Package leaflet: Information for the user

Naproxen/Esomeprazole MSN 500 mg/20 mg modified-release tablets
naproxen/esomeprazole

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, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- 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 Naproxen/Esomeprazole MSN is and what it is used for
2. What you need to know before you take Naproxen/Esomeprazole MSN
3. How to take Naproxen/Esomeprazole MSN
4. Possible side effects
5. How to store Naproxen/Esomeprazole MSN
6. Contents of the pack and other information

1. What Naproxen/Esomeprazole MSN is and what it is used for

What Naproxen/Esomeprazole MSN is
Naproxen/Esomeprazole MSN contains two different medicines called naproxen and esomeprazole. Each of these medicines works in a different way.
- Naproxen belongs to a group of medicines called "Non-Steroidal Anti-Inflammatory Drugs" (NSAIDs). It reduces pain and inflammation.
- Esomeprazole belongs to a group of medicines called "proton pump inhibitors". It reduces the amount of acid in your stomach.

Esomeprazole helps to reduce the risk of ulcers and stomach problems developing in patients who need to take NSAIDs.

What Naproxen/Esomeprazole MSN is used for
Naproxen/Esomeprazole MSN is used in adults for the relief of symptoms of:
- Osteoarthritis.
- Rheumatoid Arthritis.
- Ankylosing Spondylitis.

Naproxen/Esomeprazole MSN helps to reduce pain, swelling, redness and heat (inflammation).

You will be given this medicine if a lower dose of NSAID is considered unlikely to relieve your pain and you are at risk of getting a stomach ulcer or an ulcer in the first part (duodenum) of your small intestine (gut) when taking NSAIDs.

2. What you need to know before you take Naproxen/Esomeprazole MSN

Do not take Naproxen/Esomeprazole MSN if:
- You are allergic (hypersensitive) to naproxen,
- You are allergic to esomeprazole or other proton pump inhibitor medicines.
- You are allergic to any of the other ingredients of this medicine (listed in section 6).

- You are taking a medicine called “atazanavir” or “nelfinavir” (used to treat HIV).
- If acetylsalicylic acid, naproxen or other NSAIDS such as ibuprofen, diclofenac or COX- 2 inhibitors (e.g. celecoxib, etoricoxib) have caused you to have asthma (wheeziness) or an allergic reaction such as itchiness or skin rash (urticaria).
- You are in the last 3 months of pregnancy.
- You have severe problems with your liver, kidney or heart.
- You have an ulcer in your stomach or gut.
- You have any bleeding disorder or serious and unexpected bleeding.
- If you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking Naproxen/Esomeprazole MSN or other related medicines.

Do not take Naproxen/Esomeprazole MSN if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before taking Naproxen/Esomeprazole MSN.

Warnings and Precautions
Talk to your doctor or pharmacist before taking Naproxen/Esomeprazole MSN.

You must not take Naproxen/Esomeprazole MSN and talk to your doctor straight away, if any of the following happen to you before or while you are taking Naproxen/Esomeprazole MSN as this medicine may hide the symptoms of other disease:
- You lose a lot of weight for no reason and have problems swallowing.
- You start to vomit food or blood.
- You pass black stools (blood-stained faeces).

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking this medicine.

Check with your doctor or pharmacist before taking this medicine if:
- You have inflammation of your intestines (Crohn’s disease or ulcerative colitis).
- You have any other problems with your liver or kidneys or if you are elderly.
- You are taking medicines such as corticosteroids taken by mouth, warfarin, clopidogrel, Selective Serotonin Reuptake Inhibitors (SSRIs), acetylsalicylic acid or NSAIDs including COX-2 inhibitors (see section Other medicines and Naproxen/Esomeprazole MSN).
- You have ever had a skin reaction after treatment with a medicine similar to esomeprazole (which is a component of Naproxen/Esomeprazole MSN) that reduces stomach acid. Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), have been reported in association with naproxen and esomeprazole treatment. Stop using Naproxen/Esomeprazole MSN and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.
- You are due to have a specific blood test (Chromogranin A).

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking this medicine.

If you have previously experienced stomach ulcer or bleeding you should let your doctor know. You will be asked to report any unusual symptoms from your stomach (e.g. pain) to your doctor.

