

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **MYLAN-NAPROXEN / ESOMEPRAZOLE MR**

Naproxen / Esomeprazole Modified Release Tablets

Read this carefully before you start taking **MYLAN-NAPROXEN / ESOMEPRAZOLE MR** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **MYLAN-NAPROXEN / ESOMEPRAZOLE MR**.

Serious Warnings and Precautions

If you have, or previously had, any of the following medical conditions, see your health care provider to discuss treatment options other than MYLAN-NAPROXEN / ESOMEPRAZOLE MR:

- Heart Attack or Angina
- Stroke or Mini-stroke
- Loss of Vision
- Current Pregnancy (less than 28 weeks)
- Congestive Heart Failure

What is MYLAN-NAPROXEN / ESOMEPRAZOLE MR used for?

MYLAN-NAPROXEN / ESOMEPRAZOLE MR is used in adults to treat the signs and symptoms of:

- Osteoarthritis
- Rheumatoid arthritis
- Ankylosing spondylitis

MYLAN-NAPROXEN / ESOMEPRAZOLE MR helps to reduce pain, swelling, redness and heat (inflammation). It is used for people who:

- need to take an anti-inflammatory medicine.
- and are at risk of getting a stomach ulcer (sore) or an ulcer in the small intestine (gut).

How does MYLAN-NAPROXEN / ESOMEPRAZOLE MR work?

MYLAN-NAPROXEN / ESOMEPRAZOLE MR contains 2 drugs which work together.

- Naproxen belongs to a group of medicines called “nonsteroidal anti-inflammatory drugs” (NSAIDs). It reduces the substances in your body which cause pain and swelling.
- Esomeprazole belongs to a group of medicines called “proton pump inhibitors” (PPIs). It reduces the amount of acid produced by your stomach.
- Naproxen can damage the stomach but esomeprazole helps reduce this damage.
- MYLAN-NAPROXEN / ESOMEPRAZOLE MR only treats the symptoms of pain and inflammation of the illness as long as you use it. MYLAN-NAPROXEN / ESOMEPRAZOLE MR does not cure the illness.

What are the ingredients in MYLAN-NAPROXEN / ESOMEPRAZOLE MR?

Medicinal ingredients: naproxen (enteric-coated, delayed release core) and esomeprazole (as esomeprazole magnesium, immediate release coating).

Non-medicinal ingredients: ammonium hydroxide, colloidal silicon dioxide, croscarmellose sodium, diacetylated monoglycerides, glyceryl stearate, hypromellose, iron oxide black, iron oxide yellow, lactose monohydrate, magnesium stearate, methacrylic acid copolymer, polysorbate 80, povidone, polyethylene glycol, propylene glycol, shellac glaze, sodium carbonate anhydrous, titanium dioxide, triethyl citrate.

MYLAN-NAPROXEN / ESOMEPRAZOLE MR comes in the following dosage forms:

Modified Release Tablets: 375 mg naproxen / 20 mg esomeprazole and 500 mg naproxen / 20 mg esomeprazole

Do not use MYLAN-NAPROXEN / ESOMEPRAZOLE MR if:

- you have heart bypass surgery (planning to have or recently had)
- you have severe, uncontrolled heart failure
- you have bleeding in the brain or other bleeding disorders
- you are pregnant (after 28 weeks of pregnancy)
- you are currently breastfeeding (or planning to breastfeed)
- you are allergic to naproxen, esomeprazole, substituted benzimidazoles or to any of the non-medicinal ingredients in MYLAN-NAPROXEN / ESOMEPRAZOLE MR (see **What are the ingredients in MYLAN-NAPROXEN / ESOMEPRAZOLE MR?**)
- you have a history of asthma, hives, or symptoms of an allergic reaction after taking acetylsalicylic acid (ASA) or other NSAIDs (such as celecoxib, diclofenac and ibuprofen)
- you have an active ulcer
- you have active bleeding from the stomach or gut
- you have inflammatory bowel disease (Crohn's Disease or Ulcerative Colitis)
- you have liver disease (active or severe)
- you have kidney disease (severe or worsening)
- you have high potassium in the blood
- you are taking rilpivirine
- you are under 18 years of age

Patients who took a drug in the same class as MYLAN-NAPROXEN / ESOMEPRAZOLE MR after a type of heart surgery (coronary artery bypass grafting (CABG)) were more likely to have heart attacks, strokes, blood clots in the leg(s) or lung(s), and infections or other complications than those who did NOT take that drug. MYLAN-NAPROXEN / ESOMEPRAZOLE MR must not be used after recent CABG.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take MYLAN-NAPROXEN / ESOMEPRAZOLE MR. Talk about any health conditions or problems you may have, including if you:

- have high blood pressure.
- have high cholesterol.
- have diabetes mellitus or are on a low sugar diet.
- have atherosclerosis.

