Package leaflet: Information for the patient

PLENADREN® 5 mg modified-release tablets

(hydrocortisone)

Your medicine is known by the above name, but will be referred to as "PLENADREN" throughout this leaflet. Please note that the leaflet also contains information about other strengths (PLENADREN® 20 mg modified-release tablets).

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 PLENADREN IS AND WHAT IT IS USED FOR

PLENADREN contains a substance called hydrocortisone (sometimes called cortisol). Hydrocortisone is a glucocorticoid. It belongs to a group of medicines called corticosteroids. Glucocorticoids occur naturally in the body, and help to maintain your general health and well-being.

PLENADREN is used in adults to treat a condition known as adrenal insufficiency, or cortisol deficiency. Adrenal insufficiency occurs when your adrenal glands (just above your kidneys) do not produce enough of the hormone cortisol. Patients suffering from long-term (chronic) adrenal insufficiency need a replacement therapy to survive.

PLENADREN replaces the natural cortisol that is missing in adrenal insufficiency. The medicine delivers hydrocortisone to your body throughout the day. The cortisol levels in your blood increase rapidly to a maximum level, about 1 hour after taking the tablet in the morning, and then gradually decrease over the day with no or almost no cortisol level in the blood in the late evening and night when the levels should be low.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE PLENADREN

Do not take PLENADREN
- if you are allergic to hydrocortisone or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or pharmacist before taking PLENADREN
- when you have a condition that makes you unable to take this medicine or when the medicine is not absorbed properly from your stomach. This may happen when you have stomach problems involving vomiting and/or diarrhoea. In these situations you should seek immediate medical care in order to receive treatment with injections of hydrocortisone and extra fluid administration.
- if you have short-term or temporary illness such as infections, fever or situations causing a great amount of physical stress, such as surgery: your dose of hydrocortisone must be temporarily increased. Ask your doctor promptly for information on how you should handle these situations. If you are to have surgery, tell your doctor/dentist before the surgery that you are taking this medicine.
- if for any other reason your general health is declining although you take your medicine as prescribed; seek immediate medical care.
- if you have pheochromocytoma (a rare tumour of the adrenal glands).
- if your thyroid gland is not working normally tell your doctor since your dose of PLENADREN may need to be adjusted.

Children and adolescents

PLENADREN is not recommended for use in children and adolescents under 18 years old as it has not been studied in these patients.

Other medicines and PLENADREN

Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. During long term treatment with medicines treating infections (antibiotics) the dose of PLENADREN may need adjustment by your doctor. If used with mifepristone, a treatment used to end a pregnancy, the effect of PLENADREN may be reduced.

In addition, tell your doctor or pharmacist if you are using any of the following medicines, as the dose of PLENADREN may need to be changed:
- Phenytoin, carbamazepine and barbiturates - used to treat epilepsy
- Rifampicin or rifabutin - used to treat tuberculosis
- Ritonavir, efavirenz and nevirapine – used to treat HIV infection
- St. John's wort - used to treat depression and other conditions
- Ketoconazole, itraconazole, posaconazole and voriconazole - used to treat fungal infections
- Erythromycin, telithromycin and clarithromycin - used to treat bacterial infections

PLENADREN with food and drink

Do not take this medicine with grapefruit juice as the juice will conflict with the action of this medicine.

Pregnancy, breast-feeding 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 pharmacist for advice before taking this medicine.

It is important that you continue treatment with PLENADREN during pregnancy. Treatment in pregnant women with adrenal insufficiency is unlikely to cause any harmful effects on the mother and/or the baby. You should tell your doctor if you become pregnant as the dose of PLENADREN may have to be adjusted.

You can breast-feed during PLENADREN treatment. Hydrocortisone is excreted in breast milk. Doses of hydrocortisone used for replacement therapy are unlikely to have any effect on the child. However, talk to your doctor if you plan to breast-feed your baby.

Fertility in women with adrenal insufficiency or cortisol deficiency may be reduced. There is no indication that PLENADREN, in doses used for replacement therapy, will have an effect on fertility.