Medicines such as Naproxen/Esomeprazole MSN may be associated with a small increase in the risk of heart attack (myocardial infarction) or stroke. Any risk is more likely with high doses and long lasting treatment. Do not exceed the recommended dose or length of treatment.

Naproxen/Esomeprazole MSN contains the NSAID naproxen. As for all NSAIDs, naproxen should be used at the lowest effective dose for the shortest duration possible to reduce the risk of undesirable effects. Your doctor will therefore assess at a regular interval whether Naproxen/Esomeprazole MSN is still appropriate for you.

Naproxen/Esomeprazole MSN is not suitable to achieve rapid relief of acute pain, as it takes several hours before the painkilling substance naproxen is taken up in your blood.

Also, check with your doctor before taking this medicine if you have any heart problems, previous stroke or think you might be at risk of these problems. You may be at risk of getting these problems if:
- You have high blood pressure.
- You have problems with your blood circulation or with your blood clotting.
- You have diabetes.
- You have high cholesterol.
- You are a smoker.

Taking a proton pump inhibitor (which is a component of Naproxen/Esomeprazole MSN), especially over a period of more than one year, may slightly increase your risk of fracture in the hip, wrist or spine. Tell your doctor if you have osteoporosis or if you are taking corticosteroids (which can increase the risk of osteoporosis).

If you get a rash on your skin, especially in areas exposed to the sun tell your doctor as soon as you can, as you may need to stop your treatment with Naproxen/Esomeprazole MSN. Remember to also mention any other ill- effects like pain in your joints.

Serious skin rashes have occurred in patients taking esomeprazole (see also section 4). The rash can involve ulcers of the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). These serious skin rashes often come after flu-like symptoms such as fever, headache, body ache. The rash may cover large parts of the body with blistering and peeling of the skin.
If at any time during the treatment (even after several weeks) you develop a rash or any of these skin symptoms, stop taking this medicine and contact your doctor immediately.

When taking Naproxen/Esomeprazole MSN, inflammation in your kidney may occur. Signs and symptoms may include decreased volume of urine or blood in your urine and/or hypersensitivity reactions such as fever, rash, and joint stiffness. You should report such signs to the treating physician.

Children and adolescents
Naproxen/Esomeprazole MSN is not recommended for use in children or adolescents aged 18 years or younger.

Other medicines and Naproxen/Esomeprazole MSN
Please tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines that you buy without a prescription, including herbal medicines. This is because Naproxen/Esomeprazole MSN can affect the way some other medicines work. Also some other medicines can affect the way Naproxen/Esomeprazole MSN works.

Do not take this medicine and tell your doctor or pharmacist if you are taking:
- A medicine called “atazanavir” or “nelfinavir” (used to treat HIV).

Tell your doctor or pharmacist if you are taking any of the following medicines:
- Acetylsalicylic acid (used as a painkiller or to prevent blood clots). If you take low dose acetylsalicylic acid you may still be able to take Naproxen/Esomeprazole MSN.
- Other NSAID medicines (including COX-2 inhibitors).
- Certain drugs such as ketoconazole, itraconazole, posaconazole, or voriconazole (used to treat infections caused by a fungus).
- Erlotinib (or another anticancer drug from the same class)
- Cholestyramine (used to reduce cholesterol).
- Clarithromycin (used to treat infection).
- “Quinolone antibiotic” (for infections), such as ciprofloxacin or moxifloxacin.
- Diazepam (used to treat anxiety, to relax your muscles or used in epilepsy).
- Hydantoins such as phenytoin (used to treat epilepsy).

- Lithium (used to treat some types of depression).
- Methotrexate (used to treat rheumatoid arthritis, psoriasis and cancer).
- Probenecid (for gout).
- "Selective Serotonin Reuptake Inhibitors" (SSRIs) (used to treat major depression or anxiety disorder).
- Ciclosporin or tacrolimus (medicines used to dampen down the body's immune reactions).
- Digoxin (used to treat heart disorders).
- Sulphonylureas such as glimepiride (oral medicines used to control your blood sugar in diabetes).
- Medicines used to treat high blood pressure called diuretics (such as furosemide or hydrochlorothiazide), ACE inhibitors (such as enalapril), angiotensin II receptor antagonists (such as losartan) and beta-blockers (such as propranolol).
- Corticosteroid medicines such as hydrocortisone or prednisolone (used as anti-inflammatory medicines).
- Medicine to stop your blood clotting, like warfarin, dicoumarol, heparin or clopidogrel.
- Rifampicin (used for treatment of tuberculosis)
- St John's Wort (Hypericum perforatum) (used to treat mild depression)
- Cilostazole (used for pain in the legs due to poor blood flow)

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking Naproxen/Esomeprazole MSN.