- have poor blood flow to your extremities, for example, your hands and feet.
- are a smoker or ex-smoker.
- have kidney disease or urine problems.
- had a previous ulcer (sore) or bleeding from the stomach or gut (small or large intestine).
- previously had bleeding in the brain.
- have bleeding problems.
- are due to have a specific blood test (Chromogranin A).

Other warnings you should know about:

Heart Attack and Stroke: Medicines such as naproxen / esomeprazole may be associated with an increased risk of heart attack (myocardial infarction) or stroke. This risk may happen early in treatment.

Serious Side Effects: MYLAN-NAPROXEN / ESOMEPRAZOLE MR can cause serious side effects, including:

- **Serious Skin Reactions:** In rare cases, serious or life-threatening skin reactions listed below have been reported with some NSAIDs, such as MYLAN-NAPROXEN / ESOMEPRAZOLE MR.
 - Drug reaction with eosinophilia and systemic symptoms (DRESS),
 - Stevens-Johnson Syndrome (SJS),
 - toxic epidermal necrosis (TEN),
 - exfoliative dermatitis, and
 - erythema multiforme

You may be at a greater risk of experiencing a serious skin reaction usually during the first month of treatment. See the Serious side effects and what to do about them table, below, for more information on these and other serious side effects.

- **Serious Stomach and Intestine Problems:** MYLAN-NAPROXEN / ESOMEPRAZOLE MR can cause serious stomach and intestine problems. Tell your healthcare professional about symptoms that may be a sign of a more serious problem in your stomach or intestine such as:
 - trouble swallowing.
 - unplanned weight loss.
 - vomiting blood or food.
 - black (blood-stained) stools.

See the “Serious side effects and what to do about them” table, below, for more information on these and other serious side effects.

Antibiotics: If you take antibiotics while taking MYLAN-NAPROXEN / ESOMEPRAZOLE MR you may:

- experience symptoms such as severe (bloody or repeated watery) diarrhea, with or without fever, abdominal pain or tenderness. These are symptoms of bowel inflammation caused by a bacterial infection (*Clostridium difficile*).

If this happens, stop taking the drug combination and tell your healthcare professional immediately.

Surgery: Tell any doctor, dentist, pharmacist or healthcare professional that you see, that you are taking this medicine. This is especially important if you are planning to have heart surgery.

Pregnancy: Tell your healthcare professional if you are pregnant or planning to become pregnant. There are specific risks you must discuss with your healthcare professional.

Fertility: MYLAN-NAPROXEN / ESOMEPRAZOLE MR may affect your fertility. This means that it may be difficult for you to have a child. Talk to your healthcare professional if you have questions about this.

Driving and Using Machines: MYLAN-NAPROXEN / ESOMEPRAZOLE MR may cause you to become drowsy or tired. Be careful about driving or doing activities that require you to be alert. If you become drowsy, dizzy or light-headed after taking MYLAN-NAPROXEN / ESOMEPRAZOLE MR, do NOT drive or use machines.

Long term use of MYLAN-NAPROXEN / ESOMEPRAZOLE MR: Long-term use of MYLAN-NAPROXEN / ESOMEPRAZOLE MR may:

- interfere with the absorption of Vitamin B12 from the diet. This may cause a shortage of Vitamin B12 in your body. Talk to your healthcare professional about this risk.
- lead to low blood magnesium in some people. When blood magnesium is lower than normal, it may also lead to low blood calcium and low blood potassium.
- increase risks of broken bones of the hip, wrist or spine. This is more likely to happen if you use MYLAN-NAPROXEN / ESOMEPRAZOLE MR every day for a year or longer. Talk to your healthcare professional about this risk.
- cause a growth in your stomach (polyp), especially after one year.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with MYLAN-NAPROXEN / ESOMEPRAZOLE MR:

