1. Name of the medicinal Product

Dexamethasone Sodium Phosphate Injection USP

1.1 Strength

8 mg/2 ml

1.2 Pharmaceutical Form

Liquid Injection

2. Qualitative and Quantitative Composition

2.1 Qualitative declaration

Dexamethasone Sodium Phosphate USP

2.2 Quantitative declaration

Sr. No	Ingredients Chemical Name	Specification	Quantity (mg/tablet)	Reason for Inclusion
1	Dexamethasone Sodium Phosphate Eq. to Dexamethasone Phosphate	USP	4.40 Eq. to 4.00	Anti-inflammatory
2	Methyl Hydroxybenzoate	BP	1.80	Preservative
3	Propyl Hydroxybenzoate	BP	0.20	Preservative
4	Sodium Citrate	BP	10.0	Buffering
5	Sodium Metabisulphite	BP	1.0	Antioxidant
6	Disodium Edetate	BP	1.0	Chelating
7	Creatinine	USP-NF	4.0	Stabilizer
8	Sodium Hydroxide	BP	0.7	pH adjuster
9	Water for Injections	BP	Q.S.	Vehicle

3. Pharmaceutical Form

Liquid Injection

A clear colourless solution filled in ampoule side.

4. Clinical Particulars

4.1 Therapeutic Indications

Dexamethasone Sodium Phosphate is primarily as an anti-inflammatory or immunosuppressant agent in the treatment of a variety of diseases including those of allergic, dermatologic endocrine, hematologic, inflammatory, neoplastic, nervous system, renal, respiratory, rheumatic, and autoimmune origin. It may be used in management of cerebral edema, chronic swelling, as a diagnostic agent, diagnosis of Cushing's syndrome, antiemetic.

4.2 Posology

Dosage must be individualized on the basis of the disease and the response of the patient.

Adults:

Usual adult initial dosage is 0.5 mg-20 mg a day.

In emergencies, the usual dose of Dexamethasone Sodium Phosphate 4 mg/ml solution for injection by intravenous or intramuscular injection is 4 mg-20 mg (in shock use only the I.V. route). This dose may be repeated until adequate response is noted. After initial improvement, single doses of 2 mg-4 mg, repeated as necessary, should be sufficient. The total daily dosage usually need not exceed 80 mg, even in severe conditions.

Cerebral oedema associated with malignancy: I.V. 10 mg initially, then 4 mg by intramuscular injection every 6 hours as required for 2-4 days then gradually reduced and stopped over 5-7 days.

Mildly emetogenic therapy: I.M., I.V.: 4 mg every 4-6 hours.

Treatment of shock: Addisonian crisis/shock (e.g. adrenal insufficiency/responsive to steroid therapy): I.V.: 4-10 mg as a single dose, which may be repeated if necessary.

Pediatric: 200-400 micrograms/kg daily.

4.3 Method of Administration

I.M. / I.V.

4.4 Contraindications

Hypersensitivity to Dexamethasone or any component of the formulation.

Systemic fungal infections, cerebral malaria.

Local injection of a glucocorticoid is contraindicated in bacteraemia and systemic fungal infections, unstable joints, infection at the injection site e.g. septic arthritis resulting from

Gonorrhea or tuberculosis.

4.5 Special Warnings and Special Precautions for Use

Adrenal suppression: May cause hypercorticisni. or suppression of hypothalamic-pituitary adrenal (HP A) axis, particularly in younger children or in patients receiving high doses for prolonged periods. Particular care is required when patients are transferred from systemic corticosteroids to inhaled products due to possible adrenal insufficiency or withdrawal from steroids, including an increase in allergic symptoms.

Immunosuppression: Prolonged use of corticosteroids may also increase the incidence of secondary infection, mask acute infection (including fungal infections), prolong or exacerbate viral infections, or limit response to vaccines. Adrenal insufficiency: Dexamethasone does not provide adequate mineralocorticoid activity in adrenal insufficiency. The lowest possible dose should be used during treatment; discontinuation and/or dose reductions should be gradual.

Cardiovascular disease: Use with caution in patients with heart failure; long-term use has been associated with fluid retention and hypertension.

Diabetes: Use with caution in patients with diabetes mellitus; may alter glucose production or regulation leading to hyperglycemia.