Driving and using machines

This medicine may have minor influence on your ability to drive and use machines. Extreme tiredness and episodes of short-lasting dizziness (vertigo) have been reported. Poorly treated or untreated adrenal insufficiency reduces your ability to concentrate and will affect your ability to drive and use machines. It is therefore important to take this medicine as directed by your doctor when driving or using machines. If you are affected do not drive or use machines, until you have discussed the issue with your doctor.

3. HOW TO TAKE PLENADREN

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 is specific for you and is decided by your doctor.
- When you wake up in the morning swallow PLENADREN tablets whole with a glass of water at least 30 minutes before your breakfast, preferable between 6.00 am and 8.00 am in the morning.
- You should preferably be in an upright position.
- Do not divide, crush or chew the tablets. These tablets deliver hydrocortisone to your body throughout the day. If divided, crushed or chewed this may prevent the hydrocortisone dose in the tablet to cover the whole day, as it should.

The need for additional doses of PLENADREN

During short-term or temporary illnesses such as infection, fever, or physical stress such as surgery you will need more hydrocortisone since the body cannot produce the additional amount of cortisol required in these situations. The dose must therefore be increased temporarily and your doctor may advise you to use other hydrocortisone tablets instead of, or in addition to PLENADREN. Please discuss this with your doctor and follow the instructions on how to act in these situations.

The daily dose of PLENADREN may have to be doubled or tripled in milder conditions such as a mild infection or stress. You should then take the second dose of this medicine 6 to 10 hours after the morning dose. If it is not enough to double the daily dose, you should take a third dose 6 to 10 hours after the second dose (6-10 hour intervals between doses). When your illness is over, return to your normal maintenance dose of this medicine.

The following signs and symptoms may suggest that you need to take additional doses of PLENADREN or other forms of hydrocortisone: fatigue, weight loss, stomach discomfort, feeling light headed when you change from sitting to standing or dizziness when standing, darkening of your skin particularly skin creases and exposed areas. Contact your doctor promptly for advice if you notice any of these.

However, **seek immediate medical help** if you notice any of the following: severe weakness, fainting, abdominal pain, nausea, vomiting, back pain, confusion, reduced consciousness, delirium (very confused state).

If you take more PLENADREN than you should
A too high dose of this medicine for more than a few days may be harmful to your health. Your blood pressure may increase, you may gain extra weight and your blood sugar may become too high. An increased dose is necessary occasionally in order for the body to cope with increased stress such as fever. If extra doses are needed frequently and regularly, you should contact your doctor for re-evaluation of your maintenance dose.

If you forget to take PLENADREN
If you have forgotten to take your tablet in the morning, take it as soon as possible thereafter. Do not take a double dose to make up for a forgotten dose. If you experience any signs or symptoms listed in the section "The need for additional doses of PLENADREN", contact your doctor immediately.

If you stop taking PLENADREN
Stopping PLENADREN may be life threatening. It is therefore important to continue taking this medicine as prescribed by your doctor. Do not stop taking it without consulting 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.

If you are changing treatment from other hydrocortisone tablets to PLENADREN you may experience side effects during the first weeks. These side effects can be: stomach pain, feeling sick and tiredness. They will normally disappear with time, if not contact your doctor.

Side effects of this medicine are:

Very common (may affect more than 1 in 10 people)
- Dizziness
- Headache
- Diarrhoea
- Tiredness

Common (may affect up to 1 in 10 people)
- Stomach pain/heartburn, feeling sick or nauseated
- Pain in the joints
- Rash
- Itchiness

Additional side effects have been reported for other hydrocortisone medicines. These medicines have also been given for other indications than adrenal insufficiency replacement therapy, often in higher doses. Frequencies of these possible side effects are not known (frequency cannot be estimated from the available data). Talk to your doctor if you experience any of these side effects:
- More prone to infection
- Diabetes or problems with blood sugar levels (shown in blood tests)
- Salt and water retention causing swelling and raised blood pressure (shown on medical examination) and low potassium level in the blood
- Mood changes such as feelings of overexcitement or losing touch with reality
- Difficulty sleeping
- Raised pressure in the eye (glaucoma), clouding of the lens in the eye (cataract)
- Heartburn, aggravation of any existing stomach ulcer
- Weakening of the bones - this may cause bone fractures
- Stretch marks, bruising, acne-like rash, excessive growth of facial hair, slow wound healing.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE PLENADREN

