PART III: CONSUMER INFORMATION

ARTHROTEC 50 / ARTHROTEC 75
"diclofenac sodium and misoprostol enteric-coated tablets"

This leaflet is part III of a three-part "Product Monograph" published when ARTHROTEC was approved for sale in Canada and is designed specifically for Consumers.

Read this information each time you refill your prescription in case new information has been added.

This leaflet is a summary and will not tell you everything about ARTHROTEC. See your health care provider and pharmacist regularly and ask them questions about your health and any medications you take**.**

ABOUT THIS MEDICATION

What the medication is used for:
Your health care provider has prescribed ARTHROTEC for you for the following:

- short-term and long-term use in the relief of the signs and symptoms of rheumatoid arthritis
- short-term and long-term use in the relief of the signs and symptoms of osteoarthritis

What it does:
ARTHROTEC contains two different medicines, a nonsteroidal anti-inflammatory drug (NSAID) called diclofenac and a drug that helps to protect the lining of your stomach called misoprostol (because NSAIDs can cause damage to your stomach).

ARTHROTEC (diclofenac plus misoprostol), as a nonsteroidal anti-inflammatory drug (NSAID), can reduce the chemicals produced by your body which cause pain and swelling. It helps to relieve joint pain, swelling, and stiffness by reducing the production of certain substances (prostaglandins) and by helping to control inflammation. ARTHROTEC, as a non-steroidal anti-inflammatory drug (NSAID) does NOT cure your illness or prevent it from getting worse but it promotes suppression of the inflammation and the tissue damaging effects resulting from this inflammation. ARTHROTEC can only relieve pain and reduce swelling as long as you continue to take it.

How do NSAIDs cause stomach damage? Natural prostaglandins play an important role in protecting the stomach by working to keep a thick mucus layer on the inside surface of the stomach. If the lining of the stomach is not protected by a thick layer of mucus, it may be burned by natural stomach acids. NSAIDs lower natural prostaglandins both in the joints and in the stomach. This is good for the joints because it controls pain, swelling and stiffness. Unfortunately, lowering prostaglandins in the stomach can lead to burning stomach pain and the development of tiny holes in the lining of your stomach called "ulcers".

Oddly enough, some NSAID patients who do develop ulcers never feel any stomach pain. On the other hand, some patients who do feel stomach pain have nothing wrong with them. For this reason people must be very careful when taking NSAIDs.

How does misoprostol protect the stomach? Misoprostol is a synthetic form of a special kind of prostaglandin that is found in the stomach. Misoprostol replaces the prostaglandins that are lost when taking the NSAID medicine. It protects the thick mucus layer and reduces the acid in your stomach. This can help to protect your stomach from the NSAID.

When it should not be used:

SPECIAL NOTE FOR WOMEN OF CHILDBEARING AGE

Do not take ARTHROTEC if you are pregnant or think you are pregnant or during prolonged labour. Do not start ARTHROTEC until you have been tested to confirm that you are not pregnant. Do not get pregnant or try to get pregnant while you are taking ARTHROTEC and for at least one month (or through one menstrual cycle) after you stop taking it. This means using an effective form of birth control which you should discuss with your doctor. Stop taking ARTHROTEC, and contact your doctor immediately if you do become pregnant during ARTHROTEC therapy.

Misoprostol may cause uterine contractions (contractions of the uterus), premature birth, birth defects and abortion or may otherwise harm the unborn developing baby. Misoprostol has been reported to cause the uterus to tear when given after the eighth week of pregnancy. Tearing of the uterus can result in severe bleeding, hysterectomy, and/or maternal or fetal death. Therefore, if you are pregnant, you must not take this drug.

Diclofenac can potentially prolong labor.

Abortions caused by misoprostol are likely to be incomplete. An incomplete abortion may result in very serious medical complications, resulting in hospitalization, surgery and possibly infertility, and may result in maternal death.

Do not use ARTHROTEC if you are breastfeeding or planning to breastfeed. The body changes misoprostol to the active form of the drug, misoprostol acid, which could get into the breast milk and cause significant diarrhea in the infant.

