Package leaflet: Information for the patient

NATRIXAM 1.5 mg / 5 mg modified-release tablets
NATRIXAM 1.5 mg / 10 mg modified-release tablets

indapamide / amlodipine

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 Natrixam is and what it is used for

Natrixam is prescribed as substitution treatment of high blood pressure (hypertension) in patients already taking indapamide and amlodipine from separate tablets in the same strength.

Natrixam is a combination of two active ingredients, indapamide and amlodipine.
Indapamide is a diuretic. Diuretics increase the amount of urine produced by the kidneys. However, indapamide is different from other diuretics, as it only causes a slight increase in the amount of urine produced. Amlodipine is a calcium antagonist (which belongs to a class of medicines called dihydropyridines) and it works by relaxing blood vessels, so that blood passes through them more easily. Each of the active ingredients reduces blood pressure.

2. What you need to know before you take Natrixam

Do not take Natrixam
- if you are allergic to indapamide or any other sulfonamide (class of medicinal product for the treatment of hypertension), or to amlodipine or any other calcium antagonist (class of medicinal produt for the treatment of hypertension) or to any of the other ingredients of this medicine (listed in section 6)). This may be itching, reddening of the skin or difficulty in breathing,
- if you have severe low blood pressure (hypotension),
- if you have narrowing of the aortic heart valve (aortic stenosis) or cardiogenic shock (a condition where your heart is unable to supply enough blood to the body),
- if you suffer from heart failure after a heart attack,
- if you have severe kidney disease,
- if you have severe liver disease or suffer from a condition called hepatic encephalopathy (disease of the brain caused by liver illness),
- if you have low potassium levels in your blood,
- if you are breastfeeding.

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

You should inform your doctor if you have or have had any of the following conditions:
- recent heart attack,
- if you have heart failure, any heart rhythm problems, if you have coronary artery disease (heart disease caused by poor blood flow in the blood vessels of the heart),
- if you have problems with your kidneys,
- severe increase in blood pressure (hypertensive crisis),
- you are elderly and your dose needs to be increased,
- if you take other medicines,
- if you are malnourished,
- if you have liver problems,
- if you have diabetes,
- if you suffer from gout,
- if you need to have a test to check how well your parathyroid gland is working,
- if you had photosensitivity reactions.

Your doctor may prescribe you blood tests to check for low sodium or potassium levels or high calcium levels.
If you think any of these situations may apply to you or you have any questions or doubts about taking your medicine, you should consult your doctor or pharmacist.

Children and adolescents
Natrixam should not be given to children and adolescents.

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

You should not take Natrixam:
- with lithium (used to treat mental disorders such as mania, manic depression illness and recurrent depression) due to the risk of increased levels of lithium in the blood,
- with dantrolene (infusion for severe body temperature abnormalities).

Make sure to tell your doctor if you are taking any of the following medicines, as special care may be required:
- other medicines for treating high blood pressure,
- medicines used for heart rhythm problems (e.g. quinidine, hydroquinidine, disopyramide, amiodarone, sotalol, ibutilide, dofetilide),
- medicines used to treat mental disorders such as depression, anxiety, schizophrenia… (e.g. tricyclic antidepressants, antipsychotic drugs, neuroleptics),
- bepridil (used to treat angina pectoris, a condition causing chest pain),
- cisapride, diphemanil (used to treat gastro-intestinal problems),
- sparfloxacin, moxifloxacin, erythromycin by injection (antibiotics used to treat infections),
- vincamine IV (used to treat symptomatic cognitive disorders in elderly including memory loss),
- halofantrine (antiparasitic drug used to treat certain types of malaria),
- pentamidine (used to treat certain types of pneumonia),
- mizolastine (used to treat allergic reactions, such as hay fever),
- non-steroidal anti-inflammatory drugs for pain relief (e.g. ibuprofen) or high doses of acetylsalicylic acid,
- angiotensin converting enzyme (ACE) inhibitors (used to treat high blood pressure and heart failure),
- oral corticosteroids used to treat various conditions including severe asthma and rheumatoid arthritis,
- digitalic preparations (for the treatment of heart problems),
- stimulant laxatives,
- baclofen (to treat muscle stiffness occurring in diseases such as multiple sclerosis),
- potassium-sparing diuretics (amiloride, spironolactone, triamterene),
- metformin (to treat diabetes),
- iodinated contrast media (used for tests involving X-rays),

- calcium tablets or other calcium supplements,
- ciclosporin, tacrolimus or other medicines to depress the immune system after organ transplantation, to treat autoimmune diseases, or severe rheumatic or dermatological diseases,
- tetracosactide (to treat Crohn's disease),
- ketoconazole, itraconazole, amphotericin B by injection (anti-fungal medicines),
- ritonavir, indinavir, nelfinavir (so called protease inhibitors used to treat HIV),
- rifampicin, erythromycin, clarithromycin (antibiotics),
- hypericum perforatum (St. John's Wort),
- verapamil, diltiazem (heart medicines),
- simvastatin, an agent used to lower levels of cholesterol and fats (triglycerides) in the blood,
- allopurinol (to treat gout).

