Package leaflet: Information for the patient

Dexamethasone phosphate Noridem 4 mg/mL Solution for injection

dexamethasone phosphate

Read all of this leaflet carefully before you are given 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, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Dexamethasone phosphate Noridem is and what it is used for

Dexamethasone is a synthetic glucocorticoid (adrenocortical hormone).
Dexamethasone belongs to a group of medicines called steroids.
This medicine is given by injection to patients unable to take a tablet form of the medicine.
Dexamethasone reduces inflammation and suppresses the immune system and is used normally for patients with:

- severe allergic reactions causing swelling of the face and throat, low blood pressure and collapse (angioneurotic oedema and anaphylaxis)
- shock caused by infection or severe tuberculosis (also with anti-infective treatments e.g. antibiotics)
- raised pressure in the skull caused by tumours or infantile spasms (seizure disorder in babies)
- Sometimes, the injection is given into the painful area itself for example inflammation of the joints (rheumatoid arthritis and osteoarthritis)

Dexamethasone phosphate Noridem 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.

Dexamethasone can sometimes also be given by injection under the skin (subcutaneously) to relieve certain symptoms including pain, tiredness, weight loss and feeling and being sick.

2. What you need to know before you are given Dexamethasone phosphate Noridem

You must not be given Dexamethasone phosphate Noridem
if you have any of the following conditions:

- if you are sensitive or allergic to dexamethasone phosphate or any of the other ingredients of this medicine (listed in section 6).
- if you have a fungal infection that has spread to involve the whole body.
- if you have any other widespread infection which is not currently being treated.
- if you are to be vaccinated with live virus vaccines.
- infection at the injection site, particularly in the joint where dexamethasone phosphate will be injected (unless you are taking the appropriate antibiotic).
- unstable joints (this is a condition where joints, such as knee, can suddenly give way), where Dexamethasone phosphate Noridem will be injected.
- stomach ulcer.
- active tuberculosis.
- acute psychosis (a form of mental condition).
- you have a severe allergy to sulfites.

Warnings and precautions
Talk to your doctor or nurse before being given Dexamethasone phosphate Noridem:

- if you have ever had severe depression or manic-depression (bipolar disorder). This includes having had depression before while taking steroid medicines like dexamethasone.
- if any of your close family has had these illnesses.
- if you have or are suspected of having pheochromocytoma (a tumor of the adrenal glands).

If any of these apply to you, talk to a doctor before receiving dexamethasone.

Mental health problems while taking dexamethasone
Mental health problems can happen while taking steroids like dexamethasone (see also section 4 *"Possible side effects"*)

- These illnesses can be serious.
- Usually they start within a few days or weeks of starting the medicine.
- They are more likely to happen at high doses.
- Most of these problems go away if the dose is lowered or the medicine is stopped. However if problems do happen, they might need treatment.

Talk to a doctor if you (or someone taking this medicine), show any signs of mental health problems.
This is particularly important if you are depressed, or might be thinking about suicide. In a few cases, mental health problems have happened when doses are being lowered or stopped.

You should avoid any exposure to infectious diseases. If you do not have a definite history of chickenpox, you must avoid any contact with chickenpox (herpes simplex), shingles (herpes zoster) or measles. This precaution applies also if your child is the patient treated with this medicine. If you think you may have been exposed to these, please seek advice from a doctor immediately as the consequences can be serious (the steroids can stop your body defending itself against these diseases which can become severe and widespread). If you develop these infections, you will need immediate treatment in hospital.

If you are treated for COVID-19, you should not stop taking any other steroid medications unless your doctor has instructed you to do. Talk to your doctor, pharmacist or nurse before you take Dexamethasone phosphate Noridem. General precautions regarding steroid use in specific diseases, masking infection, concomitant medicines etc. in line with current recommendations.

Corticosteroids may mask some signs of infection and new infections may appear during their use. Your doctors will try to use the smallest dose necessary to help you. However, there may be times when an increase in dose will be needed. Any reduction in dose will need to be made more slowly than an increase.
Your doctor will explain this to you and will probably give you a "steroid treatment card" to show to other doctors while you need to take steroids (including by mouth).
Steroid treatment cards may also be available from your pharmacist.