Gastrointestinal disease: Use with caution in patients with GI diseases (peptic ulcer, ulcerative colitis) due to perforation risk.

Head injury: High-dose corticosteroids should not be used for the management of head injury.

Hepatic impairment: Use with caution in patients with hepatic impairment, cirrhosis; long-term use has been associated with fluid retention.

Myasthenia gravis: Use with caution in patients with myasthenia gravis; exacerbation of symptoms has occurred especially during initial treatment with corticosteroids.

Myocardial infarction (MI): Use with caution following acute MI; corticosteroids have been associated with myocardial rupture.

Ocular disease: Use with caution in patient with cataracts and/or glaucoma ; increased intraocular pressure, open-angle glaucoma and cataracts have occurred with prolonged use. Consider routine eye exams in chronic use.

Osteoporosis: Use with caution in patients with osteoporosis; high doses and/or long-term use of corticosteroids have been associated with increased bone loss and osteoporotic fractures.

Renal impairment: Use with caution in patients with renal impairment; fluid retention may occur.

Seizure disorders: Use with caution in patients with a history of seizure disorder; seizures have

been reported with adrenal crisis.

Thyroid disease: Changes in thyroid status may necessitate dosage adjustments; metabolic clearance of corticosteroids increases in hyperthyroid patients and decreases in hypothyroid ones.

Discontinuation of therapy: Withdraw therapy with gradual tapering of dose.

Elderly: Because of the risk of adverse effects, systemic corticosteroids should be used cautiously in the elderly in the smallest possible effective dose for the shortest duration.

Pediatrics: May affect growth velocity; growth should be routinely monitored in pediatric patients.

4.6 Paediatric Population

Not Applicable

4.7 Interaction with other medicinal products and other forms of interaction

Rifampicin, rifabutin, ephedrine, carbamazepine, phenylbutazo e, phenobarbital, phenytoin, primidone, and aminoglutethimide enhance the metabolis of corticosteroids and its therapeutic effects may be reduced. The effects of anticholinesterases are antagonised by corticosteoids in myasthenia gravis. The desired effects of hypoglycaemic agents (including insulin , anti-hypertensives, cardiac glycosides and diuretics are antagonised by corticosteroids, an the hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics and carbenoxol ne are enhanced. The effect of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy. The renal clearance of salicylates is increased by corticosteroid and steroid withdrawal may result in salicylate intoxication. There may be interaction with salicylates in patients with hypoprothrombinaemia.

4.8 Additional information on special populations

No specific Information

4.9 Paediatric Population

No specific Information

4.10 Pregnancy and Lactation

4.10.1 Pregnancy

Pregnancy: Dexamethasone crosses the placenta; and is part ally metabolized to inactive metabolites by placental enzyme.

4.10.2 Lactation

Corticosteroids may pass into breast milk, although no data are available for Dexamethasone. Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression.

4.11 Effects on ability to Drive and use Machines

There have been no studies to investigate the effect on driving performance or the ability to operate machinery.

4.12 Undesirable Effects

Cardiovascular: Arrhythmia, bradycardia, cardiac arrest, cardiomyopathy, CHF, circulatory collapse, edema, hypertension, myocardial rupture (post-MI), syncope, thromboembolism, vasculitis.

Central nervous system: Depression, emotional instability, euphoria, headache, intracranial pressure increased, insomnia, malaise, mood swings, neuritis, personality changes, pseudotumor cerebr (usually following discontinuation), psychic disorders, seizure, vertigo.

Dermatologic: Acne, allergic dermatitis, alopecia, angioedema, bruising, dry skin, erythema, fragile skin, hirsutism, perianal pruritus (following LV. injection), petechiae, rash, skin atrophy, urticaria, wound healing impaired.

Endocrine & metabolic: Adrenal suppression, carbohydrate tolerance decreased, Cushing's syndrome, diabetes mellitus, glucose intolerance decreased, growth suppression (children),hyperglycemia, hypokalemic alkalosis, menstrual irregularities, negative nitrogen balance,pituitary-adrenal axis suppression, protein catabolism, sodium retention

Gastrointestinal: Abdominal distention, appetite increased, gastrointestinal haemorrhage,gastrointestinal perforation, nausea, pancreatitis, peptic ulcer, ulcerative esophagitis, weight gain.

