

Package leaflet: Information for the user

Dexamethasone Phosphate 4 mg/ml solution for injection

Dexamethasone phosphate

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What is Dexamethasone Phosphate and what it is used for
2. What you need to know before you use Dexamethasone Phosphate
3. How to use Dexamethasone Phosphate
4. Possible side effects
5. How to store Dexamethasone Phosphate
6. Contents of the pack and other information

1. What is Dexamethasone Phosphate and what it is used for

Dexamethasone is a synthetic glucocorticoid (adrenocortical hormone).

Dexamethasone Phosphate 4 mg/ml solution for injection is indicated in the following situations:

SYSTEMIC USE

The indications are:

The same as the oral corticosteroids, in situations in which the oral therapy is unfeasible (vomits, altered consciousness);

Conditions that require a rapid therapeutic effect:

Haemorrhagic, traumatic, surgical or septic origin shock

Autoimmune inflammatory diseases: Lupus erythematosus, Dermatomyositis, Polyarthritis nodosa, Thrombocytopenic purpura, Pemphigus vulgaris, Rheumatoid arthritis

Allergies: Acute bronchial asthma, severe angioedema (in combination with antihistamines), Anaphylactic shock (in combination with adrenaline), imminent allograft rejection

Infections:

Severe typhoid fever, especially if associated with altered consciousness, shock, coma
Laryngitis stridulosa (pseudocroup) in children

Dexamethasone Phosphate is used as a treatment of coronavirus disease 2019 (COVID-19) in adult and adolescent patients (aged 12 years and older with body weight at least 40 kg) with difficulty breathing and need of oxygen therapy.

Neurological conditions: Cerebral edema secondary to tumours, abscesses, cerebral toxoplasmosis

ORL: Laryngeal dyspnoea

Oncology Pathology:

In combination with other drugs, treatment of symptomatic multiple myeloma, acute lymphocytic leukemia, acute lymphoblastic leukemia, Hodgkin's disease and non-Hodgkin's lymphoma
Prophylaxis and treatment of cytostatic-induced vomiting
Compression of the spinal cord by metastatic lesions

LOCAL USE

The same as for topical corticosteroids where the condition justifies strong local concentrations. All requirements for loco-regional injections should take into account the danger of infection, particularly the risk of facilitating bacterial proliferation.

This product is indicated in:

Dermatological conditions: Keloids

Rheumatological conditions

Periarticular injections: tendinitis, bursitis

Injections in soft tissue: heel pain, carpal tunnel syndrome, Dupuytren contracture

2. What you need to know before you use Dexamethasone Phosphate

Do not use Dexamethasone Phosphate:

- if you are allergic to dexamethasone or any of the other ingredients of this medicine (listed in section 6).
- if you have an infection affecting the whole body that is not being treated with antibiotics (treatment with dexamethasone may nevertheless be used in life-threatening situations).

Talk to your doctor or nurse if any of the above apply to you before using this medicine.

Warnings and Precautions

Talk to your doctor, pharmacist or nurse before using Dexamethasone Phosphate:

- if you have ever had a severe depression or manic-depressive psychosis (bipolar disorder). This includes having had depression earlier while taking steroid medicines such as dexamethasone.
- if someone in your immediate family has had these diseases.
- if you have or are suspected of having pheochromocytoma (a tumor of the adrenal glands).

Treatment with this medicine may cause pheochromocytoma crisis, which can be fatal. Pheochromocytoma is a rare tumor of the adrenal glands. Crisis can occur with following symptoms: headaches, sweating, palpitations, and hypertension. Contact your doctor immediately if you experience these signs.

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Take special care with Dexamethasone Phosphate and check with your doctor before use if you have:

- Liver, kidney or heart problems;
- High blood pressure;
- Epilepsy;
- History of migraines;
- Osteoporosis (brittle bones);
- You had tuberculosis in the past;
- Thyroid with decreased activity;
- Had amoebiasis in the past (specific infection of tropical countries causing diarrhea);
- Herpes infection in the eye;
- Diabetes (or family history of diabetes);
- Eye disease called glaucoma (or a family history of glaucoma);
- Ulcers in the stomach;
- You had muscle weakness caused by previous steroid treatment.

