Taking NSAIDs?

(nonsteroidal anti-inflammatory drugs)

Take a closer look at your dose.
What are NSAIDs?

Nonsteroidal anti-inflammatory drugs, or NSAIDs, are a group of medicines that can be used to manage pain and reduce inflammation and fever.

**Short-term or chronic conditions:** NSAIDs may be used for short-term conditions, such as pain from a toothache, menstrual cramps, low back pain, or inflammation associated with muscle strains or sprains; they can also be used for longer-lasting (chronic) conditions, such as osteoarthritis.

**How NSAIDs work:** It is believed that NSAIDs block enzymes that produce prostaglandin, a chemical compound involved in pain and inflammation; NSAIDs stop prostaglandins from being made in your body, which may temporarily manage pain and reduce inflammation.

**OTC or prescription:** Some NSAIDs can be found in familiar over-the-counter (OTC) products, such as aspirin, Aleve® (naproxen sodium), or Advil® (ibuprofen); other NSAIDs are only available as a prescription from your doctor.

NSAIDs are found in nearly 550 OTC and prescription medicines.

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70 million visits are made to physicians for pain-related ailments each year in the United States.

In the United States, approximately 123 million NSAID prescriptions were filled in 2014.

In 2014 62% of NSAIDs were prescribed to women.
While NSAIDs can help manage pain and reduce inflammation, studies have shown they can potentially lead to serious side effects involving the heart, stomach, and kidneys.

- Increasing doses of NSAIDs may increase the risk of serious side effects
- The risk of serious side effects may increase with longer NSAID use
- Even short-term NSAID use can lead to serious side effects

The US Food and Drug Administration (FDA) recommends that NSAIDs be used:

- Exactly as your doctor prescribes them
- At the lowest dose possible for your treatment
- For the shortest time needed
Studies have shown that the higher the NSAID dose, the higher the risk of serious side effects.

Increased NSAID doses increase:

- The chance of heart attack or stroke in people with or without heart disease or risk factors for heart disease.

- The chance of bleeding, ulcers, and tears (perforations) of the esophagus (the tube leading from the mouth to the stomach), stomach, and intestines.

- The chance of kidney problems, including kidney failure and progressive kidney damage.

The majority of commonly used NSAIDs are prescribed at the highest approved daily dose.
Doctors frequently prescribe NSAIDs to treat a wide array of painful and inflammatory conditions in adults. Here are just a few of them.

**Osteoarthritis pain**

Osteoarthritis, commonly referred to as “arthritis” or OA, is a progressive joint disease that causes cartilage—the tissue that occupies the space where bones meet—to wear away.

- NSAIDs are the most frequently used medicines to help manage the pain, inflammation, and stiffness associated with osteoarthritis
- 50% of patients with OA are treated with NSAIDs

Approximately 27 million US adults are affected by osteoarthritis.
Gout pain
Gout is a painful form of arthritis that is caused by the overproduction of uric acid, a bodily waste product. This excess of uric acid causes needle-like crystals to form in the joints, leading to painful “flares,” swelling, and stiffness.

Gout typically affects the big toe, but can also affect other joints, including ankles, heels, knees, and wrists.

For many people, gout “attacks” are initially felt in the joints of the big toe.

Mild to moderate acute pain
Acute pain is short-term pain that is linked to an injury, surgery, or other trauma to the body. NSAIDs are one of the most frequently used medicines to treat acute pain that is mild to moderate in intensity. These types of pain include:

- Headaches and toothaches
- Low back pain
- Menstrual cramps
- Sprains and strains

Low back pain is the second most common reason Americans visit their health care provider. The first reason: colds and the flu.
The science behind low-dose SoluMatrix® NSAIDs

SoluMatrix Fine Particle Technology™ is an innovative process that is applied to trusted NSAID molecules.

- This technology creates NSAID drug particles that are approximately 10 to 20 times smaller than their original size
- The result: low-dose pain medicine that is rapidly absorbed by the body

SoluMatrix Fine Particle Technology™ at a glance

Low-dose SoluMatrix® NSAIDs were developed by Iroko to align with recommendations from FDA, medical organizations, and advocacy groups: use the lowest effective NSAID dose for the shortest amount of time.
Important Safety Information

All non-steroidal anti-inflammatory drugs (NSAIDs), like ZORVOLEX, TIVORBEX and VIVLODEX, increase the risk of heart attack or stroke that can lead to death. This risk may happen early in treatment and may increase with increasing doses and longer use of NSAIDs. Avoid taking NSAIDs after a recent heart attack.