- Antacids, used to treat symptoms of excess stomach acid
- Medicines used to treat depression such as Selective Serotonin Reuptake Inhibitors (citalopram, fluoxetine, paroxetine, sertraline)
- Medicines used to treat high blood pressure such as angiotensin converting enzyme inhibitors (enalapril, lisinopril, perindopril, ramipril) or angiotensin II receptor blockers (candesartan, irbesartan, losartan, valsartan)
- Medications that prevent blood clots such as warfarin, ASA and clopidogrel. Use of MYLAN-NAPROXEN / ESOMEPRAZOLE MR with clopidogrel should be avoided as it may decrease the effectiveness of clopidogrel.
- Corticosteroids (including glucocorticoids such as prednisone), used as anti-inflammatory medicines
- Cyclosporin, used to treat rheumatoid arthritis, psoriasis, Crohn's disease, nephrotic syndrome, and in organ transplants to prevent rejection
- Digoxin, used to treat heart disorders
- Diuretics (such as furosemide, hydrochlorothiazide), used to lower your blood pressure
- Medicines used in cancer therapy such as erlotinib
- Lithium, used to treat some types of depression
- Methotrexate, used in high doses to treat cancer. Your healthcare professional may tell you to stop taking MYLAN-NAPROXEN / ESOMEPRAZOLE MR temporarily while you are taking methotrexate.
- Oral contraceptives, used to prevent pregnancy
- Oral hypoglycemics (diabetes medications), used to lower glucose levels in the blood
- Tacrolimus, used to lower the risk of organ rejection

- Diazepam, used to treat anxiety
- Phenytoin, used to treat epilepsy
- Cilostazol (not available in Canada), used to treat poor circulation in the legs
- Cisapride (not available in Canada), used to help empty the stomach
- Medicines used to treat fungal infections such as itraconazole, ketoconazole, and voriconazole
- Medicines used to treat tuberculosis such as rifampin
- Medicines used to treat HIV such as atazanavir, nelfinavir and saquinavir. MYLAN-NAPROXEN / ESOMEPRAZOLE MR may decrease the effectiveness or increase side effects of some medicines used to treat HIV. MYLAN-NAPROXEN / ESOMEPRAZOLE MR should not be used with atazanavir, nelfinavir or saquinavir.
- Herbal medicines such as St. John's Wort
- Alcohol

How to take MYLAN-NAPROXEN / ESOMEPRAZOLE MR:

- Always take MYLAN-NAPROXEN / ESOMEPRAZOLE MR exactly as your healthcare professional has told you. Do NOT increase, decrease, or stop taking MYLAN-NAPROXEN / ESOMEPRAZOLE MR without first talking to your healthcare professional.
 - Stopping MYLAN-NAPROXEN / ESOMEPRAZOLE MR after taking it for a long time may cause stomach problems.
- Take MYLAN-NAPROXEN / ESOMEPRAZOLE MR tablets at least 30 minutes before a meal.
- Swallow MYLAN-NAPROXEN / ESOMEPRAZOLE MR tablets whole with water. Do NOT chew, split or crush the tablets.

If possible, you should take the lowest dose of this medication for the shortest time period. Taking too much MYLAN-NAPROXEN / ESOMEPRAZOLE MR may increase your chances of unwanted and sometimes dangerous side effects, especially if you are elderly, have other diseases or take other medications.

Remember, this medication has been prescribed only for you. Do NOT give it to anyone else. It may harm them, even if their symptoms seem to be similar to yours.

Usual dose:

Your healthcare professional will decide on the best dosage for you based on your condition. The usual daily dose is either 375/20 mg twice a day or 500/20 mg twice a day.

Overdose:

If you think you, or a person you are caring for, have taken too much MYLAN-NAPROXEN / ESOMEPRAZOLE MR, contact a healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose of MYLAN-NAPROXEN / ESOMEPRAZOLE MR, take it as soon as you remember. If it is almost time for your dose, skip the missed dose and continue with your next scheduled dose. Go back to your regular schedule. Do not double dose.

What are possible side effects from using MYLAN-NAPROXEN / ESOMEPRAZOLE MR?

These are not all the possible side effects you may have when taking MYLAN-NAPROXEN / ESOMEPRAZOLE MR. If you experience any side effects not listed here, tell your healthcare professional.

MYLAN-NAPROXEN / ESOMEPRAZOLE MR may cause you to become more sensitive to sunlight. Sunlight or sunlamps may cause sunburn, skin blisters, skin rash, redness, itching or discoloration, or vision changes. If you have a reaction from the sun, check with your healthcare professional.

Stomach upset is a common problem with NSAIDs, such as naproxen. The esomeprazole in MYLAN-NAPROXEN / ESOMEPRAZOLE MR helps to reduce this side effect. However, side effects, usually mild, have been reported with esomeprazole use. These side effects may not be caused by esomeprazole in your case, but only a healthcare professional can assess this. If these become bothersome (or last more than 1-2 days), discuss with your healthcare professional.

