Approved Patient Information Leaflet for Medicines for Human Use: BREN-400

SCHEDULING STATUS: S3

BREN-400 Tablets

Ibuprofen

Sugar free.

Read all of this leaflet carefully before you start taking BREN-400

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- BREN-400 has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What BREN-400 is and what it is used for
2. What you need to know before you take BREN-400
3. How to take BREN-400
4. Possible side effects
5. How to store BREN-400
6. Contents of the pack and other information

1. What BREN-400 is and what it is used for

BREN-400 tablets contain the active substance ibuprofen and belongs to a group of medicines called antirheumatics used to treat any disease marked by inflammation and pain in the joints, muscles, or fibrous tissue. This medicine works as an anti-inflammatory pain killer and is also effective in the treatment of fever.

Each BREN-400 tablet contains 400 mg ibuprofen and is used for the treatment of mild to moderate pain of inflammatory origin and fever, including:

- a chronic inflammatory disorder affecting many joints, including those in the hands and feet called rheumatoid arthritis (including juvenile rheumatoid arthritis or Still's disease)
- inflammation of one or more joints affecting the spine and large joints called ankylosing spondylitis, causing pain and stiffness that can worsen with age
- inflammation of one or more larger joints when the flexible protective tissue at the ends of bones (cartilage) wears down causing pain and stiffness, most commonly in the hands, neck, lower back, knees or hips (called osteoarthritis)
- a form of arthritis characterised by severe pain, redness and tenderness in joints (called acute gouty arthritis). This causes severe pain, redness and swelling in joints, often the big toe and occurs when too much uric acid crystallises and deposits in the joints.
- pain and aches in muscles or bones which do not arise from inflamed joints (called non-articular rheumatism, including fibrositis)
- pain and inflammation caused when a bone breaks inside or around a joint. These injuries often damage cartilage at the ends of bones (articular cartilage) and other joint tissues, requiring special care in conditions like frozen shoulder (capsulitis), inflammation of the fluid-filled pads (bursae) that act as cushions at the joints (bursitis), when the tissue connecting muscle to bone becomes inflamed (tendonitis or tenosynovitis) and low-back pain
- sprains and strains
- period pain
- toothache
- pain due to a cut in the area between the vagina and anus (perineum) during childbirth (episiotomy)
- afterbirth (post-partum) pains felt as belly cramps when your uterus (womb) shrinks back

to its regular size after pregnancy

- fever.

2. What you need to know before you take BREN-400

Do not take BREN-400

- if you are hypersensitive (allergic) to ibuprofen or any of the other ingredients of BREN-400 (listed in section 6)
- if you have a history of severe allergic reactions such as wheezing or swelling of the face or throat after taking ibuprofen, aspirin or other non-steroidal anti-inflammatory medicines
- if you currently have a peptic ulcer (ulcer in your stomach or duodenum) or bleeding in your stomach, or have had two or more episodes of peptic ulcers, stomach bleeding or perforation in the past
- if you are in the last trimester (3 months) of pregnancy or in labour
- if you suffer from heart disease including heart failure
- if you have severe kidney problems.

If you are uncertain whether any of these apply to you, please discuss this with your doctor or pharmacist before taking BREN-400.

Warnings and precautions

Take special care with BREN-400

Tell your doctor before taking or whilst taking BREN-400:

- if you are taking other painkillers. If you usually take painkillers, especially combinations of different painkillers, you may damage your kidneys
- if you have or have had high blood pressure (hypertension) or other heart problems such as heart failure, angina (chest pain) or you have had a heart attack, bypass surgery or

peripheral artery disease (poor circulation in the legs or feet due to narrow or blocked arteries) or any kind of stroke

