Package leaflet: Information for the user

Lodotra 1 mgmodified-release tablets
Lodotra 2 mgmodified-release tablets
Lodotra 5 mgmodified-release tablets

Prednisone

Read all of this leaflet carefully before you start taking 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 pharmacist.
- 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 pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Lodotra is and what it is used for

Lodotra is a tablet with a delayed release behaviour of the active compound prednisone, which is a corticosteroid. Corticosteroids have an anti-inflammatory action. Anti-inflammatory medicines reduce pain, swelling, stiffness, redness and heat in affected joints.

Lodotra is used to treat:
- moderate to severe, active rheumatoid arthritis, particularly when accompanied by morning stiffness in adults

Lodotra tablets are modified-release tablets. This means that they are designed to release prednisone approximately 4 hours after swallowing. This allows you to take Lodotra at bedtime and feel an improvement in your early morning symptoms such as stiffness.

2. What you need to know before you take Lodotra

Do NOT take Lodotra if you are
- allergic to prednisone or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking Lodotra.

You must tell your doctor if you have (at the moment) or have had (in the past) any of the following conditions or treatments:
- too high a level of sugar (glucose) in your blood (diabetes). Your doctor may increase your diabetes medication and treat you under close monitoring

- weakened bones (osteoporosis)
- softened bones (osteomalacia)
- ulcers of the stomach and bowel
- severe ulcerative colitis (inflammation of the colon) with high risk of a perforation (hole) in the colon
- inflammation of the bowel (diverticulitis)
- immediately after a surgery to connect two parts of your bowel (entero-anastomosis).
- hepatitis B (a liver disease caused by a virus)
- tuberculosis (TB). A bacterial infection usually affecting the lungs
- swelling and inflammation of the lymph nodes after BCG vaccination (a vaccination against TB)
- polio (an infectious disease caused by a virus affecting the nervous system)
- approximately 8 weeks before and 2 weeks after a vaccination (if live vaccines were used)
- acute viral infection (e.g. chickenpox, lip or eye herpes, measles or shingles)
- acute bacterial infection (e.g. bacterial tonsillitis) or chronic bacterial infections (e.g. TB)
- acute fungal infection (e.g. thrush)
- parasitic infection (e.g. roundworms). In patients with known or suspected threadworm (Strongyloides) infestation Lodotra may lead to massive Strongyloides infection and widespread larval migration.
- high blood pressure. You may need more frequent blood pressure checks
- eye diseases (glaucoma). You may need closer monitoring of your conditions
- injuries or ulcers on the cornea (the transparent front of the eye that covers the iris and pupil)
- heart problems. You may need closer monitoring of your condition
- recent heart attack
- kidney disease
- mental illness
- sleep disorder occurs during the treatment and do not improve. In these situations a switch to a conventional immediate release formulation may be advisable.

Lodotra cannot achieve the desired blood concentration of prednisone if taken under fasting conditions. Therefore, Lodotra should always be taken with or after the evening meal in order to ensure sufficient efficacy. In addition, low plasma concentrations may occur in 6%-7% of Lodotra doses when taken according to the recommendations. This should be considered if Lodotra is not sufficiently effective. In these situations a switch to a conventional immediate-release formulation may be considered.

Lodotra should not be given as for acute indications instead of prednisone immediate-release tablets due to its pharmacological properties.
In one of the treatments or conditions above a different type of medicine may be more suitable for you. See also ‘Other things you should know about Lodotra’.

☞ **YOUR DOCTOR WILL ADVISE YOU ON WHAT TO DO.**

Other things you should know about Lodotra
Lodotra can affect your immune system. This affects your body’s ability to fight disease. If your immune system is affected:

- vaccination with an inactivated vaccine (e.g. flu or cholera vaccines) may not be as effective if you are taking, or start taking Lodotra
- certain viral diseases (chicken pox and measles) may be more severe. You are at particular risk if you have not been vaccinated against these diseases
- you may be at a greater risk of other severe infections.