Talk to your doctor if you experience the following symptoms:

- Symptoms of tumor lysis syndrome such as cramp, muscle weakness, disorientation, loss of vision, respiratory disorders and shortness of breath, if you suffer from hematologic disease.

Contact your doctor if you experience blurred vision or other visual disturbances.

You should not stop taking any other steroid medications unless your doctor has instructed you to do so.

General precautions regarding steroid use in specific diseases, masking infection, concomitant medicines etc. in line with current recommendations.

Children and Adolescents

Special care is required if Dexamethasone Phosphate is given to infants and children.

Dexamethasone should not be routinely used in preterm newborn infants with respiratory problems.

If dexamethasone is given to a prematurely born baby, monitoring of heart function and structure is needed.

Other medicines and Dexamethasone Phosphate

Tell your doctor or nurse if you are using, have recently used, or might use any other medicines including non-prescription medicines.

You should not be vaccinated with a live vaccine during steroid treatment. Tell your doctor or nurse if you are planning a vaccination.

Special care is needed if you are taking or using other medicines because some may interact with dexamethasone, such as:

- Barbiturates (medicines used to treat sleep disorders and epilepsy);
- Ephedrine (a medicine that is used as a nasal decongestant or in respiratory diseases);
- Rifampicin and rifabutin (antibiotics that are used to treat tuberculosis);
- Primidone, phenytoin, carbamazepine (used to treat epilepsy);
- Aminoglutethimide (used to treat cancer);
- Anticoagulants (used to thin the blood);
- Insulin and other medicines used to treat diabetes;
- Aspirin and other anti-inflammatory drugs (treatment of pain and inflammation);
- Acetazolamide (used to treat eye disease glaucoma);
- Diuretics (tablets to eliminate water);
- Carbenoxolone (used to treat gastric ulcers);
- Digoxin and other medicines that regulate the heartbeat;
- Antihypertensives (used to treat high blood pressure).

Pregnancy, breastfeeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or nurse for advice before taking this medicine.

Newborn babies of mothers who received Dexamethasone Phosphate near the end of pregnancy may have low blood sugar levels after birth.

Pregnancy

If you use dexamethasone often or for long periods during pregnancy, there may be a risk of slow baby growth. Careful observation of the baby after birth may be necessary for a short period of time.

Breast-feeding

If you are given dexamethasone for an extended period of time during breast-feeding, your baby's growth may slow down and other side effects may occur (see section 4 Possible side effects). Your physician will talk this through with you and decide if you should be given dexamethasone.

Driving and using machines

Do not drive or operate machinery if you experience any side effects that may affect your ability to do so.

This medicine contains 3.2 mg sodium (main component of cooking/table salt) per ml. This is equivalent to 0.16% of the WHO recommended maximum daily dietary intake of sodium for an adult.

3. How to use Dexamethasone Phosphate

This medicine can be given by intravenous use (injection into a vein), intramuscular use (injection into a muscle) or directly into a joint or soft tissue. This medicine may also be diluted with glucose or sodium chloride solution and given as a slow injection via a drip (infusion) system into a vein.

Dose

The dose of medicine to be given will depend on your age and medical condition and will be carefully adjusted by your doctor.

You are unlikely to need Dexamethasone Phosphate for more than one or two weeks unless you are using this medicine for the treatment of arthritic joints, in which case the treatment may last longer. If dexamethasone treatment is prolonged, tablets may be given instead of injection.

This medicine suppresses your body's natural ability to produce its own corticosteroids. As a consequence during prolonged treatment any new disease, trauma or surgical procedure will require a temporary increase in dose; if corticosteroid treatment has recently been discontinued, it may need to be restarted.

For the treatment of Covid-19

Adult patients are recommended to be given 6 mg IV once a day for up to 10 days.

Use in adolescents

Paediatric patients (adolescents of 12 years of age or older) are recommended to be given 6 mg IV once a day for up to 10 days.

Take Dexamethasone Phosphate only as prescribed by your doctor. Your doctor will decide for how long you should take dexamethasone. Check with your doctor or pharmacist if you are not sure.

Mental problems during treatment with dexamethasone

Mental health problems may occur during treatment with steroids such as dexamethasone (see also section 4 Possible side effects).

- These diseases can be serious;
- Usually occur a few days or weeks after starting treatment with this medicine;
- The bigger the dose the higher the probability of these problems to occur;
- Most of these problems go away if the dose is decreased or if treatment is stopped. However, if these problems occur, treatment may be necessary.