Very occasionally your body might give you "withdrawal effects" after taking steroids or during dose reduction, including fever, tiredness and aches and pains in muscles and joints. You should tell your doctor if you develop such symptoms even though there may be other causes for these symptoms.

Corticosteroids can lead to raised blood pressure, ankle swelling (by retention of salt) and a loss of potassium in your water. Your doctor will monitor your condition and treat these if they arise. Steroids are also used cautiously, even if necessary, if a patient taking them has a heart attack.

Corticosteroids effects can be greater in patients with hypothyroidism (when the thyroid gland doesn't make enough thyroid hormone) or cirrhosis (a serious scarring of the liver) and your doctor may need to adjust the dose.

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.

You should also tell the doctor if you:

- suffer from heart failure or have had a recent heart attack
- suffer from high blood pressure
- suffer from kidney or liver problems
- suffer from diabetes or a relative has diabetes
- suffer from or have had a stomach or duodenal ulcer
- suffer from osteoporosis (thinning and weakness of the bone)
- have suffered from muscle weakness with this or other steroids in the past
- suffer from myasthenia gravis (a disease causing weak muscles)
- suffer from an eye infection with the herpes virus
- suffer from glaucoma (increased pressure within the eye) or a relative has glaucoma
- suffer from epilepsy
- suffer from schizophrenia
- have previously had tuberculosis
- have previously had amoebiasis (an infection which is specific to tropical countries and causes diarrhoea)
- have symptoms of tumour lysis syndrome such as muscle cramping, muscle weakness, confusion, visual loss or disturbances and shortness of breath, in case you suffer from haematological malignancy.

If high doses of this medicine are administered, you may be advised to reduce salt intake and to take extra potassium in the form of tablets.

In the case of local injection of Dexamethasone phosphate Noridem (e.g. injection into a joint), your doctor will take special care to reduce the particular risk of bacterial infection. This medicine should not be injected directly into an infected site. Please tell your doctor if you suffer from complications like a marked increase in pain accompanied by local swelling, further restriction of joint motion, fever or malaise after a local injection of this medicine. Your doctor will have to check if you suffer from blood poisoning and take the appropriate action.

Injection into unstable joints should be avoided.

Please be advised not to over-use joints that are still diseased, even if you do not suffer pain!
If you have an accident, fall ill, require any surgery (including at the dentist's) or are to have any vaccinations (especially with so-called "live virus vaccines") during or after treatment with Dexamethasone phosphate Noridem you must tell the doctor treating you that you are taking or have taken steroids.

All patients taking steroid drugs for more than a few days should carry **"steroid treatment" cards**, which are available from your doctor or pharmacist. These cards carry details of your medicine and your doctor.

Children
If the patient is a child, the doctor will monitor growth and development at intervals during treatment because this medicine can cause growth retardation. Treatment will be limited, where possible, to a single dose on alternate days.

Preterm neonates (premature babies)
Dexamethasone should not be used routinely in preterm neonates 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 Noridem
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.
This is especially important with the following medicines as they may interact with your Dexamethasone phosphate Noridem:

- aspirin or similar medicines
- phenytoin (used to treat epilepsy)
- barbiturates (sedative medicines used to treat sleeplessness and epilepsy)
- ephedrine (for nose decongestion)
- antibiotics called rifampicin and rifabutin (used to treat tuberculosis)
- carbamazepine (used to treat epilepsy, pain and manic depression)
- aminoglutethimide (an anticancer medicine)
- anticoagulant medicines which thin the blood for example. warfarin
- medicines for diabetes
- certain diuretics (water tablets) – medicines that increase urine production
- antiretroviral medicines, for example, ritonavir, darunavir, indinavir, lopinavir, saquinavir and efavirenz

Because of the interactions with these medicines, your doctor might have to adjust the dosage of the medication given to you. Some medicines may increase the effects of Dexamethasone phosphate Noridem and your doctor may wish to monitor you carefully if you are taking these medicines (including some for HIV: ritonavir, cobicistat).
If you are receiving certain anticoagulants (medicines to prevent blood clots) at the same time, your doctor will frequently check your blood clotting, in order to reduce the chance of bleeding.

