ORAMORPH® 20 MG/ML

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Oramorph® 20 mg/ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active pharmaceutical ingredient: morphine (as sulphate).

1 ml oral drops, solution contains 20 mg morphine sulphate, corresponding to 15 mg morphine.
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral drops, solution
Clear, colourless solution.

4. CLINICAL PARTICULARS

WARNING: RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

- Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death [see section 4.4]
- Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation

Therapeutic indications
For the relief of moderate to severe pain.

4.1 Posology and method of administration

Posology

The dosage of Oramorph® 20 mg/ml has to be adapted to the severity of pain and to the individual sensitivity of the patient.
The recommended range of the single and daily doses for children and adults is stated in the following table based on a single dose of 0.2 to 0.3 mg morphine sulphate/kg body weight.

Age (body weight)	Single dose
Children under 3 years	contra indicated
Children 3-5 years (12.5 - 18 kg)	0.125-0.25 ml, i. e. 2-4 drops Oramorph® 20 mg/ml, corresponding to 2.5-5 mg morphine sulphate, every 4-6 hours
Children 6-12 years (20 - 40 kg)	0.25-0.5 ml, i. e. 4-8 drops Oramorph® 20 mg/ml, corresponding to 5-10 mg morphine sulphate, every 4-6 hours
Adolescents 13-18 years / Adults (40-50 kg)	0.5-1.0 ml, i. e. 8-16 drops Oramorph® 20 mg/ml, corresponding to 10-20 mg morphine sulphate, every 4-6 hours
Adults	0.5-3 ml, i. e. 8-48 drops Oramorph® 20 mg/ml, corresponding to 10-60 mg morphine sulphate, every 4-6 hours

The dose is removed from the 20 ml bottle by counting the drops (1 drop = 1.25 mg morphine sulphate).
In case of decreasing effect the single doses can be repeated after 4-6 hours. The maximum daily doses should not exceed the single doses by more than 4- to 6-fold.
If higher daily doses are needed other appropriate dosage strengths have to be considered alternatively or in combination with Oramorph® 20 mg/ml.

When patients are transferred from other morphine preparations to Oramorph oral solution dosage titration may be appropriate.
A calibrated oral dosing pipette is supplied with this dosage form for accurate and convenient dose adjustment. The required dose may be added to a soft drink immediately prior to administration.
Morphine Sulphate is readily absorbed from the gastro-intestinal tract following oral administration. However, when Oramorph oral is used in place of parenteral morphine, a 50 % to 100 % increase in dosage is usually required in order to achieve the same level of analgesia.

Renal or hepatic impairment

In patients with impaired liver or kidney function and in those with suspected delayed gastrointestinal passage Oramorph® 20 mg/ml should be dosed with special caution.

Elderly patients

Elderly patients (usually 75 years and older) and patients with poor overall physical condition may be more sensitive to morphine. Therefore, the adjustment of dose has to be done more carefully and / or the dosage intervals have to be extended. As appropriate, lower dosage strengths have to be given instead.

Special recommendations concerning dose adjustment

For initial dose adjustment pharmaceutical forms with lower active ingredient content may be applied, possibly also in addition to an existing therapy with prolonged-release tablets.
In principle, the administered dose should be sufficiently high and at the same time the lowest dose needed for pain relief in the individual case should be aimed at.

For treatment of chronic pain dosing following a fixed time schedule is preferred.

In patients receiving another additional analgesic treatment (e. g. surgery, plexus blockage) the dose should be readjusted following the respective measure.

Method and duration of administration

The oral solution is administered with a sufficient quantity of liquid. The medication can be taken independently of meals.

The physician decides about the duration of the treatment in dependence on the pain.
By no means Oramorph® 20 mg/ml should be given longer than absolutely necessary. If prolonged analgesic treatment with Oramorph® 20 mg/ml appears necessary based on the nature and severity of the disease, careful and regular monitoring within short time intervals should be installed (if required by means of temporary suspension of the medication) to evaluate if and to what extent the therapeutic necessity persists. If needed, more suitable pharmaceutical forms should be applied instead. In case of chronic pain conditions, a fixed dosage regimen is preferred.

