SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Dexamethasone Sodium Phosphate 4mg/1ml Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of Dexamethasone Sodium Phosphate injection 4mg/mL, contains dexamethasone sodium phosphate 4.37mg, USP equivalent to 4mg dexamethasone . Each mL of Dexamethasone Sodium Phosphate injection 4mg/mL, contains
dexamethasone sodium phosphate 4.37mg, USP equivalent to 4mg dexamethasone phosphate
For a full list of excipients, see 6.1.

3. PHARMACEUTICAL FORM

Solution for injection A clear, colourless liquid

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This pharmaceutical product is for prescribed use only.
Dexamethasone is a corticosteroid.

4.2 Posology and method of administration

A. Intravenous or intramuscular administration. The initial dosage of Dexamethasone Sodium Injection may very from 0.50mg/day to 9.0mg/day depending on the specific disease entity being treated. In situations of less severity, lower doses will generally suffice while in selected patients higher initial doses may be required. Usually the parenteral dosage ranges are one-third to one-half the oral dose given every 12 hours. However, in certain overwhelming, acute, life-threatening situations, administration of dosages exceeding the usual dosages may be justified and maybe in multiples of the oral dosages.
For the treatment of unresponsive shock high pharmacologic doses of this product are currently recommended. Reported regimens range from 1 to 6mg/kg of body weight as a single intravenous injection to 40mg initially followed by repeat intravenous injection very 2 to 6 hours while shock persists.
For the treatment of cerebral edema in adults an initial intravenous dose of 10 mg is recommended followed by 4mg intramuscularly very six hours until maximum response has been noted. This regimen may be continued for several days postoperatively in patients requiring brain surgery. Oral dexamethasone, 1 to 3 mg t.i.d., should be given as soon as possible and dosage tapered off over a period of five to seven days. Nonoperative cases may require continuous therapy to remain free of symptons of increased intracranial pressure. The smallest effective dose should be used in children, preferable orally. This may approximate 0.2mg/kg/24 hours in divided doses.
In treatment of acute exacerbations of multiple sclerosis daily doses of 200mg of prednisolone for a week followed by 80 mg every other day or 4-8mg dexamethasone every other day for 1 month have been shown to be effective.

The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time there is a lack of satisfactory clinical response, Dexamethasone Sodium Phosphate Injection should be discontinued and the patient transferred to other appropriate therapy. It should be emphasized that dosage requirements are variable and must be individualized on the basis of the disease under treatment and the response of the patient.

After a favourable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. It should be kept in mind that constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness and the effect of patient exposure to stressfull situations not directly related to the disease entify under treatment. In this later situation it may be necessary to increase the dosage of Dexamethasone Sodium Phosphate Injection for a period of time consistent with the patient's condition. If after a long-term theapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

B. Intra-articular, soft tissue or intralesional administration.

The dose for instrasynovial administration is usually 2 to 4 mg for large joints and 0.8 to 1 mg for small joints. For soft tissue and bursal injections a dose of 2. To 4 mg is recommended. Ganglia require a dose 1 to 2 mg. a dose of 0.4 to 1 mg is used for injection into tendon shealths. Injection into intervertebral joints should not be attempted at any time and hip joint injection cannot be recommended as office procedure.

Intrasynovial and soft tissue injections should be employed only when affected areas are limited to 1 or 2 sites. It should be remembered that corticoids provide palliation only and that other conventional or curative methods of therapy should be employed when indicated.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Frequency of injection usually ranges from once every 3 to 5 days to once every 2 to 3 weeks. Frequent intra-articular injection may cause damage to joint tissue.

4.3 Contraindications

Systemitic fungal infections .

4.4 Special warnings and special precautions for use

WARNINGS:

Serious Neurologic Adverse Reactions with Epidural Administration

Serious neurologic events, some resulting in death, have been reported with epidural injection of corticosteroids. Specific events reported include, but are not limited to, spinal cord infarction, paraplegia, quadriplegia, cortical blindness, and stroke. These serious neurologic events have been reported with and without use of fluoroscopy.