- if you suffer from a bleeding disorder, especially in the stomach or intestines. Signs of intestinal bleeding includes passing blood in your faeces (stools/motions), passing black tarry stools, vomiting any blood or dark particles that look like coffee grounds. You should stop taking BREN-400 and seek medical attention immediately (see section 4)
- if you have bowel problems (including ulcerative colitis, Crohn's disease, gastro-oesophageal reflux disease)
- if you are taking corticosteroids, anticoagulant medicine to thin your blood such as warfarin, antidepressants called selective serotonin-reuptake inhibitors or antiplatelet medicines such as aspirin
- if you use excessive alcohol
- if you have or have had asthma, bronchospasm, a chronic runny nose or allergic diseases
- if you have or have had any kind of stroke or think that you might be at risk of these conditions (e.g. if you have a family history of heart disease or stroke, high blood pressure, diabetes, high cholesterol or are a smoker)
- if you have kidney or liver problems
- if you have not been drinking fluids or has lost fluids due to continuous vomiting or diarrhoea, especially if you (or your child) are between the ages of 1 – 18 years or are an older person as there is a risk of kidney damage in dehydrated children, adolescents and the elderly
- if you have systemic lupus erythematosus (SLE), this is an autoimmune disease affecting connective tissue which causes joint pain and changes to the skin
- if you develop any skin rash, lesions of the mucous membranes, blisters or other signs of allergy, fever or swelling of your lymph glands. You should stop taking BREN-400 and

seek medical attention immediately since this can be the first signs of very serious skin reactions (see section 4)

- if you have an infection because BREN-400 may hide signs of infections such as fever and pain. It is therefore possible that BREN-400 may delay appropriate treatment of infection, which may lead to an increased risk of complications. This has been observed in pneumonia caused by bacteria and bacterial skin infections related to chickenpox. If you take this medicine while you have an infection and your symptoms of the infection persist or worsen, consult a doctor without delay
- if you develop a problem with your vision like blurred or diminished vision, or changes in colour vision
- if you develop signs of prolonged bleeding times such as unexplained and easy bruising, heavy menstrual bleeding, frequent nosebleeds, excessive bleeding from small cuts or an injury
- if you develop signs of aseptic meningitis such as severe headache, high temperature, stiffness of the neck or intolerance to bright light
- if you have frequent or daily headaches despite the regular use of BREN-400. The use of painkillers for a long period of time has in some patients been linked to headaches, a condition called medication overuse headache (MOH). You should not treat your headache with increased doses of BREN-400.

Taking BREN-400 while you are pregnant may cause kidney problems in your unborn baby and this can lead to low levels of the amniotic fluid that surrounds your baby. This fluid provides a protective cushion for the baby and helps the unborn babies' lungs, digestive system, and muscles develop. Complications can occur when the amniotic fluid is low. Use of BREN-400 in the last trimester can also cause problems with the baby's heart/ blood pressure.

Children and adolescents

BREN-400 tablets are not recommended for children under the age of one year.

Other medicines and BREN-400

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

BREN-400 may weaken the effects of the following medicines

- medicines used to help control high blood pressure and heart failure called ACE inhibitors, angiotensin receptor blockers and beta-blockers, examples include enalapril and ramipril, losartan and valsartan, atenolol, bisoprolol and propranolol
- diuretics (water tablets)
- aspirin (used at low dose) for prevention of heart attacks or stroke. This is because aspirin's anti-blood clotting properties is diminished when given together with BREN-400
- mifepristone. The combination with BREN-400 causes a decrease in the efficacy of mifepristone.

BREN-400 may strengthen the effects and/or increase your risk of side effects when used in combination with the following medicines

- cardiac glycosides, such as digoxin, used to treat heart conditions such as heart failure and irregular heart rhythm. BREN-400 may decrease the body's ability to remove digoxin from the body which can lead to a dangerous build-up of digoxin levels and cause heart failure
- lithium (a medicine used to treat some types of depression). The combination with lithium can disrupt the body's ability to remove lithium from the body which can lead to a dangerous build-up of lithium levels. You may experience increased side effects such as feeling or being sick, diarrhoea, a dry mouth and a metallic taste in the mouth