DO NOT TAKE ARTHROTEC if you have any of the following medical conditions:

- Heart bypass surgery (planning to have or recently had)
- Severe, uncontrolled heart failure
- Bleeding in the brain or other bleeding disorders
- Prolonged labor during childbirth
- Current pregnancy or in whom pregnancy has not been excluded
- Currently breastfeeding (or planning to breastfeed)
- Allergy to diclofenac sodium, misoprostol, ASA (Acetylsalicylic Acid) or other NSAIDs (Nonsteroidal Anti-Inflammatory Drugs)
- Ulcer (active)
- Bleeding from the stomach or gut (active)
- Inflammatory bowel disease (Crohn's Disease or Ulcerative Colitis)
- Liver disease (active or severe)
- Kidney disease (severe or worsening)
- High potassium in the blood
- Allergy to any other ingredients in ARTHROTEC listed in the "nonmedicinal ingredients" section below

Patients who took a drug in the same class as ARTHROTEC 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.

ARTHROTEC should NOT be used in patients under 18 years of age.

ARTHROTEC should NOT be used with other NSAIDs.

What the medicinal ingredients are:
Diclofenac sodium and misoprostol

What the important nonmedicinal ingredients are:

Lactose, Hydrogenated Castor Oil, Microcrystalline Cellulose, Colloidal Silicon Dioxide, Corn Starch, Crospovidone, Hypromellose, Magnesium Stearate, Methacrylic Acid Copolymer, Povidone K-30, Sodium Hydroxide, Talc, Triethyl Citrate.

What dosage forms it comes in:
Enteric coated Tablets:
ARTHROTEC 50: 50 mg diclofenac sodium/200 mcg misoprostol,
ARTHROTEC 75: 75 mg diclofenac sodium/200 mcg misoprostol

WARNINGS AND PRECAUTIONS

If you have, or previously had, any of the following conditions, see your health care provider to discuss treatment options other than ARTHROTEC:

- **Heart Attack or Angina**
- **Stroke or Mini-stroke**
- **Loss of Vision**
- **Congestive Heart Failure**
- **Current Pregnancy**
- **High blood pressure**
- **Diabetes**
- **High levels of fats in your blood**
- **Smoking**

It is important to take the lowest dose of ARTHROTEC that relieves your pain and/or swelling and for the shortest time possible in order to keep your risk of side effects on the heart and blood vessels as small as possible.

Use of NSAIDS, such as ARTHROTEC may cause stomach and bowel problems (such as ulceration, perforation, obstruction, and bleeding).

Use of ARTHROTEC can result in increased blood pressure and / or worsening of congestive heart failure.

BEFORE you use ARTHROTEC talk to your doctor or pharmacist if you have any of the following:

- Disease of the heart or blood vessels (also called cardiovascular disease, including uncontrolled high blood pressure, congestive heart failure, established ischemic heart disease, or peripheral arterial disease), as treatment with ARTHROTEC in these cases is not recommended.
- Risk factors for cardiovascular disease (see above) such as high blood pressure, abnormally high levels of fat (cholesterol, triglycerides) in your blood, diabetes, or if you smoke.
- Diabetes mellitus or on a low sugar diet
- Atherosclerosis
- Poor circulation to your extremities
- Smoker or ex-smoker
- Kidney disease or urine problems
- Previous ulcer or bleeding from the stomach or gut
- Previous bleeding in the brain
- Bleeding problems
- Family history of allergy to NSAIDs, such as acetylsalicylic acid (ASA), celecoxib, diclofenac, diflunisal, etodolac, fenoprofen, fluribiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, mefenamic acid, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, rofecoxib, sulindac, tenoxicam, tiaprofenic acid, tolmetin, or valdecoxib (NOT a complete list)

- Family history of asthma, nasal polyps, long-term swelling of the sinus (chronic sinusitis) or hives
- History of a severe drug hypersensitivity reaction including skin problems
- you are on any special diet, such as a low-sodium diet
- you drink alcohol;

Serious skin reactions: In rare cases, serious, life-threatening skin reactions have been reported with some NSAIDs, such as ARTHROTEC. These skin problems most often happen during the first month of treatment. **STOP taking ARTHROTEC and** tell your healthcare professional immediately if you notice any changes in your skin both during and after treatment.

ARTHROTEC may cause you to become more sensitive to sunlight. Sunlight or sunlamps may cause sunburn, skin blisters, skin rash, redness, itching or discolouration, or vision changes. If you have a reaction from the sun, talk to your healthcare professional.

The use of ARTHROTEC is contraindicated in women trying to get pregnant or in whom pregnancy has not been excluded.