Do not take ZORVOLEX, TIVORBEX or VIVLODEX right before or after a heart surgery called a “coronary artery bypass graft (CABG).”

NSAID medicines can cause ulcers, tears, and bleeding in the esophagus, stomach and intestines at any time during treatment. These events can happen without warning symptoms and may cause death. The risk of a person getting an ulcer or bleeding increases with: a past history of ulcers or bleeding in the stomach or intestines, increasing doses or longer use of NSAIDs, taking other medicines called “corticosteroids”, “anticoagulants”, “SSRIs”, or “SNRIs”, smoking, drinking alcohol, older age, and having poor health, liver disease or bleeding problems.

Please see complete Important Safety Information on pages 14 and 15, and enclosed Medication Guide.
VIVLODEX™: The lowest FDA-approved dose of meloxicam available (5 mg)

For management of osteoarthritis (OA) pain

Meloxicam is a nonsteroidal anti-inflammatory drug (NSAID) that is used to manage pain caused by OA. VIVLODEX is a low-dose SoluMatrix® meloxicam for patients with OA pain.

In a clinical study, patients with OA pain who took low-dose VIVLODEX (5 mg or 10 mg once daily) experienced greater reductions in OA pain compared with patients who took placebo.

VIVLODEX is FDA-approved at low 5-mg and 10-mg doses to be taken once daily.

For management of OA pain, the recommended starting dosage is 5 mg orally once daily. Dose may be increased to 10 mg in patients who require additional analgesia. The maximum recommended daily oral dose of VIVLODEX is 10 mg.

Important Safety Information

Tell your healthcare provider about all of your medical conditions, if you are pregnant or breast feeding, and about all of the medicines you take because NSAIDs and some other medicines can interact with each other and cause serious side effects.
Do you know your dose?

If you are currently taking meloxicam to manage OA pain, ask your doctor if you are or will be taking the lowest FDA-approved dose. Then inquire about VIVLODEX, the low-dose SoluMatrix® meloxicam from Iroko.

To learn more about VIVLODEX, including co-pay information, visit VIVLODEX.com.

Important Safety Information

ZORVOLEX, TIVORBEX or VIVLODEX should not be taken after 29 weeks of pregnancy or when breastfeeding.

Do not take ZORVOLEX, TIVORBEX or VIVLODEX if you had an asthma attack, hives, or other allergic reaction with aspirin, or any other NSAID medicine.

Life threatening allergic reactions can occur with ZORVOLEX, TIVORBEX or VIVLODEX. Get help right away if you've had swelling of the face or throat or trouble breathing.

The most common side effects reported in studies using VIVLODEX were diarrhea, nausea, and abdominal discomfort.

Please see complete Important Safety Information on pages 14 and 15, and enclosed Medication Guide.
For management of mild to moderate acute pain and osteoarthritis (OA) pain

Diclofenac is a trusted, effective NSAID that doctors use to treat different types of pain.

- ZORVOLEX is a low-dose SoluMatrix® diclofenac that can be used to treat mild to moderate acute pain and OA pain

Why ZORVOLEX?

- In clinical studies, patients taking ZORVOLEX had greater reductions in OA pain and mild to moderate acute pain compared with patients who took placebo
- ZORVOLEX can be used for the management of mild to moderate acute pain at low doses of 18 mg or 35 mg three times daily
- ZORVOLEX can be used for the management of osteoarthritis pain at a dose of 35 mg three times daily

Talk to your doctor about NSAID dosing and ask about low-dose ZORVOLEX and TIVORBEX, or visit ZORVOLEX.com and TIVORBEX.com.

Important Safety Information

The most common side effects reported in studies using ZORVOLEX were swelling, nausea, headache, dizziness, vomiting, constipation, itching, diarrhea, gas, leg or foot pain, abdominal pain, stuffy or runny nose, abnormal blood tests, high blood pressure, and heartburn.
For treatment of mild to moderate acute pain in adults

Many adults take indomethacin to manage mild to moderate acute pain conditions. Examples of acute pain include back pain, joint pain, neck pain, headaches, sprains, and gout flares.