Natrixam with food and drink
Grapefruit juice and grapefruit should not be consumed by people who are taking Natrixam. This is because grapefruit and grapefruit juice can lead to an increase in the blood levels of the active ingredient amlodipine, which can cause an unpredictable increase in the blood pressure lowering effect of Natrixam.

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.
This medicine is not recommended during pregnancy. When a pregnancy is planned or confirmed, the switch to an alternative treatment should be initiated as soon as possible.

You must not take Natrixam if you are breast-feeding. Tell your doctor immediately if you are breast-feeding or about to start breast-feeding.

Driving and using machines
Natrixam may affect your ability to drive or use machines. If the tablets make you feel sick, dizzy or tired, or give you a headache, do not drive or use machines and contact your doctor immediately. If this occurs, you should refrain from driving and other activities requiring alertness.

Natrixam contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Natrixam

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

The recommended dose is one tablet once a day, preferably in the morning.
The tablet should be swallowed as whole with water and should not be chewed.

If you take more Natrixam than you should
Taking too many tablets may cause your blood pressure to become low or even dangerously low. You may feel dizzy, drowsy, lightheaded, faint or weak. You may experience nausea, vomiting, cramps, confusion and changes in the amount of urine produced by the kidneys. If blood pressure drop is severe enough shock can occur. Your skin could feel cool and clammy and you could lose consciousness. Seek immediate medical attention if you take too many Natrixam tablets.

If you forget to take Natrixam
Do not worry. If you forget to take a tablet, leave out that dose completely. Take your next dose at the right time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Natrixam
As the treatment for high blood pressure is usually life-long, you should discuss with your doctor before stopping this medicinal product.

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.

Stop taking the medicinal product and visit your doctor immediately if you experience any of the following side effects:
- sudden wheeziness, chest pain, shortness of breath or difficulty in breathing (uncommon, may affect up to 1 in 100 people),
- swelling of eyelids, face or lips (very rare, may affect up to 1 in 10,000 people),
- swelling of the tongue and throat which causes great difficulty breathing (very rare, may affect up to 1 in 10,000 people),
- severe skin reactions including intense skin rash, hives, reddening of the skin over your whole body, severe itching, blistering, peeling and swelling of the skin, inflammation of mucous membranes (Stevens Johnson Syndrome) or other allergic reactions (very rare, may affect up to 1 in 10,000 people),
- heart attack, abnormal heart beat (very rare, may affect up to 1 in 10,000 people),
- life-threatening irregular beat (torsade de pointes) (frequency not known),
- inflamed pancreas which may cause severe abdominal and back pain accompanied with feeling very unwell (very rare, may affect up to 1 in 10,000 people).

The following common side-effects have been reported. If any of these cause you problems or if they last for more than one week, you should contact your doctor.

Common: may affect up to 1 in 10 people
- headache, dizziness, sleepiness (especially at the beginning of treatment),
- palpitations (awareness of your heart beat), flushing,
- abdominal pain, feeling sick (nausea),
- ankle swelling (oedema), tiredness,
- low potassium in the blood, which may cause muscle weakness,
- skin rashes

Other side effects that have been reported include the following list. If any of these get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Uncommon: may affect up to 1 in 100 people
- mood changes, anxiety, depression, sleeplessness,
- trembling, taste abnormalities, fainting,
- numbness or tingling sensation in your limbs, loss of pain sensation,
- visual disturbances, double vision, ringing in the ears,
- low blood pressure,
- sneezing/running nose caused by inflammation of the lining of the nose (rhinitis),
- altered bowel habits, diarrhoea, constipation, indigestion, dry mouth, vomiting (being sick),
- hair loss, increased sweating, itchy skin, red patches on skin, skin discolouration,
- disorder in passing urine, increased need to urinate at night, increased number of times of passing urine,
- inability to obtain an erection; discomfort or enlargement of the breasts in men,
- weakness, pain, feeling unwell,
- joint or muscle pain, muscle cramps, back pain,
- weight increase or decrease.

Rare: may affect up to 1 in 1,000 people
- confusion,
- feeling of dizziness.

Very rare: may affect up to 1 in 10,000 people
- changes in blood cells, such as thrombocytopenia (decrease in the number of platelets which causes easy bruising and nasal bleeding), leucopenia (decrease of white blood cells which may cause unexplained fever, soreness of the throat or other flu-like symptoms – if this occurs, contact your doctor) and anaemia (decrease in red blood cells),
- excess sugar in blood (hyperglycaemia),
- increase of calcium in blood,
- a disorder of the nerves which can cause weakness, tingling or numbness,
- cough,
- swelling of the gums,
- abdominal bloating (gastritis),
- abnormal liver function, inflammation of the liver (hepatitis), yellowing of the skin (jaundice), liver enzyme increase which may have an effect on some medical tests ; in cases of liver failure, there is a possibility of getting hepatic encephalopathy (disease in the brain caused by liver illness),
- kidney disease,
- increased muscle tension,
- inflammation of blood vessels, often with skin rash,
- sensitivity to light,
- disorders combining rigidity, tremor, and/or movement disorders.