Talk to your doctor if you (or anyone using this medicine) show any signs of mental problems. This is particularly important if you are depressed, or may be thinking about suicide. In some cases, mental problems occurred when the doses were reduced or stopped.

If you use more, or less, Dexamethasone Phosphate than you should

This medicine will be given by a doctor or nurse. It is unlikely that you will be given too much or too little, however talk to your doctor or nurse if you have any concerns.

If you stop using Dexamethasone Phosphate

Do not stop taking this medicine suddenly as this may be dangerous. Your doctor will explain how treatment should be gradually reduced. When treatment is discontinued, it can lead to a "withdrawal syndrome," which includes fever, muscle pain, joint pain, inflammation of the nose's mucous membranes, eye discomfort (conjunctivitis), painful itchy skin bumps and weight loss. In children,

increased pressure on the skull may occur: if the child complains of a headache, has seizures or is sick, report to your doctor immediately.

In some cases, mental problems have occurred when the doses have been reduced or stopped (see section 4 Possible side effects).

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If any of the following occur, inform your doctor immediately:

- **Severe allergic reaction** - Sudden rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which can cause difficulty in swallowing or breathing) may occur, and faintness may occur.
- **Severe illness and/or fever that will make you feel very sick.**

These are very serious side effects. You may need urgent medical care. All these very serious side effects are rare.

Serious effects: inform your doctor immediately.

Steroids, including dexamethasone, can cause serious mental health problems. These are common in adults and children. They can affect about 5 out of 100 people who use drugs like dexamethasone.

- Feeling of depression, including thoughts of suicide;
- Exaltation (mania) or mood swings;
- Feeling of anxiety, difficulty in sleeping, difficulty in thinking or feeling confused and loss of memory;
- Feeling, seeing or hearing things that do not exist. Have weird and scary thoughts, changes in behaviour or feeling lonely.

If you notice any of these problems **talk to your doctor immediately.**

Caregivers of patients taking/using dexamethasone should report to the physician immediately if the patient shows any signs of mental problems. This is particularly important if the patient shows signs of depression or speaks of suicidal thoughts.

Frequency not known: Thickening of the heart muscle (hypertrophic cardiomyopathy) in prematurely born babies, that generally returns to normal after stopping treatment.

If any of the following occur, talk to your doctor as soon as possible:

- Seizures;
- Aggravation of epilepsy or schizophrenia;
- Shortness of breath;
- Severe thirst or more frequent urination (may indicate increased blood sugar levels);
- Water retention (edema) and high blood pressure;
- Muscle weakness;
- Feeling of spinning or the surrounding environment is spinning;
- Eye disorders, including cataracts and glaucoma, eye infections may worsen;
- Visual disturbances, loss of vision, blurring of vision;
- Swelling and weight gain on the face and body, excess body hair;
- Osteoporosis (bone fragility) - your physician may ask you to have a bone exam to check for this condition;
- Slow growth in children or adolescents (the physician will check this situation);
- If you realize that you catch small infections very easily;
- Irregular period or absence of period in women;
- Indigestion, stomach ulcers and pain in the stomach and in the back;

- Skin diseases such as slow wound healing, bruising, spider veins or stretch marks on the skin, increased sweating, skin rashes or changes in pigmentation of the skin, coloured bumps with pruritus on the skin, itchy red rash on the skin with white scaly plaques (canker), acne;
- Headache;
- Pain, redness or swelling at the injection site (if the injection is in a joint);
- Increased appetite.

Many of the side effects described only occur after high dose or long treatments.

Reporting side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance Website: www.hpra.ie

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Dexamethasone Phosphate

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date stated on the ampoule or outer packaging after "EXP". The expiry date refers to the last day of that month.

Store below 25°C. Store in the original package in order to protect from light.

The injectable solution's physical-chemical stability after dilution in 0.9% Sodium Chloride, 5% Glucose or Ringer was demonstrated for 24 hours at room temperature.

From a microbiological point of view, the product should be used immediately. If not used immediately, the storage times and conditions are the responsibility of the user.

Do not use this medicine if you notice any particles in the solution. Only clear and particle free solutions should be used.