Pregnancy and breast-feeding
Tell your doctor or nurse before being given this medicine injection if you are pregnant or breast feeding. The doctor will then decide if the injection is suitable for you.
When dexamethasone is administered for prolonged periods or repeatedly during pregnancy, there may be an increased risk for growth retardation in the unborn child. Newborn babies of mothers who received dexamethasone near the end of pregnancy may have low blood sugar levels after birth.
If you are taking high doses of this medicine for prolonged periods and you are breast-feeding, your infant may take up dexamethasone through the breast milk. Your doctor will monitor this.

Driving and using machines
Do not drive or use machinery if you are affected by the administration of this medicine.

Dexamethasone phosphate Noridem contains sodium
This medicine contains 241.5 mg sodium (main component of cooking/table salt) per maximum single dose. This is equivalent to 12.075 % of the recommended maximum daily dietary intake of sodium for an adult.

Dexamethasone phosphate Noridem contains phosphate propylene glycol
This medicine contains 20 mg propylene glycol in each mL.
If you suffer from a liver or kidney disease, do not take this medicine unless recommended by your doctor. Your doctor may carry out extra checks while you are taking this medicine.
If your baby is less than 4 weeks old or your child is less than 5 years old, talk to your doctor or pharmacist before giving them this medicine, in particular if they use other medicines that contain propylene glycol or alcohol.
If you are pregnant or breast-feeding, do not take this medicine unless recommended by your doctor. Your doctor may carry out extra checks while you are taking this medicine.

3. How Dexamethasone phosphate Noridem is given

Your nurse or doctor will give you the injection.
Your doctor will decide the correct dosage for you and how and when the injection will be given.

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

<u>For the treatment of Covid-19</u>
Adult patients are recommended to be given *IV* 6 mg 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 *IV* 6 mg once a day for up to 10 days.

The following information is intended for healthcare professionals only:

Dexamethasone phosphate Noridem may be administered intravenously, intramuscularly, subcutaneously, intraarticularly or intralesionally. For single use only.

Dexamethasone phosphate Noridem is a clear, colourless solution.

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).

Instructions for use and handling
Dexamethasone can be diluted with the following infusion fluids:

- 5 % w/v dextrose in water and
- 0.9 % w/v sodium chloride (9 mg/mL)

When Dexamethasone phosphate Noridem is

If you are given more Dexamethasone phosphate Noridem than you should or you miss a dose
Since the injection will be given to you by a doctor or nurse, it is unlikely that you will be given too much or that you will miss a dose. If you are concerned, talk to your doctor or nurse.

If you stop the treatment with Dexamethasone phosphate Noridem
It can be dangerous to have your treatment with Dexamethasone phosphate Noridem stopped abruptly.
After prolonged therapy your body may have gotten used to the administration of this medicine and may have reduced the normal production of hormones like the one contained in this medicine.

How your treatment is stopped will depend on the disease you are being treated for and how much Dexamethasone phosphate Noridem you have been given.

It may be necessary to reduce the amount of Dexamethasone phosphate Noridem you are given gradually until you stop having it altogether. Your doctor has to make sure that the disease you have been treated for is unlikely to relapse. Dosage reduction must be adjusted if you are subjected to unusual stress (such as another illness, trauma or surgical procedures).

When the treatment is stopped too quickly, withdrawal symptoms like fever, muscle pain, joint pain and tiredness may occur. Too rapid a reduction following prolonged treatment can lead to insufficiency of hormone production in the adrenal gland and low blood pressure (symptoms of which can be tiredness, dizziness, headache, palpitation). In extreme cases this may be fatal.

In a few cases, mental health problems have occurred when doses are being lowered or stopped – see section 4.

Tell your doctor immediately if you suffer from any withdrawal symptoms.
If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

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

Some side effects can happen straight away while others may take weeks or months.
If you feel unwell in any way, keep receiving your medicine, but see your doctor straight away.