Genitourinary : Altered (increased or decreased) spermatogenesis

Local: Post injection flare (intra-articular use), thrombophlebitis

Neuromuscular & skeletal: Arthropathy, aseptic necrosis (femoral and humoral heads), fractures, muscle mass loss, myopathy (particularly in conjunction with neuromuscular disease or neuromuscular-blocking agents), neuropathy, osteoporosis, parasthesia, tendon rupture, vertebral compression fractures, weakness.

Ocular: Cataracts, exophthalmos, glaucoma, and intraocular pressure increased.

Miscellaneous: Abnormal fat deposition, anaphylactoid reaction, anaphylaxis, avascular necrosis, diaphoresis, hiccups, hypersensitivity, impaired wound healing, infections, Kaposi's sarcoma, moon face, secondary malignancy.

4.13 Overdose

Reports of acute toxicity and/or death following overdosage of glucocorticoids are rare. In the event of overdosage, no specific antidote is available; treatment is supportive and symptomatic.

5. Pharmacological Properties

5.1 Pharmacodynamics Properties

Dexamethasone is a synthetic adrenocortical steroid. Dexamethasone possesses the actions and effects of other basic glucocorticoids and is among the most active member of its class. Adrenocorticoids act on the HP A at specific receptors on the plasma membrane. On other tissues the adrenocorticoids diffuse across cell membranes and complex with specific cytoplasmic receptors which enter the cell nucleus and stimulate protein synthesis. Adrenocorticoids have anti-allergic, antitoxic, antishock, antipyretic and immunosuppressive properties. Dexamethasone has only minor mineralocorticoid activities and does therefore, not induce water and sodium retention. Dexamethasone is decrease inflammation by suppression of neutrophil migration. It decreases the production of inflammatory mediators, and reversal of increased capillary permeability. It also suppresses normal immune response

5.2 Pharmacokinetic Properties

Distribution: Dexamethasone is bound (up to 77%) to plasma proteins, mainly albumins.

There is a high uptake of Dexamethasone by liver, kidney and adrenal glands. In a small amount it is appear in breast milk and the placenta.

Metabolism and Elimination: Metabolism in the liver is slow and up to 65% excreted through urine in 24 hours, largely as conjugated steroids.

Half life: The plasma elimination half life is 3.5 to 4.5 hours. The biological half life of Dexamethasone in plasma is about I90 minutes.

5.3 Preclinical Safety Data

Not Applicable.

6. Pharmaceutical Particulars

6.1 List of Excipients

Methyl Hydroxybenzoate

Propyl Hydroxybenzoate

Sodium Citrate

Sodium Metabisulphite

Disodium Edetate

Creatinine

Sodium Hydroxide

Water for Injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

36 months

6.4 Special Precautions for Storage

Store below 30°C. Protect from light.

6.5 Nature and Contents of Container

A clear colourless liquid filled in 2ml transparent glass ampoule. Such 10 ampoules are packed in Paper-PVC blister pack. Such 10 Paper-PVC blister blisters are packed in a plain inner pack with packaging insert.

6.6 Special precaution for disposal and other handling

The prepared infusion solution should be made up immediately before use..

7. Marketing Authorization Holder and Manufacturing Site Addresses

7.1 Name and Address of Marketing Authorization Holder

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
E-mail: hiren@lincolnpharma.com;
Web site: www.lincolnpharma.com

7.2 Name and Address of manufacturing site(s)

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
E-mail: hiren@lincolnpharma.com;
Web site: www.lincolnpharma.com

8. Marketing Authorization Number

To be included after obtaining first registration.

9. Date of First <Registration> / Renewal of The <Registration>

It will be applicable after registration of this product.

10. Date of Revision of the Text

14th Febraury,2023

11. Dosimetry (If Applicable)

Not Applicale

12. Instructions for preparation of radiopharmaceuticals (if Applicable)

Not Applicable

13. Document Revision History

Date of Revision	Revision Number	Document No.	Change Made
27/07/2021	Rev_0	DAR/GDL/010A	First Issue
14/02/2023	Rev_1	DAR/GDL/010A	Changed format as per Rwanda FDA Guideline and added visual description of product in point 3