1.3.2 Patient Information Leaflet

SCHEDULING STATUS

S4

DRONAMYL 4 mg/5 ml (concentrate for dilution for infusion)

Zoledronic acid

Read all of this leaflet carefully before you receive DRONAMYL 4 mg/5 ml

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- DRONAMYL 4 mg/5 ml 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 DRONAMYL 4 mg/5 ml is and what it is used for

DRONAMYL mg/5 ml works by attaching itself to the bone and slowing down the rate of bone change.

It is used:

- To prevent bone complications, e.g. fractures, in adult patients with bone metastases (spread of cancer from primary site to the bone).
- To reduce the amount of calcium in the blood in adult patients where it is too high due to the presence of a tumour. Tumours can accelerate normal bone change in such a way that the release of calcium from bone is increased. This condition is known as tumour-induced hypercalcaemia.

2. What you need to know before you are given DRONAMYL 4 mg/5 ml

DRONAMYL 4 mg/5 ml should not be administered to you:

- if you are hypersensitive (allergic) to zoledronic acid or any of the other ingredients in the DRONAMYL 4 mg/5 ml concentrate for dilution of infusion, listed in section 6;
- if you are pregnant and breastfeeding (see '*Pregnancy and breastfeeding and fertility*');
- if you are an adolescent or a child below the age of 18 years;
- if you have or have had a severe kidney problem.

Warnings and precautions

Special care should be taken with DRONAMYL 4 mg/5 ml:

- Ensure that you are adequately hydrated before being administered DRONAMYL 4 mg/5 ml.
- Overhydration should be avoided if you are at risk of heart failure.
- Your kidney function, calcium, phosphate and magnesium levels must be carefully monitored. Short term supplemental therapy may be necessary if calcium, phosphate or magnesium levels are low.

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- If your kidneys are not functioning properly or if their function worsens then the amount of DRONAMYL 4 mg/5 ml that you are administered may be reduced or stopped.
- If you have or have had pain, swelling or numbness of the jaw, a feeling of heaviness in the jaw, loosening of a tooth or non-healing of sores or discharge, as these could be signs of a condition called osteonecrosis of the jaw.
- If you are having dental treatment or are due to undergo dental surgery, tell your dentist that you are being treated with DRONAMYL 4 mg/5 ml.
- If you are using steroids, if you are on cancer treatment or have an ear infection and you are administered DRONAMYL 4 mg/5 ml, it may lead to a condition that exposes the bone tissue in your ear.
- You may develop severe bone, joint and or muscle pain.
- You may develop sudden fractures in parts of your legs even if you may not have hurt your legs. These fractures may take long to heal and you will need orthopaedic care.
- You may develop flu-like symptoms that include fever, body pain, headache, nausea, vomiting and diarrhoea when you begin treatment with DRONAMYL 4 mg/5 ml.
- If you are being treated with DRONAMYL 4 mg/5 ml (zoledronic acid), you should not be treated with medicines that also contain zoledronic acid and are used to treat osteoporosis and other non-cancer diseases of the bone, or any other bisphosphonate, concomitantly.
- Reduced levels of calcium in the blood (hypocalcaemia), sometimes leading to muscle cramps, dry skin and a burning sensation, have been reported in patients treated with DRONAMYL 4 mg/5 ml. Irregular heartbeat (cardiac dysrhythmia), seizures, spasm and twitching (tetany) have been reported as secondary to severe hypocalcaemia. In some instances, the hypocalcaemia may be life-threatening. If any

of these apply to you, tell your doctor straight away. If you have pre-existing hypocalcaemia, it must be corrected before initiating the first dose of DRONAMYL 4 mg/5 ml. You will be given adequate calcium and vitamin D supplements.

Use in the elderly

DRONAMYL 4 mg/5 ml can be given to elderly people. There is no evidence to suggest that any additional precautions are needed.

Children and adolescents

Do not administer DRONAMYL 4 mg/5 ml to children aged 1 year to 17 years, as safety and efficacy have not been established.