Discontinuation of therapy
Since the risk of occurrence of withdrawal symptoms is increased in case of abrupt discontinuation of therapy the dose should be reduced stepwise after termination of treatment.

4.2 Contraindications

Oramorph® 20 mg/ml must not be administered in case of:
- hypersensitivity to morphine or to any of the excipients listed in section 6.1
- ileus
- acute abdomen.

4.3 Special warnings and precautions for use

Especially careful monitoring by the physician and possibly dose reduction is needed in case of:
- opioid dependence
- disturbances of consciousness
- conditions associated with a disturbance of the respiratory centre and of the respiratory function or where such disturbances must be avoided
- cor pulmonale
- conditions with increased intracranial pressure unless ventilation is performed
- hypotension in the setting of hypovolaemia
- prostatic hyperplasia with residual urine (risk of bladder rupture due to urinary retention)
- obstruction or spasms of urinary tracts
- diseases of biliary ducts
- obstructive and inflammatory bowel diseases
- phaeochromocytoma
- pancreatitis
- hypothyroidism

- epilepsia or increased propensity to seizures.

In case of an opioid overdose respiratory depression is the most important risk.

The use of morphine can be associated with physical dependence. Discontinuation after repeated use or application of an opioid antagonist can provoke typical signs of withdrawal (withdrawal syndrome).

Opioid Use Disorder (abuse and dependence) and withdrawal (abstinence) syndrome
Tolerance and physical and/or psychological dependence may develop upon repeated administration of opioids such as Oramorph 20 mg/ml.
Repeated use of Oramorph 20 mg/ml can lead to Opioid Use Disorder (OUD). A higher dose and longer duration of opioid treatment, can increase the risk of developing OUD. Abuse or intentional misuse of Oramorph 20 mg/ml may result in overdose and/or death. The risk of developing OUD is increased in patients with a personal or a family history (parents or siblings) of substance use disorders (including alcohol use disorder), in current tobacco users or in patients with a personal history of other mental health disorders (eg. major depression, anxiety and personality disorders).
Before initiating treatment with Oramorph 20 mg/ml and during the treatment, treatment goals and a discontinuation plan should be agreed with the patient (see section 4.2). Before and during treatment the patient should also be informed about the risks and signs of OUD. If these signs occur, patients should be advised to contact their physician.
Patients will require monitoring for signs of drug-seeking behavior (e.g. too early requests for refills). This includes the review of concomitant opioids and psycho-active drugs (like benzodiazepines). For patients with signs and symptoms of OUD, consultation with an addiction specialist should be considered.
Symptoms can be minimised with adjustments of dose or dosage form, and gradual withdrawal of morphine. For individual symptoms, see section 4.8

Therapeutic administration in patients with chronic pain is associated with a markedly reduced risk of psychological dependence and has to be assessed in a different light.

Morphine has an abuse potential similar to other strong agonist opioids, and should be used with particular caution in patients with a history of alcohol or drug abuse.

Compared to patients not undergoing surgery the use of Oramorph® 20 mg/ml is associated with an increased risk of ileus or respiratory depression during the postoperative phase and should therefore be administered with caution in patients before and after surgery.

Due to the analgesic effect of morphine serious intraabdominal complications such as bowel perforation can be masked.

Adrenal insufficiency
Opioid analgesics may cause reversible adrenal insufficiency requiring monitoring and glucocorticoid replacement therapy. Symptoms of adrenal insufficiency may include e.g. nausea, vomiting, loss of appetite, fatigue, weakness, dizziness, or low blood pressure.

In case of pre-existing adrenocortical insufficiency (e.g. Morbus Addison) plasma concentrations of cortisol should be monitored and possibly corticoids should be substituted.

Acute chest syndrome (ACS) in patients with sickle cell disease (SCD)
Due to a possible association between ACS and morphine use in SCD patients treated with morphine during a vaso-occlusive crisis, close monitoring for ACS symptoms is warranted.

Oramorph® 20 mg/ml must not be used in children under 3 years of age.

Decreased Sex Hormones and increased prolactin
Long-term use of opioid analgesics may be associated with decreased sex hormone levels and increased prolactin. Symptoms include decreased libido, impotence or amenorrhea. Due to its mutagenic properties, morphine should be given to males with procreative potential and to females with childbearing potential only if effective contraceptive measures are guaranteed (see section 4.6).

