1.3.2 Proposed Patient Information Leaflet

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS **S6**

ORAMORPH® ORAL DROPS 20MG/ML, 20mg/ml, Solution

Morphine sulfate

Sugar-free

Read all of this leaflet carefully before you start taking ORAMORPH® ORAL DROPS 20MG/ML

- 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.
- ORAMORPH® ORAL DROPS 20MG/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 is ORAMORPH® ORAL DROPS 20MG/ML and what it is used for

ORAMORPH® ORAL DROPS 20MG/ML is a strong-acting painkiller from the group of opiates. It is used for the relief of severe pain in adults.

2. What you need to know before you take ORAMORPH® ORAL DROPS 20MG/ML

Do not take ORAMORPH® ORAL DROPS 20MG/ML:

- if you are hypersensitive (allergic) to morphine sulphate or any of the other ingredients of ORAMORPH® ORAL DROPS 20MG/ML (listed in section 6).
- if you have an existing bowel obstruction (ileus).
- if you have unclear acute painful abdominal symptoms (acute abdomen).
- if you have a head injury or any another medical condition that's causing a growing pressure inside your skull with a decrease in the level of consciousness, unless you are being ventilated.
- if you struggle to breathe or your airways are compromised.
- if you are pregnant or breastfeeding.

Warnings and precautions

Talk to your doctor or pharmacist before taking ORAMORPH® ORAL DROPS 20MG/ML.

Special care should be taken with ORAMORPH® ORAL DROPS 20MG/ML:

- if there is dependence on opioids
- if there is loss of consciousness
- if you have disease states in which a disturbance of the respiratory center and respiratory function is present
- if you have altered heart (cor pulmonale) due to chronic congestion of the pulmonary circulation
- if you there is increased intracranial pressure
- if you have low blood pressure associated with low circulating blood volume (hypotension with hypovolaemia)
- if you have enlarged prostate gland (prostatic hypertrophy) with residual urine (risk of bladder rupture (tear of the bladder) due to urinary retention)
- if you have a urinary tract constrictions or colic biliary diseases
- if you have obstructive (associated with stenosis) and inflammatory bowel disease
- if you have an adrenal gland tumour (phaeochromocytoma)
- if you have inflammation of the pancreas (pancreatitis)
- if you have an underactive thyroid (hypothyroidism)

- if you have epileptic seizures or increased sensitivity to convulsions.

Talk to your doctor or pharmacist if you experience any of the following symptoms while taking ORAMORPH® ORAL DROPS 20MG/ML:

- increased sensitivity to pain despite the fact that you are taking increasing doses (hyperalgesia). Your doctor will decide whether you will need a change in dose or a change in strong analgesic ("painkiller"), (see section 2).
- weakness, fatigue, lack of appetite, nausea, vomiting or low blood pressure. This may be a symptom of the adrenals producing too little of the hormone cortisol, and you may need to take hormone supplement.
- loss of libido, impotence, cessation of menstruation. This may be because of decreased sex hormone production.
- if you have once been dependent on drugs or alcohol. Also tell if you feel that you are becoming dependent on ORAMORPH® ORAL DROPS 20MG/ML while you are using it. You may have started to think a lot about when you can take the next dose, even if you do not need it for the pain.
- abstinence symptoms or dependence. The most common abstinence symptoms are mentioned in section 3. If this occurs, your doctor may change the type of medicine or the times between doses.

In chronic pain patients, the risk of psychological dependence is significantly reduced or differentiated.

ORAMORPH® ORAL DROPS 20MG/ML should be administered with caution before and after surgery (increased risk of intestinal paralysis or respiratory depression).

Constipation occurs frequently with morphine treatment. Especially if you have had troubles in bowel movement before you start taking, you should take a laxative from the beginning. Please talk to your doctor.

Because of the mutagenic properties of morphine, this drug should be administered to men or women

in reproductive age only when effective prevention is ensured.

In older people, ORAMORPH® ORAL DROPS 20MG/ML is to be dosed very carefully (see section 3).

Use of ORAMORPH® ORAL DROPS 20MG/ML can lead to positive results in doping controls.