- **Keep out of the sight and reach of children.**
- Do not use this medicine after the expiry date which is stated on the bottle label and carton after EXP. The expiry date refers to the last day of that month.
- This medicine does not require any special storage conditions.
- 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 to protect the environment.
- If your medicine becomes discoloured or shows signs of any deterioration, consult your doctor or pharmacist who will tell you what to do.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What PLENADREN contains
- The active substance is hydrocortisone.
  Each modified-release tablet contains 5 mg of hydrocortisone.
- The other ingredients are hypromellose (E464), microcrystalline cellulose (E460), pregelatinised maize starch, colloidal anhydrous silica and magnesium stearate. The coating system is a mixture of macrogol (3350), polyvinyl alcohol, talc (E553b) and titanium oxide (E171). The tablets also contain yellow iron oxide (E172), red iron oxide (E172) and black iron oxide (E172).

What PLENADREN looks like and contents of the pack
The modified-release tablets are round (diameter 8 mm) and convex.
The tablets are pink.
PLENADREN comes in bottles with a screw cap containing 50 tablets.

Pack size:
Carton containing one bottle of 50 modified-release tablets.

PLGB: 15814/1871 **POM**

Manufacturer: Takeda Pharmaceuticals International AG Ireland Branch, Block 3 Miesian Plaza, 50 – 58 Baggot Street Lower, Dublin 2, Ireland.

Procured from within the EU and repackaged by the Product Licence holder: O.P.D. Laboratories Ltd., Colonial Way, Watford, Herts WD24 4PR.

Leaflet revision and issue date (Ref.): 20.02.2024
PLENADREN is a registered trademark of Takeda Pharma AB.

To request a copy of this leaflet in Braille, large print or audio please call 01923 332 796.

Package leaflet: Information for the patient

Nantrin 5 mg modified-release tablets

(hydrocortisone)

Your medicine is known by the above name, but will be referred to as "Nantrin" throughout this leaflet.
Please note that the leaflet also contains information about other strengths (Nantrin® 20 mg modified-release tablets).

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 NANTRIN IS AND WHAT IT IS USED FOR

Nantrin contains a substance called hydrocortisone (sometimes called cortisol). Hydrocortisone is a glucocorticoid. It belongs to a group of medicines called corticosteroids. Glucocorticoids occur naturally in the body, and help to maintain your general health and well-being.

Nantrin is used in adults to treat a condition known as adrenal insufficiency, or cortisol deficiency. Adrenal insufficiency occurs when your adrenal glands (just above your kidneys) do not produce enough of the hormone cortisol. Patients suffering from long-term (chronic) adrenal insufficiency need a replacement therapy to survive.

Nantrin replaces the natural cortisol that is missing in adrenal insufficiency. The medicine delivers hydrocortisone to your body throughout the day. The cortisol levels in your blood increase rapidly to a maximum level, about 1 hour after taking the tablet in the morning, and then gradually decrease over the day with no or almost no cortisol level in the blood in the late evening and night when the levels should be low.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE NANTRIN

Do not take Nantrin
- if you are allergic to hydrocortisone or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking Nantrin
- when you have a condition that makes you unable to take this medicine or when the medicine is not absorbed properly from your stomach. This may happen when you have stomach problems involving vomiting and/or diarrhoea. In these situations you should seek immediate medical care in order to receive treatment with injections of hydrocortisone and extra fluid administration.
- if you have short-term or temporary illness such as infections, fever or situations causing a great amount of physical stress, such as surgery: your dose of hydrocortisone must be temporarily increased. Ask your doctor promptly for information on how you should handle these situations. If you are to have surgery, tell your doctor/dentist before the surgery that you are taking this medicine.
- if for any other reason your general health is declining although you take your medicine as prescribed; seek immediate medical care.
- if you have pheochromocytoma (a rare tumour of the adrenal glands).
- if your thyroid gland is not working normally tell your doctor since your dose of PLENADREN may need to be adjusted.

