Defstar®
Tablets

1. Generic Name

Deflazacort

2. Qualitative and Quantitative composition

Each tablet contains

Deflazacort	6mg

3. Dosage form and strength

6mg tablets for oral administration.

4. Clinical particulars

4.1 Therapeutic indication

Defstar is indicated in patient with:

- Allergic Rhinitis
- Sudden sensory neural hearing loss
- Acute inflammatory conditions
- Acute exacerbation of chronic bronchitis
- Lower respiratory tract infection
- Arthritis
- Osteoarthritis

4.2 Posology and method of administration

As directed by physician.

4.3 Contraindication

Defstar is contraindicated in patient with:

- Systemic infection unless specific anti-infective therapy is employed.
- Hypersensitivity to deflazacort or any of the ingredients.
- Receiving live virus immunization.

4.4 Special warnings and precautions for use

- Alterations in Endocrine Function:

Hypothalamic-pituitary-adrenal axis suppression, Cushing's syndrome, and hyperglycaemia can occur; Monitor patients for these conditions with chronic use of DEFSTAR.

- Immunosuppression and Increased Risk of Infection:

Increased risk of new, exacerbation, dissemination, or reactivation of latent infections, which can be severe and at times fatal; Signs and symptoms of infection may be masked.

- Alterations in Cardiovascular/Renal Function:

Monitor for elevated blood pressure and sodium, and for decreased potassium levels

- Gastrointestinal Perforation:

Increased risk in patients with certain GI disorders; Signs and symptoms may be masked

- Behavioural and Mood Disturbances:

May include euphoria, insomnia, mood swings, personality changes, severe depression, and psychosis

- Effects on Bones:

Monitor for decreases in bone mineral density with chronic use of DEFSTAR

- Ophthalmic Effects:

May include cataracts, infections, and glaucoma; Monitor intraocular pressure if DEFSTAR is continued for more than 6 weeks

- Vaccination:

Do not administer live or live attenuated vaccines to patients receiving immunosuppressive doses of corticosteroids

- Serious Skin Rashes:

Discontinue at the first sign of rash, unless the rash is clearly not drug related

4.5 Drug interactions

- It is recommended to increase the maintenance dose of deflazacort if drugs which are liver enzyme inducers are co-administered, e.g. rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone and aminoglutethimide.
- For drugs which inhibit liver enzymes, e.g. ketoconazole it may be possible to reduce the maintenance dose of deflazacort. In patients taking estrogens, corticosteroid requirements may be reduced.
- The desired effects of hypoglycaemic agents (including insulin), anti-hypertensive & diuretics are antagonised by corticosteroids & the hypokalaemia effects of acetazolamide, loop diuretics, thiazide diuretics & carbenoxolone are enhanced.
- The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy
- Antacids may reduce bioavailability; leave at least 2 hours between administration of deflazacort and antacids.

4.6 Use in special population

- Pediatric: Deflazacort is not approved for use by anyone younger than 5 years old.
- Geriatric: No clinical data is available for elderly patients.
- Liver impairment: No dose adjustment is required in patients with mild or moderate hepatic impairment .There is no clinical experience in patients with severe hepatic impairment, and a dosing recommendation cannot be provided for patients with severe hepatic impairment.
- Renal failure: No dose adjustment is required in patients with mild, moderate or severe renal impairment.
- Pregnancy and lactation: Not recommended for use in pregnancy. Deflazacort can pass into breast milk and may cause side effects in the nursing baby.

4.7 Effects on ability to drive and use machine

No data available.

4.8 Undesirable effects

- GI – dyspepsia & peptic ulcer are the most commonly reported adverse effects
- Others - candidiasis, cataract, drug psychosis, impaired glucose tolerance, growth retardation, hirsutism, hypertension, hypokalaemia, muscle weakness, osteoporosis, pathological fracture, steroid faces, delayed wound healing.