Naproxen/Esomeprazole MSN with food and drink
Do not take Naproxen/Esomeprazole MSN with food as this may reduce and/or delay the effect of Naproxen/Esomeprazole MSN. Take your tablets at least 30 minutes before you have a meal.

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.

Pregnancy
Do not take Naproxen/Esomeprazole MSN if you are in the last 3 months of pregnancy as it could harm your unborn child or cause problems at delivery. It can cause kidney and heart problems in your unborn baby. It may affect your and your baby's tendency to bleed and cause labour to be later or longer than expected. You should not use Naproxen/Esomeprazole MSN during the first 6 months of pregnancy unless absolutely necessary and advised by your doctor. If you need treatment during this period or while you are trying to get pregnant, the lowest dose for the shortest time possible should be used. If taken for more than a few days from 20 weeks of pregnancy onward, Naproxen/Esomeprazole MSN can cause kidney problems in your unborn baby that may lead to low levels of amniotic fluid that surrounds the baby (oligohydramnios) or narrowing of a blood vessel (ductus arteriosus) in the heart of the baby. If you need treatment for longer than a few days, your doctor may recommend additional monitoring.

Breast feeding
Do not breast-feed if you are taking Naproxen/Esomeprazole MSN. This is because small amounts may pass into the mothers' milk. If you are planning to breast-feed you should not take Naproxen/Esomeprazole MSN.

Fertility
Naproxen/Esomeprazole MSN may make it more difficult to become pregnant. You should inform your doctor if you are planning to become pregnant or if you have problems to become pregnant.

Driving and using machines
You may feel dizzy or experience blurred vision while taking Naproxen/Esomeprazole MSN. If this happens, do not drive or use any tools or machines.

Naproxen/Esomeprazole MSN contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to take Naproxen/Esomeprazole MSN

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

Taking this medicine
- Swallow your tablets whole with water. Do not chew, split or crush the tablets. It is important that you take your tablets whole for your medicine to work properly.
- Take your tablets at least 30 minutes before you have a meal. Food may reduce the protective effect of Naproxen/Esomeprazole MSN on your stomach and gut. Food may also cause a considerable delay in the relief of pain and inflammation.
- If you are taking this medicine for a long time, your doctor will want to monitor you (particularly if you are taking it for more than a year).

How much to take
- Take one tablet twice a day for as long as your doctor has told you.
- Naproxen/Esomeprazole MSN is only available in 500 mg/20 mg. If your doctor thinks this dose is not suitable for you they may prescribe another treatment.

If you take more Naproxen/Esomeprazole MSN than you should
If you take more Naproxen/Esomeprazole MSN than you should, talk to your doctor or pharmacist straight away. Symptoms of an overdose may include lethargy, dizziness, drowsiness, upper abdominal pain and or discomfort, heartburn, indigestion, nausea, liver problems (shown in a blood test), kidney problems which can be severe, higher than normal levels of acid in your blood, confusion, vomiting, bleeding of the stomach or intestines, high blood pressure, breathing difficulties, coma, sudden allergic reactions (which may include breathlessness, skin rashes, swelling of the face and/or throat, and/or collapse) and uncontrolled movements of the body.

If you forget to take Naproxen/Esomeprazole MSN
- If you forget to take a dose, take it as soon as you remember it. However, if it is almost time for your next dose, skip the missed dose.
- Do not take a double dose (two doses at the same time) to make up for a forgotten dose.

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 following side effects may happen with this medicine.

Stop taking Naproxen/Esomeprazole MSN and see a doctor immediately if you notice any of the following serious side effects – you may need urgent medical treatment:
- Sudden wheezing, swelling of your lips, tongue and throat or body, rash, fainting or difficulties in swallowing (severe allergic reaction).
- Sudden onset of a severe rash or reddening of your skin with blisters or peeling may occur even after several weeks of treatment. There may also be severe blisters and bleeding in the lips, eyes, mouth, nose and genitals. The skin rashes may develop into serious widespread skin damage (peeling of the epidermis and superficial mucous membranes) with life threatening consequences. This could be 'erythema multiforme', 'Stevens-Johnson syndrome', 'toxic epidermal necrolysis' or 'drug reaction with eosinophilia and systemic symptoms'. These effects are very rare, and might affect up to 1 in 10,000 people.

