure control to the bottom of the band.

Bevacizumab

Pfizer Occupational Exposure Band (OEB): B-OEB 4 (control exposure to the range of 10 µg/day to <100 µg/day)

Exposure Controls

Engineering Controls: Engineering controls should be used as the primary means to control exposures. Use process containment, local exhaust ventilation, biosafety cabinet, or other engineering controls to maintain airborne levels within the B-OEB range. It is recommended that all large scale operations should be fully enclosed. Air recirculation is not recommended.

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8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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:	Wear impervious disposable gloves (e.g. Nitrile, etc.) as minimum protection (double recommended). (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.)
Eyes:	Wear safety glasses as minimum protection. (Safety glasses must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)
Skin:	Wear impervious disposable protective clothing when handling this compound. Full body protection is recommended (scale dependent). (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.)
Respiratory protection:	If airborne exposures are within or exceed the Biotherapeutic Occupational Exposure Band (B-OEB) range, wear an appropriate respirator with a protection factor sufficient to control exposures to the bottom of the B-OEB range. Under normal conditions of use, if the applicable Biotherapeutic Occupational Exposure Band (B-OEB) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the B-OEB (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:	Liquid	Color:	Clear, colorless
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)			
EDTA			
No data available			
Succinic acid			
No data available			
Sucrose			
No data available			
Polysorbate 80			
No data available			
SODIUM HYDROXIDE			
No data available			
Water for Injection			
No data available			
Bevacizumab			
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		

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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 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 following information is from a related compound and is presumed to be predictive of the effects produced by this material.

Short Term: Not determined, however, there may be potential for adverse reactions associated with administration of antibodies to humans, including potential systemic allergic reactions. This substance, based on the composition, may also cause eye irritation, skin irritation, and may produce allergic reactions following direct contact. This material is a novel research formulation intended to be pharmacologically active, and is assumed to be harmful if injected.

Known Clinical Effects: The following effects are based on a chemically-related material: headache, increase in blood pressure (hypertension), nose bleed, back pain, gastrointestinal perforation, hemorrhage, red, itchy, scaly skin (exfoliative dermatitis).

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

EDTA

Rat	Oral	LD50	> 2000 mg/kg
Rat	Oral	LD50	4500 mg/kg

Sucrose

Rat	Oral	LD 50	29,700 mg/kg
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Polysorbate 80

Rat	Intravenous	LD 50	1790 mg/kg
Mouse	Oral	LD 50	25 g/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.

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

Bevacizumab

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11. TOXICOLOGICAL INFORMATION

26 Week(s)	Monkey	Intravenous	<=2 mg/kg	NOAEL	Female reproductive system, Bone
1 Month(s)	Monkey	Intravenous	10 mg/kg/day *	NOAEL	None identified
1 Month(s)	Monkey	Intravenous	2 mg/kg/day (9 doses)	LOEL	Bone

Repeated Dose Toxicity Comments: * Note: Doses were administered twice weekly.

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

Bevacizumab

Embryo / Fetal Development Rabbit Intravenous <10 mg/kg NOAEL Developmental toxicity

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

12. ECOLOGICAL INFORMATION

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

Toxicity:

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

Bevacizumab

Scenedesmus subspicatus (Green Alga) OECD ErC50 72 Hours > 100 mg/L
Daphnia magna (Water Flea) OECD EC50 48 Hours > 100 mg/L

Persistence and Degradability:

Biodegradation: (Method, Inoculum, Biodeg Study, Result, Endpoint, Duration, Classification)

Bevacizumab

OECD Activated sludge Ready 96% After 28 Day(s) Ready

Bio-accumulative Potential: No data available

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.

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Transportation classification is based on data and/or procedures that may not be reflected on this document. The classification was conducted as per defining criteria in the international transportation regulations and the shipper's knowledge of the material.

15. REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture
Caution - Substance not fully tested (VIIA)

Succinic acid

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	203-740-4

Sucrose

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	200-334-9

EDTA

CERCLA/SARA 313 Emission reporting	Not Listed
CERCLA/SARA Hazardous Substances and their Reportable Quantities:	5000 lb 2270 kg
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4
EU EINECS/ELINCS List	200-449-4

Polysorbate 80

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	500-019-9

SODIUM HYDROXIDE

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15. REGULATORY INFORMATION

CERCLA/SARA 313 Emission reporting	Not Listed
CERCLA/SARA Hazardous Substances and their Reportable Quantities:	1000 lb 454 kg
California Proposition 65	Not Listed
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 for Injection

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

Bevacizumab

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

16. OTHER INFORMATION

Text of CLP/GHS Classification abbreviations mentioned in Section 3

Reproductive toxicity-Cat.2; H361fd - Suspected of damaging fertility. Suspected of damaging the unborn child.
Serious eye damage/eye irritation-Cat.2A; Skin corrosion/irritation-Cat.1A; H314 - Causes severe skin burns and eye damage

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

Reasons for Revision: Updated Section 3 - Composition / Information on Ingredients. Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking. Updated Section 2 - Hazard Identification. Updated Section 7 - Handling and Storage. Updated Section 11 - Toxicology Information.

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Prepared by: Product Stewardship Hazard Communication
Pfizer Global Environment, Health, and Safety Operations

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End of Safety Data Sheet