- methotrexate (a medicine used for suppressing the immune system, and often used in treatment of certain cancers and rheumatoid arthritis)
- ciclosporin or tacrolimus (medicines used for suppressing the immune system) - the combination may have increased side effects on kidneys function
- any other anti-inflammatory painkillers, including aspirin and other NSAIDs. This may increase the risk of adverse effects
- steroids (used in the treatment of inflammatory conditions). You may have an increased risk of gastrointestinal ulcers or bleeding
- medicines that thin your blood (anticoagulants), such as warfarin. You may experience prolonged bleeding times and an increased risk of excessive bleeding (haemorrhage)
- antibiotics called quinolones such as ciprofloxacin. You may have an increased risk of getting convulsions (seizures/fits)
- phenytoin (a medicine used to treat epilepsy). You may experience increased side effects of problems with walking and coordination, slurred speech, confusion and dizziness
- medicines known as sulphonylureas such as glibenclamide (used to treat diabetes). You may develop very low blood sugar levels (hypoglycaemia) and risk going into a coma
- medicines known as selective serotonin reuptake inhibitors (SSRIs), used for the treatment of depression. You may have an Increased risk of bleeding inside your digestive system
- zidovudine (an anti-viral drug used in treatment of HIV). You may have an increase risk of bleeding into a joint (causing symptoms like tingling, aching, or bubbling sensation at the joint, pain or tenderness, swelling, redness in the joint) and bad bruising
- aminoglycosides (a type of antibiotic). BREN-400 may decrease the body's ability to remove aminoglycosides from the body which can lead to a dangerous build-up of aminoglycosides levels which can cause increased risk of side effects such as damage to your hearing, kidneys and skeletal muscle paralysis

- *Gingko biloba* herbal medicine. There is a chance you may bleed more easily if you are taking this with BREN-400.

The following medicine may weaken the effects of BREN-400

- cholestyramine (a medicine used to lower cholesterol).

The following medicine may strengthen the effects of BREN-400

- voriconazole or fluconazole (type of anti-fungal medicines). Your doctor may want to reduce your dose of BREN-400.

BREN-400 with alcohol

BREN-400 may cause some side effects including dizziness, drowsiness and stomach problems such as bleeding in the stomach. Drinking excessive alcohol with BREN-400 might make these side effects worse.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking BREN-400.

BREN-400 should not be used in late (the last three months of) pregnancy and should only be taken in the first six months of pregnancy on the advice of your doctor.

Using pain-relieving and fever-reducing nonsteroidal anti-inflammatory drugs (NSAIDs) such as BREN-400 around 20 weeks or later in pregnancy may cause kidney problems in your unborn baby, which can lead to low levels of amniotic fluid that surrounds your baby. This fluid provides a protective cushion and helps the unborn babies' lungs, digestive system, and

muscles develop. Complications such as the permanent tightening of the muscles, tendons, skin, and nearby tissues in limbs that causes the joints to shorten and become very stiff or the delay in the foetus' lung maturation can occur with low levels of the amniotic fluid.

The use of BREN-400 during the third trimester (i.e. from 30 weeks and later) of pregnancy is contraindicated. In the third trimester BREN-400 may result in the premature closure of the foetal ductus arteriosus (i.e. the too early constriction of the normal foetal artery connecting the main body artery (aorta) and the main lung artery (pulmonary artery) allowing the foetus' blood to detour away from the lungs before birth). This can cause persistent high blood pressure of the unborn baby and lead to progressive right heart dysfunction, heart failure, a serious condition defined as abnormal accumulation of fluid in two or more foetal compartments (called foetal hydrops) and death before birth of the baby.

If you are trying to become pregnant, NSAIDs such as BREN-400 which may impair fertility in women. This effect is reversible upon stopping the medicine. It is unlikely that BREN-400, used occasionally will affect your chances of becoming pregnant, however, tell your doctor before taking BREN-400, if you have problems becoming pregnant.

Driving and using machines

BREN-400 may make you feel drowsy/sleepy, tired and disturb your vision

Do not drive or operate any tools or machines until you are aware of the measure to which BREN-400 affects you.

3. How to take BREN-400

Do not share medicines prescribed for you with any other person.

Always take BREN-400 exactly as your doctor or pharmacist has instructed you. Check with your doctor or pharmacist if you are not sure.

If you have the impression that the effect of BREN-400 is too strong or too weak, talk to your doctor or pharmacist.

Use the lowest effective dose for the shortest possible duration of treatment.