Hyperalgesia that does not respond to a further dose increase of morphine may occur in particular in high doses. A morphine dose reduction or change in opioid may be required.

Risk from concomitant use of sedative medicines such as benzodiazepines or related drugs
Concomitant use of Oramorph® 20 mg/ml and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicines should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe Oramorph® 20 mg/ml concomitantly with sedative medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible. The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms (see section 4.5).

Sleep-related breathing disorders
Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the total opioid dosage.

Severe cutaneous adverse reactions (SCARs)
Acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, has been reported in association with morphine treatment. Most of these reactions occurred within the first 10 days of treatment. Patients should be informed about the signs and symptoms of AGEP and advised to seek medical care if they experience such symptoms.
If signs and symptoms suggestive of these skin reactions appear, morphine should be withdrawn and an alternative treatment considered.

Hepatobiliary disorders
Morphine may cause dysfunction and spasm of the sphincter of Oddi, thus raising intrabiliary pressure and increasing the risk of biliary tract symptoms and pancreatitis.

Plasma concentrations of morphine may be reduced by rifampicin. The analgesic effect of morphine should be monitored and doses of morphine adjusted during and after treatment with rifampicin.

Within the first day of concomitant P2Y12 inhibitor and morphine treatment, reduced efficacy of P2Y12 inhibitor treatment has been observed (see section 4.5).

The use of Oramorph® 20 mg/ml can lead to positive results of doping tests.

4.4 Interaction with other medicinal products and other forms of interaction

The following interactions of this medicinal product have to be considered:

Concomitant application of morphine and other medicines with centrally sedating effects such as tranquilisers, anaesthetics, hypnotics and sedatives, neuroleptics, barbiturates, antidepressants, antihistamines / antiemetics, and other opioids, gabapentin or pregabalin or alcohol can result in an increase of the adverse effects of morphine at the usually recommended dose. This applies especially to the possibility of respiratory depression, sedation, hypotension and even coma.

Sedative medicines such as benzodiazepines or related drugs
The concomitant use of opioids with sedative medicines such as benzodiazepines or related drugs increases the risk of sedation, respiratory depression, coma and death because of additive CNS

Medicines with anticholinergic effect (e. g. psychotropic drugs, antihistamines, antiemetics, drugs for the treatment of Morbus Parkinson) can enhance anticholinergic adverse effects of opioids (e. g. constipation, dry mouth or disturbances of micturition).

Cimetidine and other drugs impairing liver metabolism can lead to higher morphine plasma concentrations due to the inhibition of its metabolism

Morphine can enhance the effect of muscle relaxants.
In patients pre-treated with certain antidepressants (MAO inhibitors) within 14 days prior to initiation of opioids life-threatening interactions affecting the central nervous system, the respiratory and the circulatory function have been observed in relation to pethidine. Comparable effects related to morphine cannot be excluded.

Concomitant application of rifampicin can lead to a decrease in the effect of morphine.

A delayed and decreased exposure to oral P2Y12 inhibitor antiplatelet therapy has been observed in patients with acute coronary syndrome treated with morphine. This interaction may be related to reduced gastrointestinal motility and apply to other opioids. The clinical relevance is unknown, but data indicate the potential for reduced P2Y12 inhibitor efficacy in patients co- administered morphine and a P2Y12 inhibitor (see section 4.4). In patients with acute coronary syndrome, in whom morphine cannot be withheld and fast P2Y12 inhibition is deemed crucial, the use of a parenteral P2Y12 inhibitor may be considered.

4.5 Fertility, pregnancy and lactation

Pregnancy

Data in humans are not sufficient to permit the assessment of a potential teratogenic risk. A potential correlation with a higher incidence of hernias was reported.
Morphine crosses the placental barrier. Animal studies have revealed a damaging potential for the off-spring during the entire duration of pregnancy (see section 5.3). Therefore, morphine may be applied during pregnancy only if the benefit for the mother clearly outweighs the risk for the foetus.
Due to its mutagenic properties, morphine should only be used in males with procreative potential and females with childbearing potential if effective contraception is guaranteed.