Children

ORAMORPH® ORAL DROPS 20MG/ML must not be used in children.

Other medicines and ORAMORPH® ORAL DROPS 20MG/ML

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

Concomitant use of ORAMORPH® ORAL DROPS 20MG/ML and other centrally acting medicines, i.e. on brain functions, such as medicines for anxiety disorders (tranquilizers), for depression (antidepressants) for mental disorders (neuroleptics), for anesthesia (anesthetics), for insomnia (hypnotics, sedatives, barbiturates), allergy or travel sickness (antihistamines/antiemetics) or other potent painkillers (opioids)] or alcohol can lead to an increase in side effects of morphine, especially impairment of respiratory function.

Concomitant use of ORAMORPH® ORAL DROPS 20MG/ML and sedative medicines such as benzodiazepines or related drugs increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible. However, if your doctor does prescribe ORAMORPH® ORAL DROPS 20MG/ML together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor. Please tell your doctor about all sedative medicines you are taking and follow your doctor’s dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

Medicines with anticholinergic activity (e.g. psychotropic drugs, medicines for allergies, vomiting or Parkinson's disease) may increase anticholinergic side effects of opioids (e.g. constipation, dry mouth and urination disorders).

Cimetidine (used to treat stomach ulcers) and other medicines affecting liver metabolism may cause elevated levels of morphine in the blood by inhibiting morphine degradation.

ORAMORPH® ORAL DROPS 20MG/ML should not be administered concomitantly with MAO inhibitors (medicines that are effective against depression). After administration of MAO inhibitors within the last 14 days prior to the administration of another opioid (pethidine), life-threatening effects have been observed and concerned the brain (central nervous system) as well as the respiratory and circulatory functions. The same interactions with MAO inhibitors cannot be excluded also for are ORAMORPH® ORAL DROPS 20MG/ML.

The effect of muscle relaxants medicines can be greater with morphine.

Concomitant use of rifampicin (used to treat tuberculosis) may result in a weakening of the effect of morphine.

ORAMORPH® ORAL DROPS 20MG/ML with food, drink, and alcohol

While taking ORAMORPH® ORAL DROPS 20MG/ML you must not drink alcohol because alcohol can significantly increase the depressant effect of morphine.

Pregnancy, breastfeeding and fertility

Pregnancy

ORAMORPH® ORAL DROPS 20MG/ML should not be used in pregnancy. Babies born to mothers taking ORAMORPH® ORAL DROPS 20MG/ML may suffer withdrawal (abstinence) symptoms which should be treated by a doctor.

Breastfeeding

Morphine is excreted into breast milk and may reach effective concentrations in the infant. Mothers taking ORAMORPH® ORAL DROPS 20MG/ML should not breastfeed their babies.

Fertility

Men and women of reproductive age should only take ORAMORPH® ORAL DROPS 20MG/ML if effective contraception to prevent pregnancy is used.

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 this medicine.

Driving and using machines

ORAMORPH® ORAL DROPS 20MG/ML impairs attention and responsiveness. You cannot react quickly enough to unexpected and sudden events.

Discuss with your doctor whether and under what conditions you can, for example, drive a car. A stronger impact is to be expected especially at the beginning of treatment, with increase and change of dosage as well as taking the preparation in combination with alcohol or sedatives. Do not drive a car or other vehicles. Do not use electrical tools or machines.

ORAMORPH® ORAL DROPS 20MG/ML contains sodium benzoate.

This medicine contains 1 mg sodium benzoate per ml. Sodium benzoate may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks of age).
ORAMORPH® ORAL DROPS 20MG/ML is not for use in children.

3. HOW TO TAKE ORAMORPH® ORAL DROPS 20MG/ML

Do not share medicines prescribed for you with any other person.
Always take ORAMORPH® ORAL DROPS 20MG/ML exactly as your doctor or pharmacist has told

you. Check with your doctor or pharmacist if you are not sure.

The dose of ORAMORPH® ORAL DROPS 20MG/ML must be adapted to the severity of the pain and your individual sensitivity.