Adults:

The recommended dosage of BREN-400 is 1 200 mg daily in divided doses for the relief of:

- Joint pain
- Back pain of musculo-skeletal origin
- Muscular ache and pains
- Period pain
- Toothache
- Pain after delivery of your baby
- Fever.

The recommended dosage of BREN-400 is 2 400 mg daily in divided doses (two tablets every 8 hours) for the relief of:

- Acute gout. If the acute symptoms do not resolve within three days, consult a doctor.

Children

The recommended dosage of BREN-400 in Juvenile Rheumatoid Arthritis, is the total daily dosage of 20 mg/kg of body mass given in divided doses.

Duration of administration

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms.

Talk to your doctor if the symptoms persist longer than 3 – 7 days, worsen or recur periodically.

Method of administration

Take BREN-400 tablets orally with a sufficient quantity of liquid (e.g., one glass of water).

If you take more BREN-400 than you should

The most common symptoms of overdosage are pain in the upper middle part of the abdomen and nausea. Other symptoms may include vomiting (may be blood streaked), headache, ringing in the ears, confusion and shaky eye movement. At high doses, drowsiness, chest pain, palpitations, loss of consciousness, convulsions (mainly in children), weakness and dizziness, blood in urine, cold body feeling, and breathing problems have been reported. If recently taken, gastric lavage will remove any unabsorbed BREN-400. Treatment is symptomatic and supportive.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, seek help at the nearest hospital or poison control center.

If you forget to take BREN-400

If you miss a dose of BREN-400, take it as soon as you remember unless it is almost time for your next dose. If it is, do not take the missed dose at all. Do not take/receive a double dose to make up for forgotten individual doses.

4. Possible side effects

BREN-400 can have side effects.

Not all side effects reported for BREN-400 are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking/using/receiving BREN-400, please consult your health care provider for advice.

If any of the following happens, stop taking/using BREN-400 and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause wheezing, shortness of breath, difficulty in swallowing or breathing
- rash or itching
- fainting
- any signs of bleeding from the stomach or bowels (vomiting blood and/or passing black stools)
- noticing a sudden numbness or weakness of the face, arm or leg especially on one side of the body, sudden confusion, having trouble talking or understanding, difficulty seeing in one or both eyes, sudden trouble walking, dizziness, lack of balance or coordination. These may be signs of a stroke
- pain in the chest or discomfort including pain which radiates to the arm or jaw, with shortness of breath, nausea or light-headedness. These may be signs of a heart attack
- swelling of your limbs, especially your feet or feeling short of breath or breathlessness even while resting or a persistent wheezing together with fatigue (extreme tiredness), these may be signs of your heart failing
- dark urine, yellowing of your skin or the whites of your eyes. These may be signs of a problem with your liver
- severe and serious skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis) which can involve ulcers of the mouth, throat, nose, genitals and conjunctivitis (red and

swollen eyes). These serious skin rashes are often preceded by flu-like symptoms such as fever, headache, body ache. The rash may progress to widespread blistering and peeling of the skin. The highest risk for occurrence of serious skin reactions is within the first month of treatment (see section 2. Warnings and precautions)

- a serious allergic syndrome called Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) which can involve severe rash, redness and peeling of the skin, facial swelling, enlargement of one or more lymph nodes, high fever and damage to several organs such as your lungs, pancreas, kidneys, brain and many others. This severe allergic reaction can be life-threatening (see section 2. Warnings and precautions)
- if you have difficulty urinating or notice that your urine has changed colour or if you have severe pain in the flank (area between your ribs and hips) or fluid retention, for example swollen ankles. These may be signs of effects on how your kidneys work, especially if you have kidney problems or heart failure
- neck stiffness, headache, feeling sick, being sick, fever, loss of conscious, these may be signs of aseptic meningitis.