Newborns whose mothers received opioid analgesics during pregnancy should be monitored for signs of neonatal withdrawal (abstinence) syndrome. Treatment may include an opioid and supportive care.

Withdrawal symptoms have been reported in neonates following prolonged morphine application

during pregnancy.

Delivery

Morphine can prolong or shorten the duration of labour pains. Neonates of mothers receiving opioid analgesics during delivery should be monitored with regard to signs of respiratory depression or of withdrawal syndrome; if necessary, a specific opioid antagonist should be given.

Lactation

Morphine is excreted in human milk where concentrations higher than in maternal plasma are reached. Since clinically relevant concentrations can be reached in infants breast feeding is discouraged.

Fertility

Animal studies have shown that morphine may reduce fertility (see section 5.3. preclinical safety data).

4.6 Effects on ability to drive and use machines

Morphine can impair the attentiveness and the capability to react to such an extent that the ability to drive or to use machines is impaired or inexistent.
This is to be expected especially upon initiation of treatment, dose increase and change in medication as well as in combination with alcohol or the use of sedatives.
The assessment of the individual situation in each case has to be done by the treating physician.
During a stable therapeutic regimen driving is not prohibited generally.

4.7 Undesirable effects

For the evaluation of undesirable effects the following incidences are defined:

Very common	≥ 1/10
Common	≥ 1/100 to < 1/10
Uncommon	≥ 1/1000 to < 1/100
Rare	≥ 1/10000 to < 1/1000
Very rare	< 1/10000
Not known	Cannot be estimated from the available data

Immune system disorders

Not known: anaphylactic or anaphylactoid reactions

Nervous system disorders

Depending on the dose, morphine leads to various extents of respiratory depression and sedation ranging from slight fatigue to giddiness.
Common: headache, dizziness
Very rare: tremor, involuntary muscle twitching, epileptic seizures
Not known: hyperhidrosis
Especially in high doses hyperalgesia or allodynia (see section 4.4), which do not respond to a further increase in morphine doses (possibly dose reduction or opioid rotation is necessary).

Psychiatric disorders

Morphine shows various psychiatric undesirable effects which with regard to severity and nature present differently (depending on the personality and duration of therapy).

Very common:	mood changes, mostly euphoria, but also dysphoria
Common:	changes in activity (mostly sedation, but also enhanced activity or agitation), insomnia, alterations of cognitive and sensory functions (e. g. disturbances in thinking, altered apprehensiveness/hallucinations, confusion)
Very rare:	dependence (see section 4.4), decreased libido and impaired potency

Eye disorders

Very rare:	blurred vision, diplopia, nystagmus

Miosis is a typical accompanying symptom.

Gastrointestinal disorders

Depending on the dose, nausea and dry mouth can occur.
Obstipation is a typical accompanying symptom of long-term treatment.

Common:	vomiting (especially at the beginning of therapy), anorexia, dyspepsia and taste alterations
Rare:	elevation of pancreatic enzymes and pancreatitis respectively
Very rare:	ileus, abdominal pain

Hepato-biliary disorders

Rare:	biliary colics
Very rare:	elevation of liver-specific enzymes
Not known:	spasm of sphincter of Oddi

Renal and urinary disorders

Common:	disturbances of micturition
Rare:	renal colic

Musculoskeletal and connective tissue disorders

Very rare:	muscle cramps, muscle rigidity

Respiratory, thoracic and mediastinal disorders

Rare:	bronchospasm
Very rare:	dyspnoea
Not known:	central sleep apnoea syndrome

Non-cardiogenic pulmonary oedemas have been reported in patients treated under intensive-care conditions.

Skin and subcutaneous tissue disorders

Common:	sweating, hypersensitivity reactions such as urticaria, pruritus
Very rare:	other skin reactions such as exanthema and peripheral oedema (reversible upon termination of therapy)
Not known:	acute generalised exanthematous pustulosis (AGEP)

Anaphylactic and anaphylactoid reactions can occur.

Cardiac disorders

Uncommon: clinically relevant decrease or increase in blood pressure and heart rate
Facial flushing, palpitations, generalised weakness up to loss of consciousness and heart failure can occur.