Do not throw away any medicine via the sewer or household waste. Ask your pharmacist how to dispose of medicine you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Dexamethasone Phosphate contains

- The active substance is dexamethasone.
- Each ml of solution contains 4 mg dexamethasone phosphate (as 4.37 mg dexamethasone sodium phosphate, equivalent to 3.3 mg dexamethasone base).
- The other ingredients are creatinine, trisodium citrate dihydrate, disodium edetate dihydrate, sodium hydroxide 1M (for pH adjustment) and water for injections.

What Dexamethasone Phosphate looks like and contents of the packaging

This medicine is available in amber glass ampoules.

Dexamethasone Phosphate is available in packs of 10 or 50 ampoules containing 1 ml of injectable solution.

Marketing Authorisation Holder

Fresenius Kabi Deutschland GmbH
Else-Kroner-Strasse 1
61352 Bad Homburg v.d.H
Germany

Manufacturer

Labesfal, Laboratórios Almiro, S.A.
Zona Industrial do Lagedo
3465-157 Santiago de Besteiros
Portugal

This medicinal product is authorised in the Member States of the EEA under the following names:

Name of the Member State	Name of the medicinal product
Austria	Dexamethason Kabi 4 mg/ml Injektionslösung
Bulgaria	Дексаметазон Каби 4 mg/ml инжекционен разтвор
Cyprus	Dexamethasone/Kabi 4mg/ml, ενέσιμο διάλυμα
Estonia	Dexamethasone Kabi
Finland	Dexamethasone phosphate Kabi 4 mg/ml injektioneste, liuos
Greece	Dexamethasone/Kabi 4mg/ml, ενέσιμο διάλυμα
Hungary	Dexamethasone Kabi 4 mg/ml oldatos injekció
Ireland	Dexamethasone Phosphate 4mg/ml solution for injection
Portugal	Dexametasona Kabi 4 mg/ml solução injetável
Sweden	Dexamethasone phosphate Kabi 4 mg/ml injektionsvätska, lösning
Slovenia	Deksametazon Kabi 4 mg/ml raztopina za injiciranje

This leaflet was last revised in March 2022.

The following information is intended for healthcare professionals only:

Dosage and method of administration**N. B. All doses are expressed as dexamethasone phosphate mg**

Dexamethasone Phosphate 4 mg/ml injectable solution is intended for intravenous (IV), intramuscular (IM), intra-articular and intralesional use.

The intravenous and intramuscular routes of administration of dexamethasone should only be used in case of acute illness or in life-threatening situations. Replacement by oral therapy should be done as soon as possible.

The lowest effective dose should be used and for the shortest period possible, with frequent monitoring to adequately adjust the dose to the intensity of the disease (see section Warnings and Precautions).

SYSTEMIC USE

Intravenous and intramuscular administration: IM or IV dexamethasone dosage administration is variable, depending on the condition being treated. It usually ranges from 0.4 to 24 mg (0.1 to 6 ml) daily. The patient clinical response determines treatment duration and as soon as improvements occur, the dose should be adjusted to the minimum necessary to maintain the desired clinical response. Withdrawing of the medicine after treatment completion should be gradual.

Shock: A single IV injection of 2 to 6 mg/kg body weight (0.5 to 1.5 ml/kg), which can be repeated in 2-6 hours if the shock persists. A high dose treatment should only be maintained until the condition

stabilization of the patient and generally for no more than 48-72 hours. This bolus injection can be followed by a 3 mg/kg body weight (0.75 mL/kg) continuous intravenous infusion for 24 hours. For infusion Dexamethasone Phosphate 4 mg/ml solution for injection can be diluted with the following solutions: 0.9% Sodium Chloride, 5% Glucose or Ringer.

Cerebral edema: An initial dose of 10 mg (2.5 ml) IV followed by 4 mg (1.0 ml) IM every 6 hours until symptoms of edema decrease (usually after 12 to 24 hours). After 2 to 4 days, dosage should be reduced and withdrawn gradually over a period of 5 to 7 days. In patients with recurrent or inoperable neoplasms, maintenance therapy may be effective with 2 mg dosage (0.5 ml) IM or IV 2-3 times a day.