These are very serious side effects. If you have them, you may have had a serious reaction to BREN-400. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- signs of recurrent infections such as fever, sore throat, chills, sweating cough or shortness of breath. You may have a low level of white blood cells in the blood, which can interfere with the ability to fight infection (leukopenia)
- if you develop fatigue, weakness, pale or yellowish skin, irregular heartbeats, shortness of breath, dizziness or light-headedness, chest pain, cold hands and feet. You may have a condition in which the blood doesn't have enough healthy red blood cells (anaemia)

- if you notice that it takes longer for your blood to clot after an injury. This may be due to a decrease in the cells which help your blood to clot (thrombocytopenia)
- if you develop sleeplessness, anxiety, depression (feeling in sad mood for long periods of time), and confusion
- if you experience pain in your eye and vision loss. This may be due to inflammation of the optic nerve or to optic nerve damage by a toxin
- if you experience hearing loss, ringing or other noises in one or both of your ears (tinnitus) or a sudden internal or external spinning sensation, often triggered by moving your head too quickly (vertigo)
- if your blood pressure reading is higher than normal (hypertension)
- if you experience a burning or gnawing pain in the centre of the tummy (abdomen), indigestion, heartburn and feeling sicks. This may be due to inflammation or sore that develops on the lining of the oesophagus, stomach or small intestine
- If you develop upper abdominal pain that radiates to your back, experience tenderness when touching the abdomen, fever, rapid pulse, nausea, vomiting with fat in stool and loss of appetite. You may have inflammation of the organ lying behind the lower part of the stomach (pancreas)
- if you develop diarrhoea, often with blood or pus, abdominal pain and cramping, rectal pain and rectal bleeding — passing small amount of blood with stool, an urgency to defecate often with an inability to defecate despite urgency, weight loss. You may have developed inflammation (or the worsening thereof) of your intestines (colitis or Crohn's disease)
- if you develop an itchy skin rash, a rash of purple spots due to small blood vessels leaking blood into the skin, joints, intestines or organ (purpura), painless swelling under the skin (angioedema) or if you experience heightened skin sensitivity or an unusual reaction when your skin is exposed to UV radiation from sunlight or a tanning bed

- if you develop, usually within 2 days of taking BREN-400, rapid appearance of areas of red skin studded with pinhead-sized sterile pustules. This usually starts on the face or in the armpits and groin and then becomes more widespread and there tends to be more pustules in skin folds. Facial swelling may often arise
- if you experience a build-up of fluid in the body, often seen as swelling in the legs and feet (oedema/fluid retention).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- headache
- dizziness
- indigestion
- nausea (feeling sick)
- vomiting (being sick)
- abdominal cramps or stomach pains
- flatulence or wind
- constipation
- tiredness.

Less frequent side effects:

- runny nose
- a tingling sensation in the skin “pins and needles” (paraesthesia)
- feeling drowsy or sleepy
- mouth sores.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of BREN-400**.**

5. How to store BREN-400

Store all medicines out of reach of children

- Store in a cool dry place at or below 25 °C.
- Protect from light.
- Keep the blister in the carton until required for use.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What BREN-400 contains

The active substance is ibuprofen. Each film-coated tablet contains ibuprofen 400 mg.

The other ingredients are

Tablet core

Colloidal silicon dioxide

Maize starch

Magnesium stearate

Purified talc

Sodium lauryl sulfate

Sodium starch glycolate (type A)

Film-coating

Hypromellose

Lake erythrosine

Propyl glycol

Sodium acetate

Titanium dioxide

What BREN-400 looks like and contents of the pack

BREN-400 tablets are pink coloured, circular, slightly biconvex film-coated tablets.

BREN-400 is supplied in

- Blister packs (composed of colourless PVC and aluminium foil) of 10 tablets, 15 tablets or 84 tablets per carton.
- Opaque white High Density Polyethylene (HDPE) containers containing 1 000 tablets.
- White Low Density Polyethylene (LDPE) plastic Patient Ready Packs (PRPs) containing different pack sizes.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

Shanur Healthcare (Pty) Ltd.,

Loch House Unit 003,

3A Eton Road,

Parktown,

Johannesburg 2193

This leaflet was last revised in

To be allocated by the Authority.

Registration number

36/3.1/0041

Access to the corresponding Professional Information

Professional Information for this medicine is available on the following URL:

https://austell.co.za/product-info/

Austell Pharmaceuticals (Pty) Ltd

Tel: +27 11 611 1400 or +27 860 287 835