Safety Data Sheet
Divalproex Sodium Sprinkle Capsules

Strength: 125 mg **Pack Size:** 100 and 1000 Capsules per Bottles
125mg. **Pack Size:** Blister pack of 100 unit dose **Revision No.:** 02

EMERGENCY OVERVIEW

Each Divalproex sodium sprinkle Capsules intended for oral administration contains Divalproex sodium and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

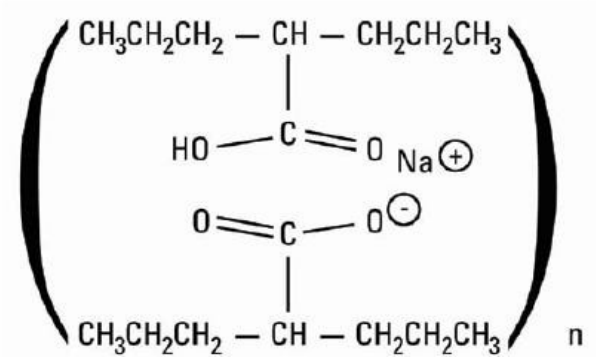
Section 1. Identification

Identification of the product

Product name: **Divalproex Sodium Sprinkle Capsules**

Formula: $(C_{16}H_{31}NaO_4)_n$

Chemical Name: Sodium hydrogen bis (2-propylpentanoate)



Manufacturer / supplier identification

Company: **Cadila Healthcare Ltd. Ahmedabad, India**

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Dist. Ahmedabad – 382210. State: Gujarat. India

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Recommended use / Therapeutic Category Monotherapy and adjunctive therapy of complex partial seizures and simple and complex absence seizures; adjunctive therapy in patients with multiple seizure types that include absence seizures.

Restriction on Use / Contraindications:

Divalproex sodium sprinkle capsules should not be administered to patients with hepatic disease or significant hepatic dysfunction.

Multi-organ hypersensitivity reactions have been rarely reported in close temporal association to the initiation of valproate therapy in adult and pediatric patients.

Urea cycle disorders.

Section 2. Hazard(s) Information

Dose and Administration

Start at 15 mg/kg/day, increasing at 1 week intervals by 5 to 10 mg/kg/day until seizure control or limiting side effects

Adverse Effects

Most common adverse reactions (reported >5%) are thrombocytopenia,) nausea, somnolence, dizziness, vomiting, asthenia, abdominal pain, dyspepsia, diarrhea, increased appetite, tremor, weight gain, weight loss, alopecia, headache, fever, anorexia, constipation, diplopia, ambylopia/ blurred vision, ataxia, nystagmus, emotional lability, thinking abnormal, amnesia, flu syndrome, infection, bronchitis, rhinitis, ecchymosis, peripheral edema, insomnia, nervousness, depression, pharyngitis, dyspnea, tinnitus.

Over Dose Effect

Over dosage with valproate may result in somnolence, heart block, and deep coma. Fatalities have been reported; however patients have recovered from valproate levels as high as 2120 mcg/mL.

Medical Conditions

- Hepatotoxicity; evaluate high risk populations and monitor serum liver tests
- Birth defects and decreased IQ following *in utero* exposure; only use to treat pregnant women with epilepsy if other medications are unacceptable; should not be administered to a woman of childbearing potential unless essential.
- Pancreatitis; divalproex sodium capsules (sprinkle) should ordinarily be discontinued.
- Suicidal behavior or ideation; Antiepileptic drugs, including divalproex sodium increase the risk of suicidal thoughts or behavior.
- Bleeding and other hematopoietic disorders; monitor platelet counts and coagulation tests.
- Hyperammonemia and hyperammonemic encephalopathy; measure ammonia level if unexplained lethargy and vomiting or changes in mental status.
- Hypothermia; Hypothermia has been reported during valproate therapy with or without associated hyperammonemia. This adverse reaction can also occur in patients using concomitant topiramate.

- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)/Multiorgan hypersensitivity reaction; discontinue divalproex sodium sprinkle capsules.
- Somnolence in the elderly can occur. Divalproex sodium capsules (sprinkle) dosage should be increased slowly and with regular monitoring for fluid and nutritional intake.

Contraindications

Divalproex sodium sprinkle capsules should not be administered to patients with hepatic disease or significant hepatic dysfunction.

Multi-organ hypersensitivity reactions have been rarely reported in close temporal association to the initiation of valproate therapy in adult and pediatric patients.

Urea cycle disorders.

Pregnancy Comments

Use of divalproex sodium during pregnancy can cause congenital malformations including neural tube defects. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. Divalproex sodium should be considered for women of childbearing potential only after the risks have been thoroughly discussed with the patient and weighed against the potential benefits of treatment.

Pregnancy Category D

Section 3. Composition / information on ingredients

Component	Exposure Limit	CAS No.
Principle Component :		
Divalproex sodium	Not Found	76584-70-8
Inactive Ingredients :		
Colloidal silicon dioxide	Not Found	7631-86-9
FD &C blue # 1	Not Found	NA
Gelatin	Not Found	9000-70-8
Hydroxypropyl methylcellulose	Not Found	9004-65-3
Methacrylic acid copolymer dispersion	Not Found	79-41-4
Microcrystalline cellulose spheres	Not Found	9004-34-6
Sodium lauryl sulfate	Not Found	151-21-3
Talc	Not Found	14807-96-6
Titanium dioxide	Not Found	13463-67-7
Triethyl citrate	Not Found	99-11-6

Section 4. First - aid measures

General Remove from exposure. Remove contiminated Clothing. Person developing serious hypersensitivity reaction must receive medical attention.