If you experience any of the following please contact your doctor immediately as you may need urgent medical attention:

- An allergic reaction which may include a sudden itchy rash, swelling of the extremeties (such as your hands and feet) and a swelling of your mouth and throat (which may cause difficulty in breathing
- If you experience sudden and (in cases of long-term therapy) unusual effects like a feeling you are going to faint, bleeding, extreme weakness, or a sudden pain in any of your organs,

The following unwanted side effects have been reported for dexamethasone and are listed below according to the organs that are affected.

Psychiatric disorders (mental health problems)
Steroids including dexamethasone can cause serious mental health problems.
These are common in both adults and children. They can affect about 5 in every 100 people taking medicines like dexamethasone.

- Feeling depressed, including thinking about suicide.
- Feeling high (mania) or moods that go up and down.
- Feeling anxious, having problems sleeping, difficulty in thinking or being confused and losing your memory.
- Feeling, seeing or hearing things which do not exist. Having strange and frightening thoughts, changing how you act or having feelings of being alone.

If you notice any of these problems talk to a doctor straight away.

Carers of patients receiving Dexamethasone phosphate Noridem should talk to a doctor immediately if the patient shows any signs of mental health problems. This is particularly important if the patient appears to be depressed, or mentions thoughts of suicide.
If you suffer from schizophrenia or epilepsy your symptoms may worsen.

Infections and infestations
You may experience more frequent and severe infections without noticing the symptoms as well as opportunistic infections (caused by a usually harmless microorganism in case of an impaired immune system) or the recurrence of dormant tuberculosis.

Abnormal growth of tissue
You may develop sterile abscesses (enclosed collections of pus, likely to turn into hard solid lumps as they scar).

Blood systems
There may be an abnormal increase in the number of white blood cells.

Hormonal (endocrine disorders)
Menstrual irregularities, lack of menstruation, abnormal hair growth, development of Cushingoid state (symptoms of which include central obesity with thin arms, thinning of the skin with easy bruising, muscle wasting and weakness, high blood pressure, uncontrolled blood sugar, osteoporosis).

Children and adolescents may have suppressed growth. Your response to stress caused by trauma, surgery or illness may be reduced. You may also experience decreased carbohydrate tolerance, onset of latent diabetes mellitus, increased need for insulin or other medicines if you are diabetic.

Metabolism and nutrition disorders
You may notice that you gain weight or have an increased appetite. Your body may also have difficulty in handling nitrogen, calcium, sodium or potassium appropriately.

Nervous system disorders
You may feel increased pressure in your head with impaired vision, vertigo, headache or in preterm infants cerebral palsy (malformation of the brain) may occur.

Eye disorders
You may develop cataracts or feel increased pressure in the eye or notice abnormal bulging out of the eyeballs or thinning of the cornea or the white, outer coat of the eyeball. Your vision may become blurred due to congestion of the optic disc or glaucoma with possible damage to the optic nerves. Secondary eye infections due to fungi or viruses can occur as can rare instances of blindness associated with local therapy around the face and head. Premature babies may suffer retinopathy. You may also develop visual disturbances or loss of vision (chorioretinopathy).

Disorders of the blood vessels or heart
High blood pressure, blood clots in the veins. Susceptible patients may develop heart failure, or the heart tissue may rupture following a recent heart attack. In infants with a low birth weight a heart muscle disease (hypertrophic cardiomyopathy) may occur.
If you are treated for multiple myeloma with dexamethasone in combination with lenalidomide or thalidomide you will have an increased risk of thromboembolic events including: Deep vein thrombosis (a blood clot in the veins of your leg) – a symptom of this is leg pain; Pulmonary embolism (a blood clot in the arteries leading to your lungs) – a symptom of this is chest pain or shortness of breath. Frequency 'Not known': Thickening of the heart muscle (hypertrophic cardiomyopathy) in prematurely born babies, that generally returns to normal after stopping treatment.

Disorders of the stomach or the digestive system
You may suffer nausea, hiccups, heartburn or reflux or infection or inflammation of the tube that leads to your stomach. Peptic ulcer may occur with possible bleeding or perforation of the small and large bowel (particularly if you have inflammatory bowel disease). Your pancreas may become inflamed (pancreatitis) or your stomach may swell.

