BioAvenir

12/2021

רופא/ה, רוקח/ת נכבד/ה,

ברצוננו להודיעך על עדכון בעלונים של התכשיר :

ORAMORPH 20 MG/ML

153-96-34100-00

צורת מינון:

SOLUTION (ORAL)

המרכיב הפעיל:

MORPHINE (AS SULFATE)

<u>התוויה:</u>

For the relief of moderate to severe pain

<u>עדכונים מהותיים בעלון לרופא:</u>

להלן עדכונים לעלון לרופא:

לתשומת לב - בהודעה זו מצוינים שינויים מהותיים והחמרות. בעלון בוצעו שינויים נוספים.

יש לעיין בעלון המצורף לאריזה (ולהודעה זו) לפני השימוש בתכשירים .

4.4 Special warnings and precautions for use

<u>Dependence and withdrawal (abstinence) syndrome</u>

Use of opioid analgesics may be associated with the development of physical and/or psychological dependence or tolerance. The risk increases with the time the drug is used, and with higher doses. Symptoms can be minimised with adjustments of dose or dosage form, and gradual withdrawal of morphine. For individual symptoms, see section 4.8

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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.

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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.

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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.

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

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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

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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.

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Risk from concomitant use of sedative medicines such as benzodiazepines or related drugs

Concomitant use of Oramorph® 20 mg/ml solution 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 solution 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).

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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.

Oral P2Y12 inhibitor antiplatelet therapy

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

4.5 Interaction with other medicinal products and other forms of interaction

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 depressant effect. The dose and duration of concomitant use should be limited (see section 4.4).

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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.

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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.

4.6 Fertility, pregnancy and lactation

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.

Fertility

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

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4.8 Undesirable effects

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

Nervous system disorders –

Depending on the dose, morphine leads to various extents of respiratory depression and sedation ranging from slight fatigue to giddiness.

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).

Eye disorders

Very rare: blurred vision, diplopia, nystagmus

Miosis is a typical accompanying symptom

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.

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Respiratory thoracic and mediastinal disorders

Very rare: dyspnoea

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

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

Hepatobiliary disorders

Rare: biliary colics

Very rare: elevation of liver-specific enzymes

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) Anaphylactic and anaphylactoid reactions can occur.

Renal and urinary disorders

Common: disturbances of micturition

Rare: renal colic

General disorders and administration site conditions

Very rare: asthenia, malaise, chills, amenorrhoea

Musculoskeletal and connective tissue disorders

Very rare: muscle cramps, muscle rigidity

Endocrine disorders

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

Drug dependence and withdrawal (abstinence) syndrome

Use of opioid analgesics may be associated with the development of physical and/or psychological dependence or tolerance. 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 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.

4.9 Overdose

Symptoms of intoxication

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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.

5.3 Preclinical safety data

In male rats, reduced fertility and chromosomal damage in gametes have been reported.

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יש לעיין בעלון המצורף לאריזה (ולהודעה זו) לפני השימוש בתכשירים .

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס ע"י פניה לבעל הרישום ביואבניר בע"מ , דוד המלך 1 הרצליה פיתוח או בטלפון 09-9544129.

בכבוד רב,

שרית קיראי-קוצ'וק

רוקחת ממונה