TIVORBEX is a low-dose SoluMatrix® indomethacin that can be used to treat mild to moderate acute pain.

Why TIVORBEX?

- In clinical studies, patients taking TIVORBEX had greater reductions in mild to moderate acute pain compared with patients who took placebo.
- TIVORBEX can be used for the treatment of mild to moderate acute pain at low doses of 20 mg (three times daily) or 40 mg (twice daily or three times daily).

Important Safety Information

The most common side effects reported in studies using TIVORBEX were: nausea, localized swelling or bleeding at the site of surgery, headache, dizziness, vomiting, constipation, itching, diarrhea, heartburn, light headedness, rash, stomach pain, drowsiness, excessive sweating, decreased appetite, hot flashes and fainting.

ZORVOLEX, TIVORBEX and VIVLODEX should be used exactly as prescribed, at the lowest dose possible, and for the shortest time needed for your treatment.

Please see complete Important Safety Information on pages 14 and 15, and enclosed Medication Guide.
Important Safety Information

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Do not take ZORVOLEX, TIVORBEX or VIVLODEX right before or after a heart surgery called a “coronary artery bypass graft (CABG).”

NSAID medicines can cause ulcers, tears, and bleeding in the esophagus, stomach and intestines at any time during treatment. These events can happen without warning symptoms and may cause death. The risk of a person getting an ulcer or bleeding increases with: a past history of ulcers or bleeding in the stomach or intestines, increasing doses or longer use of NSAIDs, taking other medicines called “corticosteroids”, “anticoagulants”, “SSRIs”, or “SNRIs”, smoking, drinking alcohol, older age, and having poor health, liver disease or bleeding problems.

Tell your healthcare provider about all of your medical conditions, if you are pregnant or breastfeeding, and about all of the medicines you take because NSAIDs and some other medicines can interact with each other and cause serious side effects.

ZORVOLEX, TIVORBEX or VIVLODEX should not be taken after 29 weeks of pregnancy or when breastfeeding.

Do not take ZORVOLEX, TIVORBEX or VIVLODEX if you had an asthma attack, hives, or other allergic reaction with aspirin, or any other NSAID medicine.

Life threatening allergic reactions can occur with ZORVOLEX, TIVORBEX or VIVLODEX. Get help right away if you’ve had swelling of the face or throat or trouble breathing.
Other serious side effects of NSAIDs include: new or worse high blood pressure, heart failure, kidney problems including kidney failure, low red blood cells (anemia), life-threatening skin or allergic reactions, and liver problems including liver failure.

The most common side effects reported in studies using ZORVOLEX were swelling, nausea, headache, dizziness, vomiting, constipation, itching, diarrhea, gas, leg or foot pain, abdominal pain, stuffy or runny nose, abnormal blood tests, high blood pressure, and heartburn.

The most common side effects reported in studies using TIVORBEX were: nausea, localized swelling or bleeding at the site of surgery, headache, dizziness, vomiting, constipation, itching, diarrhea, heartburn, light headedness, rash, stomach pain, drowsiness, excessive sweating, decreased appetite, hot flashes and fainting.

The most common side effects reported in studies using VIVLODEX were diarrhea, nausea, and abdominal discomfort.

ZORVOLEX, TIVORBEX and VIVLODEX should be used exactly as prescribed, at the lowest dose possible, and for the shortest time needed for your treatment.

These are not all the side effects reported with ZORVOLEX, TIVORBEX or VIVLODEX. Talk to your healthcare provider or pharmacist for more information about NSAID medicines. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

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Important Safety Information

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Do not take ZORVOLEX, TIVORBEX or VIVLODEX right before or after a heart surgery called a “coronary artery bypass graft (CABG).”

NSAID medicines can cause ulcers, tears, and bleeding in the esophagus, stomach and intestines at any time during treatment. These events can happen without warning symptoms and may cause death. The risk of a person getting an ulcer or bleeding increases with: a past history of ulcers or bleeding in the stomach or intestines, increasing doses or longer use of NSAIDs, taking other medicines called “corticosteroids”, “anticoagulants”, “SSRIs”, or “SNRIs”, smoking, drinking alcohol, older age, and having poor health, liver disease or bleeding problems.

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