Skin disorders
Your skin may become thin or fragile with red or blood spots or bruising or it may become lighter or darker (hypo- or hyperpigmentation). Your face may become unusually red or you may have acne, swelling around the eyes, mouth and hands, hives, allergic dermatitis or stretch marks. Wounds may take longer to heal, skin tests may be affected and you may sweat more. After injection into a vein you may feel a burning or tingling sensation especially in the perineal area (skin between anus and genital organs).

Muscle and bone disorders
You may suffer from muscle weakness, loss of muscle mass, osteoporosis (loss of bone density) especially if you are postmenopausal, vertebral compression fractures (collapsing of a bone in the spine), aseptic necrosis of femoral and humeral heads (severe knee and hip joint problem, possibly requiring replacement joints), fracture of long bones, tendon rupture, post-injection flare (following local injection e.g. into a joint).

Reproductive system
The number and activity of spermatozoa may be affected in men.

General disorders
You may have a general ill feeling.
Many of these side effects are serious therefore please tell your doctor about your symptoms as soon as possible.

Please note that it is very important that you do not suddenly stop taking this medicine (even if you are suffering from a side effect) unless your doctor tells you to (see *"If you stop the treatment with Dexamethasone phosphate Noridem"* in the previous section of this leaflet).
If you think this injection is causing you any problems, or you are at all worried, talk to your doctor, nurse or pharmacist.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via
For IE: HPRA Pharmacovigilance, Website: www.hpra.ie.
For CY: Pharmaceutical Services Ministry of Health, CY-1475, Nicosia, Tel:+ 357 608607, Fax: +357 22 608669, Website: www.moh.gov.cy/phs.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Dexamethasone phosphate Noridem

Keep this medicine out of the sight and reach of children.
Store below 25°C. Do not refrigerate or freeze.
Keep the ampoules in the outer carton in order to protect from light.
Do not use this medicine after the expiry date which is stated on the carton and ampoule after "EXP". The expiry date refers to the last day of that month.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Dexamethasone phosphate Noridem contains
- The active substance is dexamethasone phosphate. Each mL contains 4 mg of dexamethasone phosphate.
- The other excipients are disodium edetate, propylene glycol (E1520), water for injections and sodium hydroxide (*for pH adjustment*).

What Dexamethasone phosphate Noridem looks like and contents of the pack
Dexamethasone phosphate Noridem 4 mg/mL Solution for injection is a clear, colourless and sterile solution contained in clear glass ampoules.
Dexamethasone phosphate Noridem 4 mg/mL Solution for injection is available in 1 mL, 2 mL or 5 mL ampoules. Packs of 1, 5, 10, 20, 50 and 100 ampoules are available.

Not all pack sizes may be marketed.

Marketing Authorization Holder and Manufacturer
Marketing Authorisation Holder: Noridem Enterprises Ltd., Evagorou & Makariou, Mitsi Building 3, Office 115, 1065 Nicosia, Cyprus.
Manufacturer: DEMO S.A. PHARMACEUTICAL INDUSTRY, 21st Km National Road Athens-Lamia, 14568 Krioneri, Attiki, Greece,
T: +30 210 8161802, **F:** +30 210 8161587.

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

United Kingdom (Northern Ireland):	Dexamethasone 3.3 mg/mL Solution for injection
Hungary:	Dexametazon-foszfát Noridem 4 mg/ml, oldatos injekció
Cyprus:	Dexamethasone phosphate Noridem 4 mg/mL Ενέσιμο διάλυμα
Czech Republic:	Dexamethasone Noridem
Slovakia:	Dexamethasone Noridem
Greece:	Dexamethasone phosphate/DEMO 4 mg/mL Ενέσιμο διάλυμα
Ireland:	Dexamethasone phosphate Noridem 4 mg/mL Solution for injection

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given by intravenous infusion, 5 % w/v dextrose in water and 0.9 % w/v sodium chloride (9 mg/mL) 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. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
In use: Chemical and physical in-use stability has been demonstrated for 24 h at 25°C, protected from light, when diluted with the diluents stated above. Dilutions should be used within 24 hours and discarded after use. From a microbiological point of view, the product should be used immediately, while in use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled validated aseptic conditions.