WHILE taking ARTHROTEC:

- tell any other doctor, dentist, pharmacist or other health care professional that you consult or see, that you are taking this medication, especially if you are planning to have heart surgery;
- do NOT drink alcoholic beverages while taking this medication because you would be more likely to develop stomach problems;
- some NSAIDs may cause drowsiness or fatigue in some people taking them; be cautious about driving or participating in activities that require alertness if you are drowsy, dizzy or lightheaded after taking this medication;
- your regular medical checkups are essential.
- do not give ARTHROTEC to anyone else. It has been prescribed for your specific condition. ARTHROTEC may not be the correct treatment for another person, and would be dangerous if the other person were pregnant.
- Fertility may be decreased. The use of ARTHROTEC is contraindicated in women trying to get pregnant or in whom pregnancy has not been excluded.
- If you have cardiovascular disease or risks for cardiovascular disease, your doctor will periodically re-evaluate whether you should continue treatment with ARTHROTEC.

If, at any time while taking ARTHROTEC you experience any signs or symptoms of problems with your heart or blood vessels such as chest pain, shortness of breath, weakness, or slurring of speech, contact your doctor immediately.

INTERACTIONS WITH THIS MEDICATION

Talk to your health care provider and pharmacist if you are taking any other medication (prescription or non-prescription) such as any of the following (NOT a complete list):

- Acetylsalicylic Acid (ASA) or other NSAIDs (e.g. ASA, celecoxib, diclofenac, ibuprofen, indomethacin, ketorolac, meloxicam, naproxen)
- Antacids
- Antidepressants
  - Selective Serotonin Reuptake Inhibitors (SSRIs) (e.g. citalopram, fluoxetine, paroxetine, sertraline)
- Blood pressure medications
  - Diuretics (e.g. furosemide, hydrochlorothiazide)
  - ACE (Angiotensin converting enzyme) inhibitors (e.g. enalapril, lisinopril, perindopril, ramipril)
  - ARBs (angiotensin II receptor blockers) (e.g. candesartan, irbesartan, losartan, valsartan)
  - Beta-blockers
- Blood thinners (e.g. warfarin, ASA, clopidogrel)
- Corticosteroids (including glucocorticoids) (e.g. prednisone)
- Cyclosporin
- Digoxin
- Lithium
- Methotrexate
- Oral contraceptives
- Oral hypoglycemics (diabetes medications)
- Phenytoin (a medicine used to treat seizures)
- Tacrolimus
- Sulfinpyrazone (a medicine used to treat gout)
- Voriconazole (a medicine used to treat fungal infections)

Do not take ASA (acetylsalicylic acid), ASA-containing compounds, ibuprofen or other drugs used to relieve symptoms of arthritis while taking ARTHROTEC unless directed to do so by your physician.

Your health care provider may prescribe low dose ASA (acetylsalicylic acid) as a blood thinner to reduce your risk of having a heart attack or stroke while you are taking ARTHROTEC. Take only the amount of ASA prescribed by your healthcare provider. You are more likely to upset or damage your stomach if you take both ARTHROTEC and ASA than if you took ARTHROTEC alone.

Using ARTHROTEC with a blood-thinner increases the risk of bleeding. This can occur in the stomach or anywhere.

Using ARTHROTEC with blood pressure drugs may increase your risk of kidney failure. This is more likely if

you are elderly or dehydrated.

Do not take antacids that contain magnesium (because they can cause diarrhea) while you are taking ARTHROTEC. Ask your pharmacist to help you select a suitable brand.

Stomach problems may be more likely to occur if you drink alcoholic beverages. Therefore, do not drink alcoholic beverages while taking this medication.

PROPER USE OF THIS MEDICATION

Usual Dose for Patients 18 Years of Age and Older:

Medical Condition	Recommended daily dose	Maximum Dose (per day)*
Rheumatoid arthritis	50 mg twice a day	100mg
Osteoarthritis	50 mg twice a day	100mg

ARTHROTEC should be swallowed whole.

To lessen stomach upset, take ARTHROTEC immediately after a meal or with food or milk. Also, you should remain standing or sitting upright (i.e. do not lie down) for about 15-30 minutes after taking the medicine. This helps to prevent irritation that may lead to trouble swallowing.

Take ARTHROTEC only as directed by your health care provider. **Do NOT take more of it, do NOT take it more often and do NOT take it for a longer period of time than your healthcare provider ordered. If possible, you should take the lowest dose of this medication for the shortest time period.** Taking too much ARTHROTEC may increase the chance of unwanted and sometimes dangerous side effects, especially if you are an elderly patient, have other disease or take other medications.

If you will be using ARTHROTEC for more than 7 days, see your healthcare provider regularly to discuss whether this medicine is working for you and if it is causing you any unwanted effects. Be sure to take ARTHROTEC regularly as prescribed. In some types of arthritis, up to two weeks may pass before you feel the full effects of this medicine. During treatment, your doctor may decide to adjust the dosage according to your response to the medication.