- Yellowing of the skin or the whites of your eyes, having dark urine and tiredness which can be symptoms of liver problems.
- Medicines such as Naproxen/Esomeprazole MSN may be associated with a small increased risk of heart attack (myocardial infarction) or stroke. Signs include chest pain spreading to your neck and shoulders and down your left arm, confusion or muscle weakness or numbness which may only be on one side of your body.
- You pass black sticky bowel motions (stools) or have bloody diarrhoea.
- You vomit any blood or dark particles that look like coffee grounds

Talk to your doctor as soon as possible if you experience any of the following:

Naproxen/Esomeprazole MSN may in rare cases affect the white blood cells leading to immune deficiency.

If you have an infection with symptoms such as fever with a severely reduced general condition or fever with symptoms of a local infection such as pain in the neck, throat or mouth or difficulties in urinating, you must consult your doctor as soon as possible so that a lack of white blood cells (agranulocytosis) can be ruled out by a blood test. It is important for you to give information about your medication at this time.

Other possible side effects include:

Common (may affect up to 1 in 10 people)
- Headache.
- Feeling tired.
- Feeling thirsty.
- Feeling depressed.
- Feeling breathless.
- Increased sweating.
- Itchy skin and skin rashes.
- Spinning feeling (vertigo).
- Red or purple marks, bruising or spots on your skin.
- Feeling sick (nausea) or being sick (vomiting).
- A fluttering feeling in your heart (palpitations).
- Disturbed sleep or trouble sleeping (insomnia).
- Hearing problems or ringing in your ears.
- Dizziness, feeling drowsy or feeling light-headed.
- Swelling of your hands, feet and ankles (oedema).
- An inflammation inside the mouth.
- Eyesight problems.
- Diarrhoea, stomach pain, heartburn, indigestion, constipation, burping or wind (flatulence).
- Stomach ulcer or ulcer in the first part (duodenum) of the small intestine.
- Inflammation of the lining of the stomach (gastritis).
- Benign polyps in the stomach.

Uncommon, rare or very rare (may affect up to 1 in 100 people or less)
- A sore mouth or mouth ulcers.
- Eyesight problems such as blurred vision, conjunctivitis or eye pain.
- Strange dreams.
- Feeling sleepy.
- An increased in the amount of sugar (glucose) in your blood. The symptoms may include feeling thirsty and increased amount of urine.
- Low levels of sugar (glucose) in your blood. The symptoms may include feeling hungry or weak, sweating and a fast heartbeat.
- Coma.

- Inflammation of the blood vessels.
- Perforation (hole) of the stomach or intestine.
- Systemic lupus erythematosus (SLE), a disease where the body's immune system attacks the body, which causes joint pain, skin rashes and fever.
- Enlarged lymph glands.
- Fracture of the hip, wrist or spine (if Naproxen/Esomeprazole MSN is used in high doses and over long duration).
- Fever.
- Fainting.
- Dry mouth.
- Aggression.
- Hearing loss.
- Asthma attack.
- Fits or seizures.
- Period problems.
- Weight changes.
- Hair loss (alopecia).
- Lumpy rash (hives).
- Joint pain (arthralgia).
- Enlarged breasts in men.
- Sore or swollen tongue.
- Twitching or muscle tremor.
- Appetite problems or taste changes.
- Muscle weakness or pain (myalgia).
- Your blood may take longer to clot.
- Problems for women in getting pregnant.
- Fever, redness or other signs of infection.
- An irregular, slow or very fast heartbeat.
- Tingling feelings such as "pins and needles".
- Difficulty with your memory or concentration.
- Feeling agitated, confused, anxious or nervous.
- Generally feeling unwell, weak and lacking energy.
- Swollen or painful parts of your body because you have gained water.
- High or low blood pressure. You may feel faint or dizzy.
- Skin rash or blistering, or your skin becoming more sensitive on exposure to sunlight.
- Seeing, feeling or hearing things that are not there (hallucinations).
- Changes in your blood test results, such as to see how your liver is working. Your doctor can explain more.
- An infection called "thrush" which can affect the gut and is caused by a fungus.
- Blood in your urine (water) or other kidney problems. You may have back pain.
- Difficulty breathing, which may get slowly worse. This may be signs of pneumonia or swelling of your lungs developing.
- Low levels of salt (sodium) in your blood. This may cause weakness, being sick (vomiting) and cramps.
- Symptoms of meninigitis such as fever, feeling or being sick, a stiff neck, headache, sensitivity to bright light and confusion.
- Problems with your pancreas. Signs include severe stomach pain which spreads to your back.
- Pale coloured stools which are a sign of serious liver problems (hepatitis). Serious liver problems may lead to liver failure and disorder of the brain.
- Colitis or worsening of inflammatory bowel disease such as Crohn's disease or ulcerative colitis. Signs include stomach pain, diarrhoea, vomiting and weight loss.
- Blood problems such as a reduced number of red cells (anaemia), white cells or platelets. This can cause weakness, bruising, fever, severe chills, sore throat or make infections more likely.
- Increased number of a certain type of white blood cells (eosinophilia).