The safety and effectiveness of epidural administration of corticosteroids have not

been established, and corticosteroids are not approved for this use.
In patients on corticosteroid therapy subject to any unusual stress, increased dosage of rapidly acting corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used.
Prolonged use of corticosteroids may produce posterior subcapsular cataracts. Glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.
Children who are on immunosuppressant drugs are more susceptible to infections than healthy children. Chickenpox and measles, for example, can have a more serious or even fatal course in children on immunosuppressant corticosteroids. In such children, or in adults who have not have these diseases, particular care should be taken to avoid exposure. If exposed, therapy with varicella zoster immune globulin(VZIG) or pooled intravenous immunoglobulin(IVIG), as appropriate, may be indicated. If chicken develops, treatment with antiviral agents may be considered.
Similarly, corticosterioids should be used with great care in patients with known or suspected Strongyloides(threadworm) infestation. In such patients, corticosteroidinduced immunosuprression may lead to Strongyloides hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia.
PRECAUTIONS- Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy: therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.
There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.
Corticosteroids should be used cautiously in patients with ocular herpes simplex for fear of corneal perforation.
The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction must be gradual.
Pysychic derangements may appear when corticosteroids are used ranging from euphoria, insomnia, mood swings, personality changes, and severe depression to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.
Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.
Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection, also in diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, and myasthenia gravis.

Growth and development of infants and children on prolonged corticosterioid therapy should be carefully followed.
Patients who are on immunosuppressant dosed of corticosteroids should be warned to avoid exposure to chickenpox or measles and, if exposed, to obtain medical advice.
Intra-articular injection of a corticosteroid may produce systemic as well as local effects.
Appropriate examination of any joint fluid present is necessary to exclude a septic process.
A marked increase in pain accompanied by local swelling, further restriction of joint motion, fever, and malaise are suggestive of septic arthritis. If this complication occurs and dthe diagnosis of sepsis is confirmed, appropriate antimicrobial therapy should be instituted.
Local injection of a steroid into a previously infected joint is to be avoided.
Corticosteroids should not be injected into unstable joints.
Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis they do not show that they affect the ultimate outcome or natural history of the disease. The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect. (see pology and administration section) Since complications of treatment with glucocorticoids are dependent on the size of
the dose and the duration of treatment a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermitten therapy should be used.

4.5 Interaction with other FPPs and other forms of interaction

Rifabutin (for example)
Ketoconazole (for example)
Itraconazole (for example)
Nevirapine (for example)
HMG -CoA reductase inhibitors (for example)
Rifampicin (for example).

4.6 Pregnancy and lactation

Use during pregnancy. Since adequate human reproduction studies have not been done with corticosteroids, use of these drugs in pregnancy, nursing mothers or women of childbearing potential requires that the possible benefits of the drug be weighed against the potential hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.
Average and large doses of cortisone or hydrocortisone can cause elevation of blood pressure, salt and water retention, and increased exacretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Patients with a stressed myocardium should be observed carefully and the drug administered slowly since premature ventricular contractions may occur wit hrapid

administration. Dietry salt restriction and potassium supplementation may be necessary.
All corticosteroids increase calcium excretion.
While on corticosteroid therapy patients should not be vaccinated against smallpox. Other immunization procedures should not be undertaken in patients who are on corticosteroids, especially in high doses, because of possible hazards of neurological complications and lack of antibody response.
The use of Dexamethasone Sodium Phosphate Injection in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate anti-tuberculosis regimen.
If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur.
During prolonged corticosteroid therapy, theses patients should receive chemoprophylaxis
Because rare instances of anaphylactoid reactions have occurred in patients receiving parenteral corticosteroid therapy, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug.
Dexamethasone Sodium Phosphate Injection contains sodium sulfite, a sulphite that may cause allergic type reactions including anaphylactic symptoms and lifethreatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulphite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

Summary of Use during Lactation

Because no information is available on the use of systemic dexamethasone during breastfeeding, an alternate corticosteroid may be preferred, especially while nursing a newborn or preterm infant. Local injections, such as for tendinitis, would not be expected to cause any adverse effects in breastfed infants, but might occasionally cause temporary loss of milk supply.