Unless otherwise prescribed, the usual range of single and daily doses for adults is according to the following table on the basis of a single dose of 0,2 to 0,3 mg morphine sulphate/kg of body weight:

Age	Single dose	Daily dose
Adults	0,5-3 ml, i.e.8-48 drops of ORAMORPH® ORAL DROPS 20MG/ML corresponding to 10-60 mg morphine sulfate	Up to 18 ml, i.e. 288 drops of ORAMORPH® ORAL DROPS 20MG/ML corresponding up to 360 mg morphine sulfate

The doses can be repeated after 4 to 6 hours. The maximum daily dose should not exceed 4 - 6 times the single doses. If higher daily doses are required, appropriate dosage can be obtained using the other alternative strengths or in combination with ORAMORPH® ORAL DROPS 20MG/ML.

Hepatic or renal dysfunction

In patients with hepatic or renal impairment and suspected delayed gastrointestinal passage, ORAMORPH® ORAL DROPS 20MG/ML is to be dosed very carefully.

Elderly

Patients in advanced age (usually 75 years of age) and patients with poor body general conditions may be more sensitive to morphine. Therefore, make sure that the dose adjustment is conservative and/or to select longer dosing intervals. If necessary, switch to lower dosage strengths.

Special instructions for dose adjustment

For readjustment of the dosage, possibly use forms with a lower content of active substance, also in addition to an existing therapy with prolonged-release tablets.

In principle, a sufficiently high dose should be given, while the smallest effective dose should be sought in the individual analgesic case. In case you undergo with another additional pain treatment (e.g. surgery, plexus blockade), the dose will be reset. This will be done by your doctor in the given case.

Method of administration

The prescribed dose is measured as drops.

The drops are taken with sufficient liquid, mixed in water or fruit juice.

2 drops = 2,5 mg morphine sulfate

4 drops = 5 mg morphine sulfate

8 drops = 10 mg morphine sulfate

16 drops = 20 mg morphine sulphate

24 drops = 30 mg morphine sulphate

Duration of treatment

Your doctor will tell you how long your treatment with ORAMORPH® ORAL DROPS 20MG/ML will last, depending on the pain symptoms. ORAMORPH® ORAL DROPS 20MG/ML should be taken in any case no longer than it is necessary. If a long-term pain treatment with ORAMORPH® ORAL DROPS 20MG/ML appears to be necessary according to type and severity of the disease, careful and regular review should take place at short intervals (possibly making breaks in treatment, see section "If you stop taking ORAMORPH® ORAL DROPS 20MG/ML "), whether and to what extent a medical need still exists. If necessary, switch to more appropriate forms. In the treatment of chronic pain, a fixed dose schedule is to be preferred.

If you have the impression that the effect of ORAMORPH® ORAL DROPS 20MG/ML is too strong or too weak, tell your doctor or pharmacist.

If you take more ORAMORPH® ORAL DROPS 20MG/ML than you should

Your caregiver must be informed of the signs of overdose and must be aware of what steps to take if such an event occurs.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison center. Specifically, the following symptoms can occur: small pupils, impaired breathing to respiratory arrest, loss of consciousness up to coma, hypotension leading to shock, increase in heart rate, dizziness. The overdose of strong opioids can lead to a fatal outcome.

People who have taken an overdose may get pneumonia from inhaling vomit or foreign matter. Symptoms may include breathlessness, cough, and fever.
Under no circumstances you can go into situations that require more attention, such as driving a car.

The following measures are useful in case of overdose until the arrival of a doctor: keep awake, give orders to breath, provide breathing assistance.

If you forget to take ORAMORPH® ORAL DROPS 20MG/ML

If you forgot to take a dose of ORAMORPH® ORAL DROPS 20MG/ML, this will lead to poor or a lack of pain relief. Continue the application in the recommended manner. In any circumstances you should not double the dose.

If you stop taking ORAMORPH® ORAL DROPS 20MG/ML

If you want to interrupt or stop the treatment, you should talk to your doctor about the reasons for the interruption and other modes of treatment.