- A shortage of all types of blood cells (pancytopenia).
- Problems with the way your heart pumps blood around the body or damage to your blood vessels. Signs may include tiredness, shortness of breath, feeling faint, chest pain or general pain.

Not known (frequency cannot be estimated from the available data)
- If you are on Naproxen/Esomeprazole MSN for more than three months it is possible that the levels of magnesium in your blood may fall. Low levels of magnesium can be seen as fatigue, involuntary muscle contractions, disorientation, convulsions, dizziness or increased heart rate. If you get any of these symptoms, please tell your doctor promptly. Low levels of magnesium can also lead to a reduction in potassium or calcium levels in the blood. Your doctor may decide to perform regular blood tests to monitor your levels of magnesium.
- Rash, possibly with pain in the joints.

Do not be concerned by this list of possible side effects. You may not get any of them.

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

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

5. How to store Naproxen/Esomeprazole MSN

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, bottle or blister after EXP. The expiry date refers to the last day of that month.

Blister: Do not store above 25°C. Store in the original package in order to protect from moisture.

Bottle: Do not store above 25°C. Store in the original package and keep the bottle tightly closed in order to protect from moisture.

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 Naproxen/Esomeprazole MSN contains
- The active substances are naproxen and esomeprazole. Each modified-release tablet contains 500 mg naproxen and 20 mg esomeprazole (as magnesium trihydrate).
- The other ingredients are
  Tablet core: cellulose, microcrystalline, croscarmellose sodium (E468), povidone, silica, colloidal anhydrous, magnesium stearate (E470b).
  Coating Tablet: hypromellose 2910, macrogol 8000, methacrylic acid-ethyl acrylate copolymer (1:1) dispersion 30 percent, triethyl citrate, titanium dioxide (E171), polydextrose, polysorbate 80, glycerol monostearate 40-55, iron oxide yellow (E172), carnauba wax.
  Printing ink: iron oxide black (E172), propylene glycol.

What Naproxen/Esomeprazole MSN looks like and contents of the pack
Naproxen/Esomeprazole MSN are yellow, oval modified-release tablets, marked with “NE2” in black on one side.

Naproxen/Esomeprazole MSN are available in blisters containing 10, 30, or 60 modified-release tablets, or HDPE bottle with a child-resistant polypropylene screw closure and silica-gel desiccant canister containing 10, 30, or 60 modified-release tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
MSN Labs Europe Limited,
KW20A, Corradino Park,
Paola PLA 3000,
Malta

Manufacturer
Pharmadox Healthcare Limited,
KW20A Kordin Industrial Park, Paola,
PLA3000
Malta

MSN Labs Europe Limited
KW20A Corradino Park, Paola,
PLA3000
Malta

This medicine is authorised in the Member States of the European Economic Area under the following names:

Germany:	Naproxen/Esomeprazol Vivanta 500 mg/20 mg Tabletten mit veränderter Wirkstofffreisetzung
Spain:	Naproxeno/Esomeprazol Vivanta 500 mg/20 mg comprimidos de liberación modificada EFG
Ireland:	Naproxen/Esomeprazole MSN 500 mg/20 mg modified-release tablets

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