Life-threatening cerebral edema:

High dosage scheme (all doses are expressed as dexamethasone phosphate mg):

	<u>Adults</u>	<u>Children > 35 kg</u>	<u>Children < 35 kg</u>
Initial dose	50 mg (12,5 ml) IV	25 mg (6,25 ml) IV	20 mg (5,0 ml) IV
1st day	8 mg (2.0 ml) IV every 2 hours	4 mg (1.0 ml) IV every 2 hours	4 mg (1.0 ml) IV every 3 hours
2nd day	8 mg (2.0 ml) IV every 2 hours	4 mg (1.0 ml) IV every 2 hours	4 mg (1.0 ml) IV every 3 hours
3rd day	8 mg (2.0 ml) IV every 2 hours	4 mg (1.0 ml) IV every 2 hours	4 mg (1.0 ml) IV every 3 hours
4th day	4 mg (1.0 ml) IV every 2 hours	4 mg (1.0 ml) IV every 4 hours	4 mg (1.0 ml) IV every 6 hours
5th-8th day	4 mg (1.0 ml) IV every 4 hours	4 mg (1.0 ml) IV every 6 hours	2 mg (0.5 ml) IV every 6 hours
After 8 days	Decrease: 4 mg (1.0 ml) daily reduction	Decrease: 2 mg (0.5 ml) daily reduction	Decrease: 1 mg (0.25 ml) daily reduction

Note: Dexamethasone by intravenous and intramuscular use should only be used in case of acute illness or in life-threatening situations.

Replacement with oral therapy should be done as soon as possible.

For the treatment of Covid-19:

Adult patients 6 mg IV, once a day for up to 10 days.

Paediatric population

Paediatric patients (adolescents aged 12 years and older) are recommended to take 6mg/dose IV once a day for up to 10 days.

Duration of treatment should be guided by clinical response and individual patient requirements.

Elderly, renal impairment, hepatic impairment

No dose adjustment is needed.

LOCAL USE

Intra-articular and soft tissue injections

Dosage changes according to degree of inflammation and affected area size and location. Injections can be repeated once every 3-5 days (for example, for bursae) up to once every 2-3 weeks (for joints).

Injection site

1. Large joints

Dose

2 mg to 4 mg (0.5 ml to 1.0 ml)

2. Small joints	800 micrograms to 1 mg (0.2 ml to 0.25 ml)
3. Bursae	2 mg to 3 mg (0.5 ml to 0.75 ml)
4. Tendon sheaths	400 micrograms to 1 mg (0.1 ml to 0.25 ml)
5. Soft tissue infiltration	2 mg to 6 mg (0.5 ml to 1.5 ml)
6. Ganglia	1 mg to 2 mg (0.25 ml to 0.5 ml)

SPECIAL POPULATIONS

Children

Required dosage is variable and may need to be adjusted according to individual needs. Typically, daily dosage ranges from 200 micrograms/kg body weight to 400 micrograms/kg body weight (0.05 ml/kg body weight to 0.1 ml/kg body weight).

Corticosteroids cause growth retardation in childhood and adolescence, which may be irreversible. Treatment should be limited to the minimum dose for the shortest period possible. In order to minimize suppression of the hypothalamic-pituitary-adrenal axis and growth delay, treatment should be limited, as far as possible, to a single dose on alternate days.

Infant and children growth and development on prolonged corticosteroid therapy should be closely monitored.

Elderly

Treatment of elderly patients, especially in the long term, should be planned, taking into account the most serious consequences in old age. Such effects include osteoporosis, hypertension, hypokalemia, diabetes, susceptibility to infection, and thin, fragile skin. Careful clinical supervision is necessary to avoid potentially fatal reactions.

Incompatibilities

Sodium phosphate dexamethasone is physically incompatible with daunorubicin, doxorubicin, vancomycin, diphenhydramine (with lorazepam and metoclopramide) and metaraminol bitartrate and should not be mixed with solutions containing these medicinal products. It is also incompatible with doxapram and glycopyrrolate in syringes and with ciprofloxacin, idarubicin and midazolam in injections in Y system (1:1 mix).

Storage Precautions in Use

Shelf-life after dilution:

The physical-chemical stability after dilution of the solution for injection in 0.9% Sodium Chloride, 5% Glucose or Ringer was demonstrated for 24 hours under 25°C and protected from light.

From a microbiological point of view, the product should be used immediately. If not used immediately, the storage times and conditions are the responsibility of the user.