Your treatment with Lodotra may make you more likely to develop an infection. If you are developing an infection, it may be more difficult to be detected while you are taking Lodotra.

You may need a smaller dose of Lodotra if you have:
- hypothyroidism (an underactive thyroid gland)
- cirrhosis of the liver (liver disease caused by alcoholism or hepatitis).

You may need a higher dose of Lodotra during stressful events such as:
- a surgical procedure
- during infection.

If you take Lodotra for several months or more, your doctor will carry out regular check-ups including:
- eye examination
- blood test
- blood pressure check.

Treatment with Lodotra may have a negative effect on the way calcium is metabolised in your bones. Therefore, you should clarify with your doctor the risk of osteoporosis (bone loss and fractures), particularly if you have family members who have a history of bone fractures, you do not take exercise regularly, you are a woman during or after menopause or if you are elderly.

When stopping Lodotra there is a risk of:
- the symptoms of your rheumatoid arthritis returning
- adrenal failure. This is when your adrenal gland does not produce enough cortisol (a hormone). This is especially likely in stressful situations such as:
  - during infections
  - after accidents
  - when you are under increased physical strain
- cortisone withdrawal syndrome (a serious illness caused by your body not producing cortisol).

☞ **YOUR DOCTOR WILL ADVISE YOU ON WHAT TO DO.**

Other medicines and Lodotra
Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines.

<u>The effects of the following medicines may be increased by your Lodotra treatment:</u>
- heart medication such as cardiac glycosides (e.g. digoxin)
- laxatives or salt depleting drugs such as some diuretics (water tablets)
- cyclosporine, a drug used after transplant surgery or occasionally in severe rheumatoid arthritis
- muscle relaxants, such as suxamethonium, used in hospitals
- cyclophosphamide, a treatment for various types of cancer.

<u>The effects of the following medicines may be decreased by your Lodotra treatment:</u>
- somatropin, a growth hormone
- praziquantel, a treatment for parasitic infections
- diabetes medicines, e.g. insulin, metformin, glibenclamide.

<u>The following medicines may reduce the effect of Lodotra on your rheumatoid arthritis symptoms:</u>
- treatments for epilepsy such as barbiturates, phenytoin and primidone
- rifampicin, a treatment for infection
- bupropion, a treatment for depression
- aluminium and magnesium antacids.

The following medicines may increase the effect of Lodotra on your rheumatoid arthritis symptoms:

- oestrogen containing medicines, for example oral contraceptives, Hormone Replacement Therapy (HRT)
- liquorice (used as an expectorant in cough medicines and also present in confectionery).

Other effects of medicines:

- non-steroidal anti-inflammatory drugs (NSAIDs) such as acetylsalicylic acid, diclofenac and ibuprofen increase the risk of gastrointestinal bleeding
- warfarin may have reduced or increased blood thinning effects depending upon the individual
- treatment with ACE inhibitors (e.g. captopril or enalapril) for high blood pressure or heart failure may increase the risk of changes in the numbers of blood cells
- anticholinergic medicines (e.g. atropine) may increase the risk of raised pressure in the eye (glaucoma)
- medications to treat or prevent malaria (e.g. chloroquine, hydroxychloroquine, mefloquine) may increase the risk of muscle weakness, including heart muscle weakness
- amphotericine B, an antifungal drug, may increase the risk of hypokalaemia
- some diagnostic tests may be affected, for example:
  - skin tests for allergies
  - a blood test to measure your levels of a hormone produced by the thyroid gland.

☞ **YOUR DOCTOR WILL ADVISE YOU ON WHAT TO DO.**

Lodotra with food and drink
Take your Lodotra in the evening usually around 10 pm. Ideally, you should take your tablets with or after your evening meal. You should swallow the tablets whole, with sufficient liquid, e.g. glass of water.
You should NOT break, divide or chew the tablets.
If more than 2-3 hours have passed since eating, you should take Lodotra with a light meal or snack.