Drug Levels

Maternal Levels. Relevant published information was not found as of the revision date.

Infant Levels. Relevant published information was not found as of the revision date.

Effects in Breastfed Infants

None reported with any corticosteroid.

Effects on Lactation and Breastmilk

Dexamethasone can cause a decrease in basal serum prolactin and thyrotropinreleasing hormone stimulated serum prolactin increase in nonnursing women.[1][2]
Published information on the effects of dexamethasone on serum prolactin or on lactation in nursing mothers was not found as of the revision date. However, medium to large doses of depot corticosteroids injected into joints have been reported to cause temporary reduction of lactation.[3][4]

A study of 46 women who delivered an infant before 34 weeks of gestation found that a course of another corticosteroid (betamethasone, 2 intramuscular injections of 11.4 mg of betamethasone 24 hours apart) given between 3 and 9 days before delivery resulted in delayed lactogenesis II and lower average milk volumes during the 10 days after delivery. Milk volume was not affected if the infant was delivered less than 3 days or more than 10 days after the mother received the corticosteroid.[5] An equivalent dosage regimen of dexamethasone might have the same effect.
A study of 87 pregnant women found that betamethasone given as above during pregnancy caused a premature stimulation of lactose secretion during pregnancy. Although the increase was statistically significant, the clinical importance appears to be minimal.[6] An equivalent dosage regimen of dexamethasone might have the same effect.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects

Fluid and electrolyte disturbances:

Sodium retention
Fluid retention
Congestive heart failure in susceptible patients
Potassium loss
Hypokalemic alkalosis
Hypertension

Musculoskeletal:

Muscle weakness
Steroid myopathy
Loss of muscle mass
Osteoporosis
Vertebral compression fractures
Aseptic necrosis of femoral and humeral heads
Pathologic fracture of long bones

Gastrointestinal:

Peptic ulcer with possible subsequent perforation and haemorrhage
Pancreatitis
Abdominal distention
Ulcerative esophagitis

Dermatological:

Impaired wound healing
Thin fragile skin
Facial erythema
Increased sweating

DEXAMETHASONE SODIUM PHOSPHATE INJECTION 4MG/ML

May suppress reactions to skin tests
Petechiae and ecchymoses

Neurological:
Convulsions
Increased intracranial pressure with papilledema(pseudotumor cerebri) usually after treatment
Vertigo
Headache
Ophthalmic:
Posterior subcapsular cataracts
Increased intraocular pressure
Glaucoma
Exophthalmos
Endocrine:
Menstrual irregularities
Development of cushingoid state
Suppression of growth in children
Secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery, or illness
Decreased carbohydrate tolerance
Manifestations of latent diabetes mellitus
Increased requirements for insulin or oral hypoglycmic agents in diabetics
Metabolic:
Negative nitrogen balance due to protein catabolism
Miscellaneous:
Hyperpigmentation or hypopigmentation
Subcutaneous and cutaneous atrophy
Sterile abscess
DEXAMETHASONE SODIUM PHOSPHATE INJECTION 4MG/ML
Postinjection flare, following intra-articular use
Charcot-like arthropathy
Itching, burning, tingling in the ano-genital rgion
Laboratory test findings (for example)
Post-marketing experience (for example)
4.9 Overdose
Corticosteroids are a type of anti-inflammatory medicine. Corticosteroid overdose occurs when someone accidentally or intentionally takes more than the normal or recommended amount of this medication.
Corticosteroids come in many forms, including:
• Creams and ointments that are applied to the skin
• Inhaled forms that are breathed into the nose or lungs
• Pills or liquids that are swallowed
• Injected formulas delivered to the skin, joints, muscles, or veins
Most corticosteroid overdoses occur with pills and liquids
Symptoms of corticosteroid overdose can include:

- Burning or itching skin
- Convulsions
- Deafness
- Depression
- Dry skin
- High blood pressure
- Muscle weakness
- Nervousness
- Psychosis
- Sleepiness
- Stopping of menstrual cycle
- Swelling in lower legs, ankles, or feet
- Weakness

- Worsening of health conditions such as ulcers, diabetes

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Glucocorticoids
ATC code: S02AB02

Dexamethasone possesses the actions and effects of other basic glucocorticoids and is among the most active members of its class.

Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. They cause profound and varied metabolic effects and in addition, they modify the body's immune responses to diverse stimuli. Naturally-occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used primarily for their potent anti-inflammatory effects in disorders of many organ systems.

Dexamethasone has predominant glucocorticoid activity with little propensity to promote renal retention of sodium and water. Therefore it does not offer complete replacement therapy and must be supplemented with salt or desoxycorticosterone.

5.2 Pharmacokinetic properties

The biological half-life of dexamethasone in plasma is about 190 minutes.

Binding of dexamethasone to plasma proteins is less than for most other corticosteroids and is estimated to be about 77%.

Up to 65% of a dose is excreted in the urine in 24 hours, the rate of excretion being increased following concomitant administration of phenytoin.

The more potent halogenated corticosteroids such as dexamethasone, appear to cross the placental barrier with minimal inactivation.

5.3 Preclinical safety data

In animal studies, cleft palate was observed in rats, mice, hamsters, rabbits, dogs and primates; not in horses and sheep. In some cases these divergences were combined with defects of the central nervous system and of the heart. In primates, effects in the brain were seen after exposure. Moreover, intra-uterine

growth can be delayed. All these effects were seen at high dosages.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol
EDTA-2Na
Propylene Glycol
Water for Injection

6.2 Incompatibilities

Dexamethasone is physically incompatible with daunorubicin, doxorubicin, vancomycin, diphenhydramine (with lorazepam and metoclopramide) and metaraminol bitartrate and should not be admixed with solutions containing these drugs. It is also incompatible with doxapram and glycopyrrolate in syringe and with ciprofloxacin, idarubicin and midazolam in Y-site injections (1:1 mixture).

6.3 Shelf life

36 months

From a microbiological point of view, the product should be used immediately after opening. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 h at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Any unused portion of the product should be discarded immediately after use.

Chemical and physical in-use stability of dilutions has been demonstrated for 24 h at 30°C. Dilutions should be used within 24 hours and discarded after use.

6.4 Special precautions for storage

Keep container in the outer carton.

Do not freeze.

Store below 30°C.

Any unused portion should be discarded immediately after use.

6.5 Nature and contents of container

Type I clear glass ampoule containing 1 ml solution for injection.

Type I clear glass ampoule containing 2 ml solution for injection.

1 ml	**2 ml**
Package of 10 ampoules of 1 ml each	Package of 10 ampoules of 2 ml each

Not all pack sizes may be marketed.

6.6 Instructions for use and handling

When Dexamethasone 4 mg/ml solution for injection is given by intravenous infusion, dextrose 5% in water and sodium chloride 0.9% have been

recommended as diluents. The exact concentration of dexamethasone per infusion container should be determined by the desired dose, patient fluid intake and drip rate required

7. Marketing Authorisation Holder

Jeil Pharmaceuticals co,ltd.

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8. Number(S) In The National Register Of Finished Pharmaceutical Products

Dexamethasone Sodium Phosphate Injection 4mg/ml:

06704/07913/REN/2021

9. Date of First Authorisation/Renewal Of The Authorisation

Oct 22, 2021

10. Date Of Revision Of The Text

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