With prolonged use of ORAMORPH® ORAL DROPS 20MG/ML a physical dependence can develop. Abrupt discontinuation of treatment will therefore be accompanied by withdrawal symptoms. These can be body aches, headache, muscle pain, tremors, anxiety, dissatisfaction, tension, agitation, confusion, irritability, recurrent insomnia, mood swings, hallucinations seizures, diarrhoea, stomach pain, nausea, flu-like symptoms, fast heartbeat and large pupils.

Since the risk of the occurrence of withdrawal symptoms upon sudden discontinuation of treatment is

higher, the dosage should be reduced gradually when discontinuing the treatment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

ORAMORPH® ORAL DROPS 20MG/ML can have side effects.

Not all side effects reported for ORAMORPH® ORAL DROPS 20MG/ML are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while taking ORAMORPH® ORAL DROPS 20MG/ML, please consult your health care provider for advice.

If any of the following happens, stop taking / using ORAMORPH® ORAL DROPS 20MG/ML and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Serious allergic reaction which causes difficulty in breathing and dizziness.

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

Tell your doctor if you notice any of the following:

Frequent side effects:

- Headache
- Dizziness
- Mood changes
- Changes in awareness
- Sleep disturbances
- Disturbance in thinking and feeling (e.g. thought disorders, cognitive problems or hallucinations, confusion)
- Nausea
- Dry mouth
- Constipation
- Vomiting (especially at the beginning of treatment)
- Loss of appetite

- Taste disturbances
- Problems in emptying the bladder
- Sweating
- Hives
- Itching

Less frequent side effects:

- Drop in blood pressure and / or shortness of breath (anaphylactic reactions)
- Shaking (tremor)
- Involuntary muscle twitching
- Epileptic seizures
- Particularly at high doses, Increased sensitivity to pain that does not respond to further increase in the dose of morphine
- Dependence
- Decrease in libido or erectile dysfunction
- Blurred vision
- Double vision
- Nystagmus
- Pupillary constriction
- High level of pancreatic enzymes (seen on blood test)
- Inflammation of the pancreas
- Intestinal obstruction
- Severe abdominal pain
- Biliary colic
- High level of liver enzymes (seen on blood test)
- Renal colic
- Muscle cramps
- Muscle rigidity
- Convulsions of the muscles of the airways (bronchospasm)
- Shortness of breath (dyspnea)

- For patients in intensive care have been observed fluid retention in the lungs that is not due to failure of cardiac function (non-cardiogenic pulmonary oedema)
- Water accumulation in the tissues (peripheral edema) - they resolve after discontinuation
- Clinically significant drop and rise in blood pressure and heart rate
- Facial flushing
- Palpitation
- General weakness
- Fainting
- Heat failure
- Habituation and eventually come to decrease in the activity (development of tolerance)
- Withdrawal symptoms
- Chills
- Absence of menstruation
- A syndrome of inappropriate release of the diuretic hormone (SIADH; symptom: lack of sodium (hyponatraemia) can be triggered).

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 or nurse. 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 ORAMORPH® ORAL DROPS 20MG/ML.

5. HOW TO STORE ORAMORPH® ORAL DROPS 20MG/ML

Store all medicines out of reach of children.

Store at or below 25 °C.

Store in the original package / container.

Keep the bottle in the carton to protect from light.

After opening the bottle, ORAMORPH® ORAL DROPS 20MG/ML shelf-life is of 90 days.

Do not use this medicine after the expiry date which is stated on the packaging after "EXP". The expiry date refers to the last day of the month.

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 ORAMORPH® ORAL DROPS 20MG/ML contains:

The active substance is morphine sulfate.

The other ingredients are purified water, citric acid, sodium benzoate, sodium edetate.

What ORAMORPH® ORAL DROPS 20MG/ML looks like and contents of the pack

ORAMORPH® ORAL DROPS 20MG/ML is a clear, colorless solution.

The medicine is available in packs of 20 ml oral drops, solution.

Holder of Certificate of Registration

Eurolab (Pty) Ltd

Woodmead Office Park, 3 Stirrup Lane

Van Reenens Avenue, Woodmead, 2144

This leaflet was last revised in

Registration Number

To be allocated