Children and adolescents
Nantrin is not recommended for use in children and adolescents under 18 years old as it has not been studied in these patients.

Other medicines and Nantrin
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. During long term treatment with medicines treating infections (antibiotics) the dose of Nantrin may need adjustment by your doctor. If used with mifepristone, a treatment used to end a pregnancy, the effect of Nantrin may be reduced.

In addition, tell your doctor or pharmacist if you are using any of the following medicines, as the dose of Nantrin may need to be changed:
- Phenytoin, carbamazepine and barbiturates - used to treat epilepsy
- Rifampicin or rifabutin - used to treat tuberculosis
- Ritonavir, efavirenz and nevirapine – used to treat HIV infection
- St. John's wort - used to treat depression and other conditions
- Ketoconazole, itraconazole, posaconazole and voriconazole - used to treat fungal infections
- Erythromycin, telithromycin and clarithromycin - used to treat bacterial infections

Nantrin with food and drink
Do not take this medicine with grapefruit juice as the juice will conflict with the action of this medicine.

Pregnancy, breast-feeding 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 pharmacist for advice before taking this medicine.

It is important that you continue treatment with Nantrin during pregnancy. Treatment in pregnant women with adrenal insufficiency is unlikely to cause any harmful effects on the mother and/or the baby. You should tell your doctor if you become pregnant as the dose of Nantrin may have to be adjusted.

You can breast-feed during Nantrin treatment. Hydrocortisone is excreted in breast milk. Doses of hydrocortisone used for replacement therapy are unlikely to have any effect on the child. However, talk to your doctor if you plan to breast-feed your baby.

Fertility in women with adrenal insufficiency or cortisol deficiency may be reduced. There is no indication that Nantrin, in doses used for replacement therapy, will have an effect on fertility.

Driving and using machines
This medicine may have minor influence on your ability to drive and use machines. Extreme tiredness and episodes of short-lasting dizziness (vertigo) have been reported. Poorly treated or untreated adrenal insufficiency reduces your ability to concentrate and will affect your ability to drive and use machines. It is therefore important to take this medicine as directed by your doctor when driving or using machines. If you are affected do not drive or use machines, until you have discussed the issue with your doctor.

3. HOW TO TAKE NANTRIN

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 is specific for you and is decided by your doctor.
- When you wake up in the morning swallow Nantrin tablets whole with a glass of water at least 30 minutes before your breakfast, preferable between 6.00 am and 8.00 am in the morning.
- You should preferably be in an upright position.
- Do not divide, crush or chew the tablets. These tablets deliver hydrocortisone to your body throughout the day. If divided, crushed or chewed this may prevent the hydrocortisone dose in the tablet to cover the whole day, as it should.

The need for additional doses of Nantrin
During short-term or temporary illnesses such as infection, fever, or physical stress such as surgery you will need more hydrocortisone since the body cannot produce the additional amount of cortisol required in these situations. The dose must therefore be increased temporarily and your doctor may advise you to use other hydrocortisone tablets instead of, or in addition to Nantrin. Please discuss this with your doctor and follow the instructions on how to act in these situations.

The daily dose of Nantrin may have to be doubled or tripled in milder conditions such as a mild infection or stress. You should then take the second dose of this medicine 6 to 10 hours after the morning dose. If it is not enough to double the daily dose, you should take a third dose 6 to 10 hours after the second dose (6-10 hour intervals between doses). When your illness is over, return to your normal maintenance dose of this medicine.

The following signs and symptoms may suggest that you need to take additional doses of Nantrin or other forms of hydrocortisone: fatigue, weight loss, stomach discomfort, feeling light headed when you change from sitting to standing or dizziness when standing, darkening of your skin particularly skin creases and exposed areas. Contact your doctor promptly for advice if you notice any of these.