Pregnancy and breast-feeding

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

Driving and using machines
Lodotra is unlikely to affect your ability to drive or using machines. However, if you develop eye pain or a blurred vision during the treatment, you should avoid these activities.

Lodotra contains lactose
The medicinal product contains a sugar called lactose. If you have been told that you have an intolerance to some sugars, contact your doctor before taking Lodotra.

3. How to take Lodotra

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The dose of Lodotra your doctor will prescribe will depend on the severity of your disease. This should not usually be more than 10 mg prednisone per day.

Your starting dose can be reduced on your doctor's advice in steps to a lower maintenance dose depending on:

- your rheumatoid arthritis symptoms
- your response to Lodotra.

For doses not realisable/practicable with this strength other strengths of this medicinal product are also available.

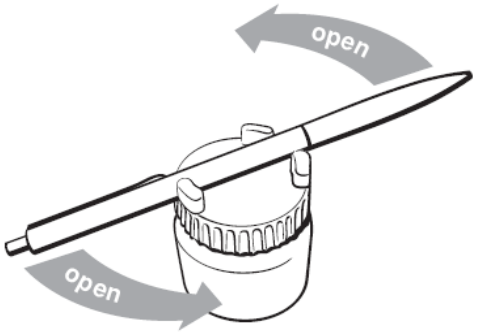
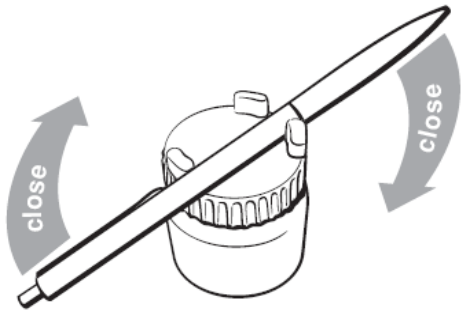
If you are changing over from taking standard corticosteroid tablets in the morning to taking Lodotra in the evening, your dose should contain the same amount of active substance (prednisone).

Method of administration:

- How to open and close the Lodotra bottle especially designed for rheumatoid arthritis patients: see "Directions for opening and closing the container"
- Take the number of tablets that your doctor has told you
- Do not break the tablet as the coating is important for Lodotra to work properly
- Swallow the tablets whole: Do not break, divide or chew the tablets
- Take Lodotra in the evening (usually at about 10 pm) with a glass of water
- You should take Lodotra with or after the evening meal. If more than 2 - 3 hours have passed since eating, take the tablet with a light meal or snack
- Always take the tablets after dinner or a light snack.

Lodotra modified-release tablets are usually taken for several months or longer. Your doctor will talk to you about how long you need to take your tablets.

Directions for opening and closing the container:
Please follow the instructions below:

	
To Open Place pen or similar object between the raised sections of the lid and turn in the direction shown (anticlockwise).	To Close Place pen or similar object between the raised sections of the lid and turn in the direction shown (clockwise).

If you take more Lodotra than you should
Acute intoxications with Lodotra are not known. In case of overdosing, you are likely to experience an increase in undesirable effects including:

- disturbances in hormone function
- effects on your metabolism
- effects on your electrolyte (salt) balance, leading to increased risk of abnormal heartbeats.

☞ **CONTACT YOUR DOCTOR IF YOU ARE CONCERNED OR EXPERIENCE AN INCREASE IN ADVERSE EFFECTS.**

If you forget to take Lodotra

☞ **YOU SHOULD CONTACT YOUR DOCTOR ON HOW TO PROCEED**

If you stop taking Lodotra
Do not suddenly stop taking your Lodotra modified-release tablets.
If you stop taking Lodotra your rheumatoid arthritis symptoms may return.
It is important that your Lodotra dose is reduced slowly. Your doctor will advise you how to reduce your dose gradually.
Lodotra should not be substituted by prednisone immediate-release tablets without first talking to your doctor.

☞ **IF YOU HAVE ANY FURTHER QUESTIONS ON THE USE OF THIS MEDICINE, ASK YOUR DOCTOR OR PHARMACIST.**

4. Possible side effects

Like all medicines, this medicine can cause side effects although not everybody gets them.
The frequency and severity of the undesirable effects listed below depend on dosage and duration of treatment.

