Otezla®
Safety Data Sheet

Revision Number: 4 **Date Issued** 17-Jul-2023

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

1.1 Product identifier

Product Name: Otezla®
Common Name: Apremilast
Chemical Name: N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-1,3-dioxo-1H-isoindol-4-yl]acetamide
Synonyms: AMG 407

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

Recommended Use: Pharmaceutical
Uses advised against: No information available

Manufacturer:
Amgen Inc.
One Amgen Center Drive
Thousand Oaks, California 91320-1799
1-805-447-7233
1-805-447-1000

Emergency Telephone Number:
Chemtrec
NORTH AMERICA 1-800-424-9300,
INTERNATIONAL 1-703-527-3887

2. HAZARDS IDENTIFICATION

Emergency Overview

Pharmaceutical product intended for clinical and commercial manufacturing purposes only. Product contains apremilast, an active pharmaceutical ingredient, for treatment of various inflammatory diseases. Dosage contents may pose a health hazard only if significant absorption occurs (e.g. inhalation after a major spill). Avoid inhalation, skin contact, eye contact and accidental ingestion.

2.1 - Classification of the drug substance or mixture (drug product in final form, not applicable)

REGULATION (EC) No 1272/2008

Acute Oral Toxicity	Category 4
Reproductive Toxicity	Category 2
Specific TOST - Single Exposure. Oral	Category 2
Specific TOST - Repeated Exposure Oral	Category 2

2.2 Label elements

Signal Word **Warning**

SGHH0999
H302 - Harmful if swallowed
H361 - Suspected of damaging fertility or the unborn child
H371 - May cause damage to organs
H373 - May cause damage to organs through prolonged or repeated exposure

GHSPO642
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 advice/ attention
P260 - Do not breathe dust/fume/gas/mist/vapors/spray
P314 - Get medical advice/ attention if you feel unwell
P501 - Dispose of contents/ container to an approved waste disposal plant
P309 + P311 - If exposed or if you feel unwell: Call a POISON CENTER or doctor/ physician

2.3 Other Hazards
No information available

3. COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

Ingredients:	Active Ingredient - apremilast, Inactive Ingredients - Proprietary Information
Chemical Name:	N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-1,3-dioxo-1H-isoindol-4-yl]acetamide
CAS-No:	608141-41-9

4. FIRST AID MEASURES

4.1 Description of first-aid measures

Eye Contact:	In the case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
Skin Contact:	Wash off immediately with soap and plenty of water removing all contaminated clothes and shoes. Consult a physician if necessary.
Inhalation:	Move to fresh air. If symptoms persist, call a physician.
Ingestion:	If symptoms persist, call a physician. Do not induce vomiting without medical advice. Never give anything by mouth to an unconscious person.
Notes to Physician:	Treat symptomatically.

5. FIRE-FIGHTING MEASURES

5.1 Extinguishing media

Flammable Properties: No information available.

Extinguishing Media: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

5.2 Special hazards arising from the substance or mixture

Hazardous Combustion Products: No information available.

5.3 Advice for firefighters

Protective Equipment and Precautions for Firefighters: As in any fire, wear self-contained breathing apparatus pressure-demand, NIOSH (approved) and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

Spill Procedures: If material is released or spilled, cordon off spill area. Take proper precautions to minimize exposure by using appropriate personal protective equipment in cleaning up a spill. If in powder form, wet down spilled material to minimize airborne dispersion. Soak up material with absorbent e.g., paper towels, and wash spill area thoroughly with appropriate cleaning materials. Dispose of collected material in accordance with applicable waste disposal regulations. Avoid release to the environment.