4.9 Overdose

There is limited experience of overdose with Defstar Tablets. Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

5. Pharmacological properties

5.1 Mechanism of action

Glucocorticoids bind to the cytosolic glucocorticoid receptor (GR). This type of receptor is activated by ligand binding. After a hormone binds to the corresponding receptor, the newly formed receptor-ligand complex translocate itself into the cell nucleus, where it binds to glucocorticoid response elements (GRE) in the promoter region of the target genes resulting in the regulation of gene expression and modification of transcription and, hence, protein synthesis in order to achieve inhibition of leukocyte infiltration at the site of inflammation, interference in the function of mediators of inflammatory response, suppression of humoral immune responses, and reduction in edema or scar tissue. The anti-inflammatory actions of dexamethasone are thought to involve phospholipase A_2 inhibitory proteins, lipocortins, which control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotriene.

5.2 Pharmacodynamic properties

Deflazacort exerts anti-inflammatory activity in DMD, likely improving various symptoms, including muscle weakness and cardiorespiratory symptoms in addition to delaying their

onset. This allows for an increased quality of life and prevents the necessity for surgical procedures, such as those for scoliosis, which is associated with DMD. Studies showed significant preservation of muscle mass in patients generally treated with 0.9 mg/kg/day of Deflazacort compared to a control group. The following findings are based on clinical studies using deflazacort on a long term basis:

- Effects on muscle strength

At age 16, individuals treated with long-term deflazacort had 63 ± 4% score in muscle strength compared to a mean muscle strength score of 31 ± 3% for control patients6. Significant improvements in climbing stairs and rising from a supine position were also seen in patients taking deflazacort.6

- Effects on ambulation

Ambulation was significantly higher by 12 years of age and 18 years of age in patients taking deflazacort when compared with the control group. The control group showed a mean loss of ambulation of 2 years sooner than with deflazacort treatment.8

- Effects on cardiac function

Mean left ventricular ejection fraction (a measure of cardiac function) was higher in patients treated with deflazacort over the long term. Preservation of cardiac function was demonstrated by a mean difference in ejection fraction of about 7%, favouring study groups taking deflazacort over control groups.8

- Effects on spinal alignment

Children treated with deflazacort also significantly lowered the rate and severity of scoliosis and eliminated the need for scoliosis surgery after long-term treatment.

5.3 Pharmacokinetic properties

After oral administration in the fasted state, the median Tmax with deflazacort tablets or suspension is about 1 hour. The protein binding of the active metabolite of deflazacort is about 40%. Deflazacort is rapidly converted to the active metabolite 21-desDFZ by esterases after oral administration. 21-desDFZ is further metabolized by CYP3A4 to several other

inactive metabolites. Urinary excretion is the predominant route of deflazacort elimination (about 68% of the dose), and the elimination is almost completed by 24 hours post dose. 21-desDFZ accounts for 18% of the eliminated drug in the urine.

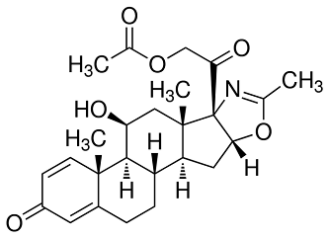
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

NA.

7. Description

Deflazacort belongs to Deflazacort is in a class of medications called corticosteroids. Its chemical name is [2-[(1*S*,2*S*,4*R*,8*S*,9*S*,11*S*,12*S*,13*R*)-11-hydroxy-6,9,13-trimethyl-16-oxo-5-oxa-7-azapentacyclo[10.8.0.0^{2,9}.0^{4,8}.0^{13,18}]icosa-6,14,17-trien-8-yl]-2-oxoethyl] acetate and its structure is:



Its empirical formula is $C_{25}H_{31}NO_6$ and its molecular weight is 441.5 g/mol.

8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

18 months

8.3 Packaging Information

Defstar tablets are available in a strip of 10 tablets.

8.4 Storage and handling instructions

Store in cool and dry place.

9. Patient Counselling Information

9.1 Adverse Reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.5

9.3 Dosage

Refer part 4.2

9.4 Storage

Refer part 8.4

9.5 Risk Factors

Refer part 4.4

9.6 Self-monitoring information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

10. Manufactured by

Hetero Labs Limited.

11. Details of permission or license number with date

LIC NO. MNB/09/780-FORM 25- 22.03.2020.

12. Date of revision: January 2021