Overdose Treatment In overdose situations, the fraction of drug not bound to protein is high and hemodialysis or tandem hemodialysis plus hemoperfusion may result in significant removal of drug. The benefit of gastric lavage or emesis will vary with the time since ingestion. General supportive measures should be applied with particular attention to the maintenance of adequate urinary output.

Naloxone has been reported to reverse the CNS depressant effects.

Section 5. Fire - fighting measures

Flash point	Not Found	**Upper Flammable Limit:**	Not Found
Auto-Ignition Temperature:	Not Found	**Lower Flammable Limit:**	Not Found
Extinguishing Media	Water Spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and material.	**Fire and Explosion Hazard**	This material is assumed to be combustible. As with all dry powders it is advisable to ground mechanical equipment in contact with the dry material to dissipate the potential build-up of static electricity.

Fire Fighting Procedure As with all fires, evacuate personnel to a safe area. Fire fighter should use self- contained breathing equipment and protective clothing.

Section 6. Accidental Release Measures

Spill Response Wear approved respiratory protection, chemically compatible gloves and protective clothing. Wipe up spillage or collect spillage using high efficiency vacuum cleaner. Avoid breathing dust. Place spillage in appropriately labelled container for disposal. Wash spill site.

Section 7. Handling and Storage

Storage Store at 20° to 25°C (68° to 77°F)**.**
Dispense in a tight, light-resistant container.

Incompatibilities: No Data available.

Section 8. Exposure controls / personal protection

Respiratory Protection	Protection from inhalation is not normally necessary. If ventilation is inadequate or dust is likely to generate, use of suitable dust mask would be appropriate.
Skin Protection	Skin protection is not normally necessary, however it is good practice to avoid contact with chemical to use suitable gloves when handling.
Eye protection	Eye protection is not normally necessary. If concerned wear protective goggles or glasses. Wash hands prior to touching eye and in particular handling contact lenses.
Protective Clothing	Protective clothing is not normally necessary, however it is good practice to use apron.

Section 9. Physical and chemical properties

Appearance Divalproex Sodium Sprinkle Capsules (divalproex sodium coated particles in capsules), 125 mg are white to off-white free flowing pellets filled in size '0' hard gelatin capsules with blue colored cap printed with "ZA66" in black ink and white body printed with "125mg" in black ink.

Solubility in water	No Data Available.	**Odour**	Odourless
Boiling point	No Data Available	**Melting Point**	No Data Available
Evaporation rate	No Data Available	**Vapour density**	No Data Available
Reactivity in water	No Data Available	**Evaporation rate**	No Data Available
% Volatile by volume	No Data Available	**Specific gravity**	No Data Available
		Vapour pressure	No Data Available
Other information	No Data Available		

Section 10. Stability and Reactivity

Condition to avoid	Avoid exposure to extreme heat, light and moisture.	**Stable**	Stable under normal ambient and anticipated storage and handling conditions.

Decomposition Products	No Data Available	**Hazardous Reaction**	No data available.
Incompatibilities:	No Data Available		

Section 11. Toxicological information

General

Handling of formulated product is not expected to cause any toxicological affects. The data pertains to the ingredient in formulations, rather than this specie formulation.

Target organ

Eye contact, Skin contact and inhalation is not great risk as this product is tablet.

Other

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Carcinogenesis

Valproate was administered orally to rats and mice at doses of 80 and 170 mg/kg/day (less than the maximum recommended human dose on a mg/m^2 basis) for two years. The primary findings were an increase in the incidence of subcutaneous fibrosarcomas in high dose male rats receiving valproate and a dose-related trend for benign pulmonary adenomas in male mice receiving valproate. The significance of these findings for humans is unknown.

Mutagenesis

Valproate was not mutagenic in an in vitro bacterial assay (Ames test), did not produce dominant lethal effects in mice, and did not increase chromosome aberration frequency in an in vivo cytogenetic study in rats. Increased frequencies of sister chromatid exchange (SCE) have been reported in a study of epileptic children taking valproate, but this association was not observed in another study conducted in adults. There is some evidence that increased SCE frequencies may be associated with epilepsy. The biological significance of an increase in SCE frequency is not known.

Fertility

Chronic toxicity studies of valproate in juvenile and adult rats and dogs demonstrated reduced spermatogenesis and testicular atrophy at oral doses of 400 mg/kg/day or greater in rats (approximately equivalent to or greater than the maximum recommended human dose (MRHD) on a mg/m^2 basis) and 150 mg/kg/day or greater in dogs (approximately 1.4 times the MRHD or greater on a mg/m^2 basis). Fertility studies in rats have shown no effect on fertility at oral doses of valproate up to 350 mg/kg/day (approximately equal to the MRHD on a mg/m^2 basis) for 60 days. The effect of valproate on testicular development and on sperm production and fertility in humans is unknown.

Section 12. Ecological information

Do not allow product to enter drinking water supplies, waste water or soil

Section 13. Disposal Consideration

Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 14. Transport Information

The product is not hazardous when shipping via air (IATA), ground (DOT), or sea (IMDG).

Section 15. Regulatory Information

Generic Medicine. Approved by USFDA & the ANDA Number is 78919

Section 16. Other information

None

Date of issue: 28/05/2015 **Supersedes edition of:** 01

The information contained herein is based on the state of our knowledge. It Characterises the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.