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

ARTHROTEC is NOT recommended for use in patients under 18 years of age.

Missed Dose:
If you miss a dose of ARTHROTEC, take the next dose at the regular time. It is important that ARTHROTEC be taken as prescribed. Try to remember to take ARTHROTEC at the appropriate time. Having a regular routine associated with taking your medicine will help.

Do not take a double dose.

Overdose:
Symptoms of overdose may include stomach pain, confusion, drowsiness, low muscle tone, shaking hands that you cannot control, seizures, shortness of breath, diarrhea, fever, rapid or pounding heartbeat, slow heartbeat, dizziness or fainting

Seek immediate medical attention if you think that you or anyone else may have taken too much ARTHROTEC. Do this even if there are no signs of discomfort or poisoning.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

ARTHROTEC may cause some undesirable reactions especially when used for a long time or in large doses. When these side effects occur, you may require medical attention. Report all symptoms or side effects to your health care provider.

ARTHROTEC may cause you to become drowsy or tired. Be careful about driving or participating in activities that require you to be alert. If you become drowsy, dizzy or light-headed after ARTHROTEC, do NOT drive or operate machinery.

Check with your healthcare provider IMMEDIATELY if you develop 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 this medication.

If you are not getting any relief of your arthritis or if any problems develop, check with your doctor.

Elderly, frail, or debilitated patients often seem to experience more frequent or more severe side effects.

Stomach upset is one of the common problems with NSAIDs. If stomach upset (indigestion, nausea, vomiting, stomach pain or diarrhea) occurs and continues, contact your doctor.
Because misoprostol increases mucus production some patients experience diarrhea. Keep taking your ARTHROTEC. It is just a sign that the drug is working. Usually the diarrhea goes away in two to three days. If it is not gone after a week, check with your doctor.

While your body gets used to misoprostol you may feel a crampy pain in your stomach. Like the diarrhea it usually goes away in a few days. If it doesn't, check with your doctor.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM		
Symptom	**STOP taking ARTHROTEC and get emergency medical attention IMMEDIATELY**	**STOP taking ARTHROTEC and talk your doctor or pharmacist**
Bloody or black tarry stools, vomiting blood	✓	
Shortness of breath, wheezing, any trouble in breathing or tightness in the chest	✓	
Blurred vision or any visual disturbance	✓	
Any change in the amount or colour of your urine (red or brown)	✓	
Nausea, fatigue, lethargy, diarrhea, pruritus, yellow discolouration of the skin or eyes with or without itchy skin, right upper quadrant tenderness, and «flu-like» symptoms	✓	
Change in heart rate or rhythm, change in blood pressure, heart failure, blood clot	✓	
Infections: Sepsis (infection of the whole body) Lung infection	✓	
Seizure, shaking, loss of consciousness, strange dreams, change in mood or thoughts	✓	
Benign mass in the intestine, trouble with swallowing	✓	
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, eyes and genitals and spread to other areas of the body, swelling of face, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feeling thirsty, urinating less often, less urine or dark urine, hives, red or dry itchy skin, purple or red spots on skin, bruising	✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM		
Symptom	**STOP taking ARTHROTEC and get emergency medical attention IMMEDIATELY**	**STOP taking ARTHROTEC and talk your doctor or pharmacist**
Any pain or difficulty experienced while urinating		✓
Swelling of the feet or lower legs; weight gain		✓
Vomiting or persistent indigestion, nausea, stomach pain or diarrhea		✓
Malaise, fatigue, loss of appetite		✓
Headaches, stiff neck		✓
Dizziness, light headedness		✓
Hearing problems		✓
Agranulocytosis: fever, chills. Sore throat or mouth sores. Flu-like symptoms. Weakness.		✓
Hemolytic Anemia: Fatigue and short of breath. Yellow skin or eyes. Dark urine. Abdominal pain, nausea, vomiting, loss of appetite.		✓
Increased sensitivity or nerve pain		✓

This is not a complete list of side effects. For any unexpected effects while taking ARTHROTEC, contact your doctor or pharmacist.

HOW TO STORE IT

Store at 15-25°C and protect from heat and humidity.
Do NOT keep outdated medicine or medicine no longer needed. Any outdated or unused medicine should be returned to your pharmacist.

Keep out of the reach of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:

- Fax toll-free to 1-866-678-6789, or
- Mail to:
Canada Vigilance Program
Health Canada
Postal Locator 1908C
Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: ***Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.***

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals may be obtained by contacting the sponsor, Pfizer Canada ULC, at: 1-800-463-6001

This leaflet was prepared by
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