Not known (frequency cannot be estimated from the available data):
- changes may occur in your laboratory parameters and your doctor may need to give you blood tests to check your condition. The following changes in laboratory parameters may occur:
  . low sodium in the blood that may lead to dehydration and low blood pressure,
  . increase in uric acid, a substance which may cause or worsen gout (painful joint(s) especially in the feet),
  . increase in blood glucose levels in diabetic patients,
- abnormal ECG tracing,
- short sightedness (myopia).
- blurred vision.
- visual impairment.

If you suffer from systemic lupus erythematosus (a type of collagen disease), this might get worse.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Natrixam

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 carton and the blister or container. The expiry date refers to the last day of that month.

Blisters: store below 30°C.
Bottles: this medicinal product 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 protect the environment.

6. Contents of the pack and other information

What Natrixam contains

- The active substances are indapamide and amlodipine.
  One tablet of Natrixam 1.5 mg / 5 mg contains 1.5 mg indapamide and 6.935 mg amlodipine besilate equivalent to 5 mg amlodipine.
  One tablet of Natrixam 1.5 mg / 10 mg contains 1.5 mg indapamide and 13.87 mg amlodipine besilate equivalent to 10 mg amlodipine.
- The other ingredients are:
  - Tablet core for Natrixam 1.5mg/5mg and 1.5mg/10mg: lactose monohydrate, hypromellose (E464), magnesium stearate (E572), povidone (E1201), silica colloidal anhydrous, calcium hydrogen phosphate dihydrate, cellulose microcrystalline (E460), croscarmellose sodium (E468), pregelatinized maize starch,
  - Tablet film-coating for Natrixam 1.5mg/5mg: glycerol (E422), hypromellose (E464), macrogol 6000, magnesium stearate (E572), titanium dioxide (E171),
  - Tablet film-coating for Natrixam 1.5mg/10mg: glycerol (E422), hypromellose (E464), iron oxide red (E172), macrogol 6000, magnesium stearate (E572), titanium dioxide (E171).

What Natrixam looks like and contents of the pack
Natrixam 1.5 mg / 5 mg tablets are white, round, film-coated, modified-release tablets of 9 mm diameter engraved with on one face.
Natrixam 1.5 mg /10 mg tablets are pink, round, film-coated, modified-release tablets of 9 mm diameter engraved with on one face.

The tablets are available in blisters of 15, 30, 60, 90 tablets and containers of 100 and 500 tablets. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Les Laboratoires Servier
50, rue Carnot
92284 Suresnes cedex– France

Manufacturers
Les Laboratoires Servier Industrie
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45520 Gidy - France

and

Servier (Ireland) Industries Ltd (SII)
Moneylands, Gorey Road
Arklow – Co. Wicklow – Ireland

and

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and

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and

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Hungary

and

Egis Pharmaceuticals PLC
H- 9900 Körmend ,
Mátyás király u. 65,
Hungary

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

Austria	NATRIXAM®, Tabletten mit veränderter Wirkstofffreisetzung
Belgium	NADREXAM® comprimé à libération modifiée
Bulgaria	NATRIXAM®, таблетки с изменено освобождаване
Cyprus	NATRIXAM®, δισκία ελεγχόμενης αποδέσμευσης
Czech Republic	NATRIXAM®, tablety s řízeným uvolňováním
Estonia	NATRIXAM®
Finland	NATRIXAM®, depottabletti
France	NATRIXAM®, comprimé à libération modifiée
Germany	NATRIXAM®, Tabletten mit veränderter Wirkstofffreisetzung
Greece	NATRIXAM®, δισκία ελεγχόμενης αποδέσμευσης
Hungary	NATRIXAM® módosított hatóanyagleadású tabletta
Ireland	NATRIXAM®, modified-release tablets
Italy	NATRILOR®, compresse a rilascio modificato
Latvia	TERTENSAM®, ilgstošās darbības tabletes
Lithuania	NATRIXAM®, modifikuoto atpalaidavimo tabletės
Luxembourg	NADREXAM®, comprimé à libération modifiée
Malta	NATRIXAM®, modified-release tablets
Netherlands	NATRIXAM®, tabletten met gereguleerde afgifte
Poland	TERTENS-AM®
Portugal	NATRIXAM®, comprimidos de libertação modificada
Romania	NATRIXAM® comprimate cu eliberare modificată
Slovakia	NATRIXAM®, tablety s riadeným uvoľňovaním
Slovenia	NADEXAM® tablete s prirejenim sproščanjem
Spain	NATRIXAM® comprimidos de liberación modificada

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

<[To be completed nationally]>

<Other sources of information>

<Detailed information on this medicine is available on the web site of {MA/Agency}>