Common side effects of Lodotra (may affect up to 1 in 10 people):
A hormone imbalance causing Cushing's syndrome (typical symptoms: a round face often called a 'moon face', upper body weight gain and rash on the face) as well as a reduced production of glucocorticoids in the body.

Disturbances of the balance of sugars, fats and salts in the body possibly resulting in:
- increased appetite and weight gain
- diabetes
- high cholesterol
- heart rhythm disturbances (because of increased potassium excretion)
- accumulation of water (oedema, because of reduced sodium excretion).

Reduced ability to fight infections. Infections may be more severe or the symptoms may be masked. Increases susceptibility to and severity of infections. Clouding of the lens (cataract) and increased pressure in the eye (glaucoma) with or without eye pain. Stretch marks, bruising or red marks on the skin or in the mouth, wasting of the skin. An increase or decrease in the number of blood cells. Muscle wasting and weakness, bone wasting resulting in an increased risk of bone fractures (osteoporosis). Headache. Sleeping difficulties.

Uncommon side effects of Lodotra (may affect up to 1 in 100 people):
- High blood pressure
- Thickening or inflammation of the lining of the blood vessels and blood clots
- Stomach ulcers and bleeding in the bowel
- Increased hair growth, spots and other skin blemishes and delayed healing of skin wounds, acne.

Rare side effects of Lodotra (may affect up to 1 in 1,000 people):
- Allergic reactions including blistering on the skin
- Inflammation of the pancreas causing severe abdominal pain
- Disturbances in sex hormone secretion, possibly resulting in absence of monthly periods in women or impotence in men
- Disturbance of the thyroid function
- Depression (feeling sad), irritability, feelings of happiness that are not justified by reality, increased impulse, loss of contact with reality (psychosis)
- Increased pressure in the head resulting in headache, vomiting and double vision

- Development or worsening of epileptic fits
- Worsening of existing eye ulcers or infections
- Loss of bone (osteonecrosis).

Side effects of Lodotra where the frequency is not known (frequency cannot be estimated from the available data):

- Reversible fat overgrowth in the spine, heart or chest (lipomatosis).
- Accelerated heart beat
- Acid-base imbalance in the blood due to low potassium level (hypokalaemic alkalosis)
- Leakage of fluid under the retina resulting in visual distortion (central serous chorioretinopathy
- Nausea, diarrhea, vomiting
- Extra hair growth in women (hirsutism)
- Muscle wasting of the upper arms and legs, tendon rupture, vertebral and long bone fractures

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

Pharmacovigilance Section
Irish Medicines Board
Kevin O'Malley House
Earlsfort Centre
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6767836
Website: www.imb.ie
e-mail: imbpharmacovigilance@imb.ie

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

5. How to store Lodotra

- Keep this medicine out of the sight and reach of children
- Do not use this medicine after the expiry date which is stated on the bottle and the carton. The expiry date refers to the last day of that month
- After first opening the container, the tablets can be stored in the bottle for up to 14 weeks. After that time, dispose of the remaining tablets
- Do not store above 25°C
- 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 Lodotra contains
The active substance is prednisone.
One Lodotra 1 mg modified-release tablet contains 1 mg of prednisone.
One Lodotra 2 mg modified-release tablet contains 2 mg of prednisone.
One Lodotra 5 mg modified-release tablet contains 5 mg of prednisone.

The other ingredients are:
Tablet core: **Tablet shell:**

- Colloidal anhydrous silica
- Croscarmellose sodium
- Lactose monohydrate
- Magnesium stearate
- Povidone K 29/32
- Red ferric oxide E 172.

- Colloidal anhydrous silica
- Calcium hydrogen phosphate dihydrate
- Glycerol dibehenate
- Magnesium stearate
- Povidone K 29/32
- Yellow ferric oxide E 172.