Other medicines and DRONAMYL 4 mg/5 ml

Always tell your healthcare provider if you are taking any other medicine (this includes complementary or traditional medicines).

Tell your doctor if you are taking any of the following medicines:

- Aminoglycosides (medicines used to treat severe infections), calcitonin (hormone that reduces calcium levels when it is above the normal level or loop diuretics (medicine used to treat hypertension), since the combination of these with bisphosphonates may cause the calcium level in the blood to become too low.
- Thalidomide (a medicine used to treat a certain type of blood cancer involving the bone) or any other medicines which may harm your kidneys.
- Chemotherapy and the use of corticosteroids together with DRONAMYL 4 mg/5 ml may cause the development of a condition called osteonecrosis of the jaw. The condition causes the jawbone to become exposed.

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- Medicines that also contains zoledronic acid and is used to treat osteoporosis and other non-cancer diseases of the bone), or any other bisphosphonate, since the combined effects of these medicines taken together with DRONAMYL 4 mg/5 ml are unknown.
- Anti-angiogenic medicines (used to treat cancer), since the combination of these with DRONAMYL 4 mg/5 ml has been associated with an increased risk of osteonecrosis of the jaw (ONJ).

Pregnancy and breastfeeding and fertility

You should not receive DRONAMYL 4 mg/5 ml if you are pregnant. Tell your doctor if you are or think that you may be pregnant.

You must not receive DRONAMYL 4 mg/5 ml if you are breastfeeding.

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking DRONAMYL 4 mg/5 ml.

Women of child-bearing potential should be advised to avoid becoming pregnant and advised of the potential hazard to the foetus while receiving DRONAMYL 4 mg/5 ml. There may be a risk of foetal harm e.g. skeletal and other abnormalities if a woman becomes pregnant while receiving DRONAMYL 4 mg/5 ml therapy.

Driving and using machinery

It is not always possible to predict to what extent DRONAMYL 4 mg/5 ml may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which DRONAMYL 4 mg/5 ml affects them. There have been cases of drowsiness and sleepiness with the use of DRONAMYL 4 mg/5 ml. You should therefore be careful when driving, using machinery or performing other tasks that need full attention.

3. How DRONAMYL 4 mg/5 ml is given

You will not be expected to give yourself DRONAMYL 4 mg/5 ml. It will be given to you by a person who is qualified to do so.

- Your doctor will decide on a dose which is right for you. The usual single dose given is 4 mg.
- Your doctor will recommend that you drink enough water before each treatment to help prevent dehydration.
- Carefully follow all the other instructions given to you by your doctor, healthcare provider or pharmacist. Your doctor will tell you how long your treatment with DRONAMYL 4 mg/5 ml will last.
- If you have the impression that the effect of DRONAMYL 4 mg/5 ml is too strong or too weak, tell your doctor or pharmacist.

How often will you receive DRONAMYL 4 mg/5 ml:

- If you are being treated for the prevention of bone complications due to bone metastases, you will be given one infusion of DRONAMYL 4 mg/5 ml every three to four weeks.
- If you are being treated to reduce the amount of calcium in your blood, you will normally only be given one infusion of DRONAMYL 4 mg/5 ml.

How will you receive DRONAMYL 4 mg/5 ml:

- DRONAMYL 4 mg/5 ml is given as a drip (infusion) into a vein which should take at least 15 minutes and should be administered as a single intravenous solution in a separate infusion line.

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- Patients whose blood calcium levels are not too high will also be prescribed calcium and vitamin D supplements to be taken each day.

If you receive more DRONAMYL 4 mg/5 ml than you should

Since a healthcare professional will administer DRONAMYL 4 mg/5 ml, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you have received doses higher than those recommended, you must be carefully monitored by your doctor. This is because you may develop serum electrolyte abnormalities (e.g. abnormal levels of calcium, phosphorus and magnesium) and/or changes in kidney function, including severe kidney impairment. If your level of calcium falls too low, you may have to be given supplemental calcium by infusion.