However, **seek immediate medical help** if you notice any of the following: severe weakness, fainting, abdominal pain, nausea, vomiting, back pain, confusion, reduced consciousness, delirium (very confused state).

If you take more Nantrin than you should
A too high dose of this medicine for more than a few days may be harmful to your health. Your blood pressure may increase, you may gain extra weight and your blood sugar may become too high. An increased dose is necessary occasionally in order for the body to cope with increased stress such as fever. If extra doses are needed frequently and regularly, you should contact your doctor for re-evaluation of your maintenance dose.

If you forget to take Nantrin
If you have forgotten to take your tablet in the morning, take it as soon as possible thereafter. Do not take a double dose to make up for a forgotten dose. If you experience any signs or symptoms listed in the section "The need for additional doses of Nantrin", contact your doctor immediately.

If you stop taking Nantrin
Stopping Nantrin may be life threatening. It is therefore important to continue taking this medicine as prescribed by your doctor. Do not stop taking it without consulting 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.

If you are changing treatment from other hydrocortisone tablets to Nantrin you may experience side effects during the first weeks. These side effects can be: stomach pain, feeling sick and tiredness. They will normally disappear with time, if not contact your doctor.

Side effects of this medicine are:

Very common (may affect more than 1 in 10 people)
- Dizziness
- Headache
- Diarrhoea
- Tiredness

Common (may affect up to 1 in 10 people)
- Stomach pain/heartburn, feeling sick or nauseated
- Pain in the joints
- Rash
- Itchiness

Additional side effects have been reported for other hydrocortisone medicines. These medicines have also been given for other indications than adrenal insufficiency replacement therapy, often in higher doses. Frequencies of these possible side effects are not known (frequency cannot be estimated from the available data). Talk to your doctor if you experience any of these side effects:
- More prone to infection
- Diabetes or problems with blood sugar levels (shown in blood tests)
- Salt and water retention causing swelling and raised blood pressure (shown on medical examination) and low potassium level in the blood
- Mood changes such as feelings of overexcitement or losing touch with reality
- Difficulty sleeping
- Raised pressure in the eye (glaucoma), clouding of the lens in the eye (cataract)
- Heartburn, aggravation of any existing stomach ulcer
- Weakening of the bones - this may cause bone fractures
- Stretch marks, bruising, acne-like rash, excessive growth of facial hair, slow wound healing.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE NANTRIN

- **Keep out of the sight and reach of children.**
- Do not use this medicine after the expiry date which is stated on the bottle label and carton after EXP. The expiry date refers to the last day of that month.
- This medicine does not require any special storage conditions.
- 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 to protect the environment.
- If your medicine becomes discoloured or shows signs of any deterioration, consult your doctor or pharmacist who will tell you what to do.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Nantrin contains
- The active substance is hydrocortisone.
  Each modified-release tablet contains 5 mg of hydrocortisone.
- The other ingredients are hypromellose (E464), microcrystalline cellulose (E460), pregelatinised maize starch, colloidal anhydrous silica and magnesium stearate. The coating system is a mixture of macrogol (3350), polyvinyl alcohol, talc (E553b) and titanium oxide (E171). The tablets also contain yellow iron oxide (E172), red iron oxide (E172) and black iron oxide (E172).

What Nantrin looks like and contents of the pack
The modified-release tablets are round (diameter 8 mm) and convex.
The tablets are pink.
Nantrin comes in bottles with a screw cap containing 50 tablets.

Pack size:
Carton containing one bottle of 50 modified-release tablets.

PLGB: 15814/1871 **POM**

Manufacturer: Takeda Pharmaceuticals International AG Ireland Branch, Block 3 Miesian Plaza, 50 – 58 Baggot Street Lower, Dublin 2, Ireland.

Procured from within the EU and repackaged by the Product Licence holder: O.P.D. Laboratories Ltd., Colonial Way, Watford, Herts WD24 4PR.

Leaflet revision and issue date (Ref.): 20.02.2024

To request a copy of this leaflet in Braille, large print or audio please call 01923 332 796.