What Lodotra looks like and contents of the pack
Lodotra 1 mg modified-release tablets are pale yellowish-white, cylindrical with 'NP1' embossed on one side.
Lodotra 2 mg modified-release tablets are yellowish-white, cylindrical with 'NP2' embossed on one side.
Lodotra 5 mg modified-release tablets are light yellow, cylindrical with 'NP5' embossed on one side.

Pack sizes: Bottles with 30 and 100 modified-release tablets.
Hospital packs: Bottles with 30, 100 and 500 modified-release tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Mundipharma Pharmaceuticals Ltd., Millbank House, Arkle Road, Sandyford, Dublin 18, Ireland.

Manufacturer
HORIZON Pharma GmbH, Joseph-Meyer-Str. 13-15, 68167 Mannheim, Germany.

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

Austria	Lodotra 1 mg/2 mg/5 mg Tabletten mit verzögerter Wirkstofffreisetzung
Belgium	Lodotra 1 mg/2 mg/5 mg tabletten met gereguleerde afgifte/comprimé à libération modifiée/Tabletten mit verzögerter Wirkstofffreisetzung
Bulgaria	Лодотра 1 mg/2 mg/5 mg таблетки с изменено освобождаване
Cyprus	Lodotra 1 mg/2 mg/5 mg δισκία ελεγχόμενης αποδέσμευσης
Czech Republic	Lodotra 1 mg/2 mg/5 mg tablety s řízeným uvolňováním
Denmark	Lodotra 1 mg/2 mg/5 mg tabletter med modificeret udløsning
Estonia	Lodotra 1 mg/2 mg/5 mg toimeainet modifitseeritult vabastav tabletid
Finland	Lodotra 1 mg/2 mg/5 mg depottabletit
France	Lodotra 1 mg/2 mg/5 mg comprimé à libération modifiée
Germany	Lodotra 1 mg/2 mg/5 mg Tabletten mit verzögerter Wirkstofffreisetzung
Greece	Lodotra 1 mg/2 mg/5 mg δισκία ελεγχόμενης αποδέσμευσης
Hungary	Lodotra 1 mg/2 mg/5 mg módosított hatóanyagleadású tabletta
Iceland	Lodotra 1 mg/2 mg/5 mg töflur með breyttan losunarhraða
Italy	Lodotra 1 mg/2 mg/5 mg compresse a rilascio modificato
Ireland	Lodotra 1 mg/2 mg/5 mg modified-release tablets
Latvia	Lodotra 1 mg/2 mg/5 mg ilgstošās darbības tabletes
Lithuania	Lodotra 1 mg/2 mg/5 mg modifikuoto atpalaidavimo tabletės
Luxembourg	Lodotra 1 mg/2 mg/5 mg tabletten met gereguleerde afgifte/comprimé à libération modifiée/Tabletten mit verzögerter Wirkstofffreisetzung
Malta	Lodotra 1 mg/2 mg/5 mg modified-released tablets
Netherlands	Lodotra 1 mg/2 mg/5 mg tabletten met gereguleerde afgifte
Norway	Lodotra 1 mg/2 mg/5 mg tabletter med modifisert frisetting
Poland	Lodotra 1 mg/2 mg/5 mg tabletki o zmodyfikowanym uwalnianiu

Portugal	Lodotra 1 mg/2 mg/5 mg comprimidos de libertação modificada
Romania	Lodotra 1 mg/2 mg/5 mg comprimate cu eliberare modificată
Sweden	Lodotra 1 mg/2 mg/5 mg tabletter med modifierad frisättning
Slovak Republic	Lodotra 1 mg/2 mg/5 mg tablety s riadeným uvoľňovaním
Slovenia	Lodotra 1 mg/2 mg/5 mg tablete s prirejenim sproščanjem
Spain	Lodotra 1 mg/2 mg/5 mg comprimidos de liberación modificada
United Kingdom	Lodotra 1 mg/2 mg/5 mg modified-released tablets

This leaflet was last revised in {MM/YYYY}.