7. HANDLING AND STORAGE

7.1 Precautions for Safe Handling

Handling and Storage: Avoid contact with skin, eyes or clothing. Do not eat, drink or smoke in work areas. Use adequate ventilation to minimize exposure. Wash hands, face and other potentially exposed areas immediately after handling this material. Remove contaminated clothing prior to entering eating areas. Clean protective equipment thoroughly after each use. Store in a well ventilated area.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1 Control parameters

Occupational Exposure Limit: No exposure guidelines established by ACGIH, NIOSH or OSHA. Amgen recommends an occupational exposure limit (OEL) of 60 µg/m^3 as an 8-hour time weighted average over a 40-hour work week. The OEL is designed as an acceptable airborne concentration of a substance for which it is believed that workers may be repeatedly exposed day after day without adverse health effects. Apremilast has been classified per Amgen's Hazard Classification System as an Occupational Exposure Band 3 compound (20 µg/m^3 - 100 µg/m^3) with the following suffixes: A (acute toxicity), R (reproductive and/or developmental effects) STOT-SE (Specific Target Organ Toxicity - Single Exposure), and STOT-RE (Specific Target Organ Toxicity - Repeated Exposure)

Engineering Controls: When practicable, handle material in enclosed processes or in processes with effective local exhaust ventilation or within a chemical hood.

8.2 Exposure controls

Personal Protective Equipment

Eye/face Protection: Wear safety glasses with side shields, chemical splash goggles, or safety glasses with side shields and a full-face shield to prevent contact with eyes. The choice of protection should be based on the job activity and potential for exposure to the eyes and face.

Skin Protection: Use gloves or other appropriate personal protective equipment if skin contact with formulation is possible. Wear lab coat or other protective over garment if splashing is possible. The choice of protection should be based on the job activity and potential for skin contact.

Respiratory Protection: When possible, handle material in enclosed processes or containers. If it is properly handled with effective local exhaust ventilation or containment, respiratory protection may not be needed. For procedures involving larger quantities or dust/aerosol generating procedures such as weighing or a large transfer of liquids, an air-purifying respirator with NIOSH approval for dusts and mists may be needed. The choice of protection should be based on the job activity and the potential for exposure.

Other: Wash hands, face and other potentially exposed areas after handling material (especially before eating, drinking or smoking). Clean protective equipment thoroughly after each use.

8.3 Environmental exposure controls

Environmental Exposure Controls Avoid release to the environment.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	Drug Substance - white to pale yellow powder Final Drug Product (diamond shaped tablets) - Pink (10-mg), brown (20-mg), or beige (30-mg)
Molecular Weight:	460.5
Odor:	No information available
Odor Threshold:	No information available
pH:	No information available
Melting point (°C) VALUE	156.1°C
Flash Point:	No information available
Evaporation Rate:	No information available
Lower explosive limit:	No information available
Upper explosive limit:	No information available
Vapor Pressure:	No information available
Vapor Density (air = 1):	No information available
Relative density:	No information available
Water Solubility:	10 µg/mL (water)
Partition Coefficient (log Kow):	1.77 @ pH 7
Viscosity:	No information available

10. STABILITY AND REACTIVITY

10.1 Reactivity No information available

10.2 Chemical stability No information available

10.3 Possibility of hazardous reactions No information available

10.4 Conditions to avoid Warning: Apremilast, the active pharmaceutical ingredient in Otezla, can form combustible dust concentrations in air during processing and present an explosion hazard risk.

- Minimize dust generation and accumulation. Fine dust dispersed in air in sufficient concentrations and in the presence of an ignition source is a potential dust explosion hazard.
- Routine housekeeping should be instituted to ensure that dusts do not accumulate on surfaces.
- Dry powders are sensitive to electrostatic ignition. Provide adequate precautions, such as electrical grounding, bonding, or inert atmospheres for process equipment, and grounding and bonding of personnel who are open handling the powder.
- Appropriately classified electrical equipment should be used.
- Explosion hazards should be considered when using dust control equipment, such as local exhaust ventilation, air material separators, portable vacuums, etc.
- Antistatic or fire-retardant PPE maybe required for the task dependent on risk assessment.
- Grounding, anti-static tools, and/or an electrically rated vacuum should be used to clean up spills.
- Refer to NFPA 652, Standard on the Fundamentals of Combustible Dust

10.5 Incompatible materials No information available

10.6 Hazardous decomposition products No information available

10.7 Other information

Dust Explosion Properties:

Dust Explosion Hazard Properties tested on apremilast (drug substance) -
MIE: 3-5 mJ
MIT (dust cloud): 450-460 ^{o}C
Kst: 215 bar-m/sec
Pmax: 7.7