General disorders and administration site conditions

Tolerance can develop.
Rare: drug withdrawal (abstinence) syndrome
Very rare: asthenia, malaise, chills, amenorrhoea

Endocrine disorders

Very rare: syndrome of inadequate ADH secretion (SIADH, with hyponatraemia as the main symptom).

Drug dependence and withdrawal (abstinence) syndrome
Repeated use of Oramorph 20 mg/ml can lead to drug dependence, even at therapeutic doses. The risk of drug dependence may vary depending on a patient's individual risk factors, dosage, and duration of opioid treatment (see section 4.4).
An abstinence syndrome may be precipitated when opioid administration is suddenly discontinued or opioid antagonists administered, or can sometimes be experienced between doses. For management, see section 4.4.
Physiological withdrawal symptoms include: Body aches, tremors, restless legs syndrome, diarrhoea, abdominal colic, nausea, flu-like symptoms, tachycardia and mydriasis. Psychological symptoms include dysphoric mood, anxiety and irritability. In drug dependence, “drug craving” is often involved.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form /https://sideeffects.health.gov.il

4.8 Overdose

Symptoms of intoxication

The sensitivity towards morphine varies greatly from patient to patient. Therefore, symptoms of intoxication can occur in adults after application of single doses which correspond to a subcutaneous and intravenous dose of about 30 mg. In patients with carcinoma these doses are frequently exceeded without provoking serious adverse reactions.

The manifestation of an opioid intoxication comprises the triad of miosis, respiratory depression and coma. At first pinpoint pupils are observed; however, in case of marked hypoxia the pupils are dilated. Respiration is markedly reduced (breath rate of 2-4 per minute). The patient becomes cyanotic.

Morphine overdosage leads to giddiness and stupor up to coma. The blood pressure remains normal initially, but decreases markedly with progression of intoxication. Persistent decrease in blood pressure can result in shock. Tachycardia, bradycardia and rhabdomyolysis can occur. The body temperature decreases. The skeletal muscles relax; occasionally generalised seizures can develop, especially in children. Death may occur from respiratory failure. Death occurs mostly due to respiratory insufficiency or due to complications such as pulmonary oedema.
Aspiration pneumonia can develop.

Therapy of intoxication

In unconscious patients with respiratory arrest ventilation, intubation and intravenous administration of opioid antagonists (e. g. 0.4 mg naloxone intravenously) are indicated. In case of persistent respiratory insufficiency the single dose has to be repeated 1 to 3 times in 3-minute intervals until the respiratory rate is back to normal and the patient responds to painful stimuli.

The patient has to be strictly monitored (at least for 24 hours) since the duration of action of the opioid antagonist is shorter compared to that of morphine so that recurrence of the respiratory insufficiency has to be expected.

The single dose of the opioid antagonist is 0.01 mg per kg body weight in children. Additionally measures to prevent a decrease in body temperature and to supplement volume may be necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Opioids
ATC-code: N02A A01

Morphine is a phenanthrene alkaloid from *Papaver somniferum* with opioid-agonistic properties. It shows distinct affinity to μ-receptors.

Central effects

Morphine has analgesic, antitussive, sedative, tranquilising, and antidiuretic effects. It provokes respiratory depression and miosis. Emetic and antiemetic effects have been described, the latter occurring as a delayed effect, furthermore a slight decrease in blood pressure and heart rate was reported.

Peripheral effects

Constipation, contraction of the sphincters of the bile ducts, increase in tone of the urinary bladder muscles and the vesical sphincter, prolonged stomach passage effected by pylorus constriction, flushing, urticaria and pruritus due to the release of histamine, and in asthmatic patients bronchospasm, influence on the hypophyseal-hypothalamic axis and consequently influence on hormone effects of corticoids, sex hormones, prolactin and antidiuretic hormone. Manifestation of clinical symptoms due to these hormonal changes may be feasible.

Onset of action after oral application is after 30-90 minutes. The duration of action lasts about 4-6 hours and markedly longer in prolonged-release formulations.