If you missed a dose of DRONAMYL 4 mg/5 ml

Since a healthcare provider will administer DRONAMYL 4 mg/5 ml, it is unlikely that the dose will be missed.

4. Possible side effects

DRONAMYL 4 mg/5 ml can have side effects.

Not all side effects reported for DRONAMYL 4 mg/5 ml are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking DRONAMYL 4 mg/5 ml, please consult your healthcare provider for advice.

At the beginning of treatment with DRONAMYL 4 mg/5 ml you may experience flu-like symptoms such as fever, tiredness, weakness, drowsiness, chills and pain in various parts of

the body. This condition is called acute reaction phase and occurs because your body is having a response to the treatment that you are receiving.

If any of the following happens, stop taking DRONAMYL 4 mg/5 ml and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching, increased sweating,
- fainting,
- skin reactions (pain, redness and swelling) at the infusion site.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to DRONAMYL 4 mg/5 ml. 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:

- Pain in the mouth, teeth and/or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth. These could be signs of bone damage in the jaw.
- Unusual break of the thigh bone, particularly in patients on long-term treatment for osteoporosis. Early signs experiencing may be pain, weakness or discomfort in your thigh, hip or groin and you should contact your doctor immediately.

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

Tell your doctor if you notice any of the following:

The following side effects have been reported frequently:

- tiredness, which may indicate that you have a low level of red blood cells (anaemia) as well as other blood disorders which your doctor will establish by doing the necessary tests,
- headache,
- inflammation of the membrane lining the eyelid,
- nausea, vomiting, decreased appetite,
- bone, joint and/or muscle pain, joint stiffness,
- kidney disorders. kidney failure will be determined by your doctor with certain specific blood tests,
- low counts of white blood cells and blood platelets, which your doctor will establish by doing the necessary tests.

The following side effects have been reported less frequently:

- anxiety, sleep disturbance, mental disturbances,
- dizziness, taste abnormality, sleepiness, tremor,
- tearing of the eyes; eyes sensitive to light, painful redness and/or swelling of the eyes,
- low blood pressure or high blood pressure,
- irregular heartbeat,
- difficulty in breathing with wheezing or coughing,
- diarrhoea, constipation, stomach pain, dry mouth,
- muscle cramps,
- ear pain or discharge from the ear,
- pain in chest,
- increase in weight,
- red patches on the skin,

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- low level of magnesium and potassium in the blood. Your doctor will monitor this and take necessary steps.

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

Reporting of side effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions 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 DRONAMYL 4 mg/5 ml.

5. How to store DRONAMYL 4 mg/5 ml

Store all medicines out of reach of children.

Store at or below 25 ˚C.

Protect from light.

Do not use the medicine after the expiry date which is shown on the carton and label.

Do not remove ampoule from carton until required for use.

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

Do not store in a bathroom.

After aseptic dilution, it is preferable to use the diluted product immediately. If not used immediately, the duration and conditions of storage prior to use are the healthcare provider's

responsibility. The total time between dilution, storage in a refrigerator at 2 to 8 °C and end of administration must not exceed 24 hours. Do not freeze the reconstituted solution.

Only clear solution free from particles and discoloration should be used.

6. Contents of the pack and other information

What DRONAMYL 4 mg/5 ml contains:

The active substance is zoledronic acid.

The other ingredients are:

Sodium citrate

Sodium hydroxide (pH adjuster)

Hydrochloric acid, concentrated (pH adjuster)

Water for injections

What DRONAMYL 4 mg/5 ml looks like and contents of the pack:

What DRONAMYL 4 mg/5 ml looks like:

Clear and colourless solution, free from particulate matter.

Contents of the pack:

15 ml colourless type 1 glass vial containing 4 mg of zoledronic acid in a 5 ml solution with a bromobutyl rubber stopper coated with a tetrafluoroethylene and ethylene copolymer and aluminium crimp cap with plastic flip-off button. The vials are packed in 1’s in a cardboard carton.

Holder of Certificate of Registration and Manufacturer

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Access to the corresponding Professional Information

Can be obtained on the SAHPRA website.