Common side effects include:

- Nausea
- Stomach upset
- Diarrhea
- Headache

Uncommon side effects include:

- Dry mouth
- Dizziness
- Insomnia
- Feeling of burning / prickliness / numbing
- Swelling of extremities
- Feeling sleepy
- Feeling like you or your surroundings are moving (vertigo)

Rare side effects include:

- Taste disorders
- Nervousness
- Hair loss
- Increased sweating

Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Serious side effects of esomeprazole and what to do about them			
RARE			
Blood disorders (low white and/or red blood cell count): feeling tired or weak, pale skin, bruising or bleeding for longer than usual if you hurt yourself, fever, chills		✓	
Gastrointestinal fungal infection: diarrhea,		✓	

Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
vomiting, melena, hemorrhage, abdominal pain, and fever			
Hepatitis (inflammation of liver): skin and eyes appear yellow			✓
Myalgia (muscle pain): aching muscles, tenderness or weakness		✓	
Photosensitivity (sensitivity to sunlight): itchy, red skin when exposed to sunlight		✓	
Severe allergic reactions: shortness of breath, chest pain or discomfort, feeling thirsty, urinating less often, less urine or dark urine, swelling or anaphylactic reaction/shock			✓
Skin reactions: rash, dermatitis, itching and/or hives		✓	
Stomatitis (mouth sores, redness and swelling of the lining of the mouth): inflammation in the mouth		✓	
VERY RARE			
Aggressive behaviour		✓	
<i>Clostridium difficile</i> colitis (bowel inflammation): severe or persistent diarrhea, abdominal pain, nausea and vomiting, fever		✓	
Decreased consciousness		✓	
Gynecomastia: Breast enlargement in men (and /or women)		✓	
Hallucinations: seeing or hearing things that are not there		✓	
Hypomagnesemia (low level of magnesium in the blood): abnormal eye movements, fatigue, muscle spasms or cramps, muscle weakness, numbness		✓	
Liver failure (serious disturbance of liver function, hepatic failure): yellow colour to skin, whites of the eyes (jaundice), bleeding easily, swollen abdomen, mental disorientation or confusion, sleepiness, coma		✓	
Muscular weakness		✓	
Nephritis (inflammation of the kidney): decreased appetite, difficulty breathing, fatigue, frequent urination, itchiness,		✓	

Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
nausea, vomiting			
Serious skin reactions: <ul style="list-style-type: none"> • Skin peeling, scaling, or blistering (with or without pus) which may also affect your eyes, mouth, nose or genitals, itching, severe rash, bumps under the skin, skin pain, skin color changes (redness, yellowing, purplish) • Swelling and redness of eyes or face • Flu-like feeling, fever, chills, body aches, swollen glands, cough 			✓
UNKNOWN			
Subacute cutaneous lupus erythematosus: new or worsening joint pain, rash on your cheeks or arms that gets worse in the sun			✓
Serious side effects of NSAIDs and what to do about them			
RARE			
Serious Skin Reactions: fever, severe rash, swollen lymph glands, flu-like feeling, blisters and peeling skin that may start in and around the mouth, nose, and genitals and spread to other areas of the body, swelling of face and/or legs, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feeling thirsty, urinating less often, less urine or dark urine			✓
UNKNOWN			
Asthma: shortness of breath, wheezing, any trouble breathing or chest tightness			✓
Blurred vision, or any visual disturbance			✓
Chills, fever, muscle aches or pains, or other flu-like symptoms, especially if they occur before or together with a skin rash; these symptoms may be the first signs of a serious allergic reaction to the medication			✓
Colitis: bloody or black tarry stools			✓
Dizziness, light-headedness		✓	
Edema: swelling of the feet, lower legs; weight gain		✓	
Headaches, stiff neck		✓	
Hearing problems		✓	
Jaundice: yellow discoloration of the skin or eyes, with or without itchy skin			✓

Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Malaise, fatigue, loss of appetite		✓	
Mental confusion, depression		✓	
Renal disease: any change in the amount or colour of your urine (red or brown), any pain or difficulty experienced while urinating			✓
Skin rash, hives, swelling or itching			✓
Vomiting or persistent indigestion, nausea, stomach pain or diarrhea		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

MYLAN-NAPROXEN / ESOMEPRAZOLE MR tablets should be kept in their original container. Keep bottles tightly closed to protect from moisture. Do not keep MYLAN-NAPROXEN / ESOMEPRAZOLE MR in the bathroom medicine cabinet or other warm, moist places.

Store at controlled room temperature (15°C to 30°C).

Do NOT keep expired medicine or medicine no longer needed. Return to your pharmacist. Medicines should not be disposed of via wastewater or household waste. Your healthcare professional will throw away any medicines that are no longer being used. These measures will help protect the environment.

Keep out of reach and sight of children.

If you want more information about MYLAN-NAPROXEN / ESOMEPRAZOLE MR:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this

Patient Medication Information by visiting the Health Canada website:
(<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website www.mylan.ca, or by calling 1-844-596-9526.

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