Onset of action after intramuscular or subcutaneous application is after 15-30 minutes, after intravenous application within a few minutes. Independent of these routes of administration the duration of action last about 4-6 hours. Following epidural and intrathecal application locally limited analgesic effects are evident after a few minutes. The duration of action lasts about 12 hours following epidural use and is even longer in case of intrathecal administration.
In vitro as well as animal studies show different effects of opioids of natural origin such as morphine on components of the immune system. The clinical relevance of these findings is not known.

5.2 Pharmacokinetic properties

Following oral application morphine is absorbed fairly rapidly, primarily from the upper small

intestine and to a minor extent also from the stomach. The low absolute bioavailability (20%-40%) is attributed to an extensive first-pass effect.

About 20-35% of morphine is bound to plasma proteins, primarily to the albumin fraction.
After intravenous administration of 4-10 mg as a single dose the distribution volume of morphine is reported at 1.0 to 4.7 l/kg. High tissue concentrations are encountered in the liver, the kidneys, in the gastrointestinal tract and in muscles. Morphine crosses the blood brain barrier.

Metabolism of morphine occurs primarily in the liver but also in bowel epithelium. The main step is the glucuronidation of the phenolic hydroxyl moiety effected by the hepatic UDP-glucuronyltransferase and N-demethylation.

Main metabolites are morphine-3-glucuronide and to a minor extent morphine-6-glucuronide. Among other components sulphate conjugates and oxidative metabolites such as normorphine, morphine-N-oxide and a morphine derivative hydroxylised in position 2 are formed. The half- life of the glucuronides is markedly longer than that of morphine itself. Morphine-6-glucuronide is biologically active. A prolonged effect in patients with renal insufficiency may be attributable to this metabolite.

Following oral and parenteral application, about 80% of the administered morphine is recovered in urine (10% of unchanged morphine, 4% of normorphine, and 65% as glucuronides with a ratio of 10:1 for morphine-3-glucuronide: morphine-6-glucuronide). The elimination half-life of morphine is subject to high interindividual variability. Following parenteral application it ranges from 1.7 to 4.5 hours on average, occasionally about 9 hours were reported. Approximately 10% of the morphine glucuronides are excreted via the bile with the faeces.

5.3 Preclinical safety data

During continuous application of morphine the sensitivity of the CNS towards morphine decreases. This habituation effect can be so marked that doses are tolerated which at a first application would be toxic due to respiratory depression. Due to the euphoric effect of morphine dependence can develop (see section 4.4).

Clearly positive findings on mutagenicity are available which indicate that morphine has a clastogenic potential and does exert this effect on germ cells, too. For this reason morphine has to be regarded as a substance with mutagenic effect; it has to be assumed that this kind of effect occurs also in humans.
Morphine should be administered only as long as effective contraceptive measures are ensured.
Long-term studies in animals assessing a carcinogenic potential of morphine are not available.

Animal studies have revealed a damaging potential for the off-spring during the entire duration of pregnancy (CNS malformation, growth retardation, testis atrophia, changes concerning the neurotransmitter systems and behavioural changes, dependence). In male rats, reduced fertility and chromosomal damage in gametes have been reported. Furthermore in several animal species morphine had an effect on the sexual performance of males and on the fertility of females.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified water, citric acid anhydrous, sodium benzoate (1 mg/ml), disodium edetate (dihydrate).

6.2 Incompatibilities

Not known.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.
After opening of the bottle Oramorph® 20 mg/ml is stable for 90 days.

6.4 Special precautions for storage

Store below 25°C. Store the bottle in the original carton in order to protect from light.

6.5 Nature and contents of container

Container equipped with a dropping device containing 20 ml oral drops, (N1).

6.6 **Special precaution for disposal**

No special instructions.

7. MANUFACTURER

L. Molteni & C. dei F.lli Alitti Società di Esercizio S.p.A. Strada Statale 67,
Tosco Romagnola, 50018 - Fraz. Granatieri- Scandicci
(Firenze) Italy

8. LICENSE HOLDER AND IMPORTER

BioAvenir Ltd.
1 David Hamelech St.
Herzelia Pituach 4666101

9. REGISTRATION NUMBER: 153-96-34100-00

Revised in January 2024.