Dust Explosion Hazard Properties tested on apremilast (30 mg blend) -
MIE: 100-300 mJ
MIT (dust cloud): 370-380 ^{o}C
Kst: 166 bar-m/sec
Pmax: 7.5

11. TOXICOLOGICAL INFORMATION

11.1 Information on toxicological effects

Acute Toxicity:
LC50 Rat Inhalation > 5800 mg/m^3/4h
LD50 Oral Rat > 5000 mg/kg
LD50 Dermal Rabbit > 2000 mg/kg
MLD Oral Mouse > 2000 mg/kg
MLD Oral Rat (male) 2000 kg/kg
MLD Oral Rat (female) 300 mg/kg
MLD IV Mice (male) 120 mg/kg
MLD IV Mice (female) > 120 mg/kg
MLD IV Rat > 60 mg/kg
Acute Toxicity - GHS Category 4

Skin corrosion/irritation: Based on available data, the GHS classification criteria are not met.

Serious eye damage/eye irritation: Based on available data, the GHS classification criteria are not met.

Respiratory or skin sensitization: Based on available data, the GHS classification criteria are not met.

Germ cell mutagenicity: Based on available data, the GHS classification criteria are not met.

Carcinogenicity: Based on available data, the GHS classification criteria are not met.

Reproductive toxicity: Based on several reproductive toxicity studies conducted in male and female mice, GHS classification criteria were met.
GHS Category 2

STOT - single exposure: Based on available data, GHS classification criteria were met.
STOT-SE Category 2 (immune system, central nervous system gastrointestinal tract).

STOT - repeated exposure: Based on available data, GHS classification criteria were met.
STOT-SE Category 2 (immune system, central nervous system gastrointestinal tract).

Aspiration Hazard: No information available

12. ECOLOGICAL INFORMATION

12.1 Toxicity

Ecotoxicity effects: NOEC Algae 3.5 mg/L (OECD 201) - GHS Category 2
NOEC Daphnia magna (crustacea) 6.3 mg/L (OECD 211) - Does not meet GHS classification criteria
NOEC Fish (sp. not specified) 7.2 mg/L (OECD 210) - Does not meet GHS classification criteria
EC50 (presumed) Activated sludge 1000 mg/L (OECD 209) - Does not meet GHS classification criteria

12.2 Persistence and degradability

Persistence/Degradability: Alpremilast is not readily biodegradable (OECD 301).

12.3 Bioaccumulative potential

Bioaccumulation/ Accumulation: Partition Coefficient (log Kow) (OECD 107) of 1.77 @ pH 7, bioaccumulation potential is expected to be low.

12.4 Mobility in soil

Mobility in Environmental Media: Apremilast does not significantly adsorb to soil (OECD 106).

12.5 Results of PBT and vPvB assessment

Results of PBT and vPvB assessment: No information available

12.6 Other adverse effects

Other Adverse Effects: Koc = 263-457 L/kg (not likely to adsorb to sludge) (OECD 106).

13. DISPOSAL CONSIDERATIONS

13.1 Waste treatment methods

Waste Disposal Method: Dispose of waste according to prescribed federal, state, local and competent authority guidelines.

14. TRANSPORT INFORMATION

DOT: Not regulated by U.S. DOT, IATA, or IMDG.

15. REGULATORY INFORMATION

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

International Inventories

TSCA:	-
EINECS/ELINCS	-
DSL/NDSL	-
PICCS:	-
ENCS:	-
CHINA:	-
AICS:	-
KECL:	-

Legend

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
EINECS/ELINCS - European Inventory of Existing Commercial Chemical Substances/EU List of Notified Chemical Substances
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List
PICCS - Philippines Inventory of Chemicals and Chemical Substances
ENCS - Japan Existing and New Chemical Substances
IECSC - China Inventory of Existing Chemical Substances
AICS - Australian Inventory of Chemical Substances
KECL - Korean Existing and Evaluated Chemical Substances

State Regulations

California Proposition 65: This product does not contain any Proposition 65 chemicals.

15.2 Chemical safety assessment

No CSA has been conducted.

16. OTHER INFORMATION

Revision Number: 4

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections, which pertain to their particular conditions.No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it may be biologically active. Translation of this SDS is available upon request.

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