

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

<Morphine hydrochloride trihydrate> 10 (30, 60, 100, 200) mg prolonged-release film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

10 mg: 1 tablet contains 10 mg morphine hydrochloride trihydrate equivalent to 7.59 mg morphine.
30 mg: 1 tablet contains 30 mg morphine hydrochloride trihydrate equivalent to 22.78 mg morphine.
60 mg: 1 tablet contains 60 mg morphine hydrochloride trihydrate equivalent to 45.55 mg morphine.
100 mg: 1 tablet contains 100 mg morphine hydrochloride trihydrate equivalent to 75.92 mg morphine.
200 mg: 1 tablet contains 200 mg morphine hydrochloride trihydrate equivalent to 151.84 mg morphine.

Excipients with known effect:

10 mg:	Lactose monohydrate	8 mg per tablet.
30 mg:	Lactose monohydrate	24.74 mg per tablet.
60 mg:	Lactose monohydrate	49.48 mg per tablet.
	Colouring agent Sunset yellow (E 110)	0.00128 mg per tablet.
100 mg:	Lactose monohydrate	82.20 mg per tablet.
	Colouring agent Sunset yellow (E 110)	0.0332 mg per tablet.
200 mg:	Lactose monohydrate	164.40 mg per tablet.
	Colouring agent Ponceau 4R (E 124)	0.0475 - 0.0625 mg per tablet.
	Colouring agent Sunset yellow (E 110)	0.0250 - 0.0300 mg per tablet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Prolonged-release film-coated tablet.

10 mg: White round and biconvex tablets
30 mg: Blue to green round and biconvex tablets
60 mg: Yellow round and biconvex tablets
100 mg: Yellow to orange round and biconvex tablets
200 mg: Red round and biconvex tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the prolonged relief of severe and most severe pain (such as cancer pain) that is resistant to other analgesics.

4.2 Posology and method of administration

The treatment is initiated by titration with an immediate-release morphine formulation (tablets or solution) to a morphine dose which gives adequate pain control. Thereafter, the patient is transferred to the same daily dose of <Morphine hydrochloride trihydrate> prolonged-release tablets. Breakthrough pain should be treated with immediate-release morphine.

<Morphine hydrochloride trihydrate> prolonged-release tablets should be used at 12-hour intervals. The dose has to be adjusted according to the severity of the pain, the patient's age and previous history of analgesic requirements.

Posology

Paediatric population

<Morphine hydrochloride trihydrate> prolonged-release tablets are not recommended for the use in children below 12 years due to insufficient data on safety and efficacy.

The use of morphine is contraindicated in children below 1 year.

Adults and adolescents >12 years

In patients with severe pain the usual initial dose is 10-30 mg morphine hydrochloride at 12-hour intervals. Patients with low body weight (less than 70 kg) require a lower starting dose.

Increased intensity of pain requires an increased dose of morphine. The correct dose for every patient is a dose that is sufficient to control pain with no or tolerable side effects for 12 hours.

Usually, <Morphine hydrochloride trihydrate> 200 mg prolonged-release tablets are intended for the relief of particularly cancer pain in patients who tolerate morphine and require a daily morphine dose of more than 200 mg.

Patients receiving <Morphine hydrochloride trihydrate> prolonged-release tablets in place of parenteral morphine should be treated cautiously, based on individually different sensitivity. That means that the dose requirement per day should not be overestimated.

Elderly patients and patients with impaired hepatic or renal function

Caution should be exercised and the initial dose should be reduced.

Method of administration

The tablets should be swallowed as a whole with a sufficient amount of liquid.

<Morphine hydrochloride trihydrate> prolonged-release tablets must not be divided or dissolved before administration. Dissolving or dividing of the tablets will damage the prolonged-release system, leading to a rapid release of morphine which may cause substantial side effects up to a fatal dose of morphine.

Treatment goals and discontinuation

Before initiating treatment with <Morphine hydrochloride trihydrate>, a treatment strategy including treatment duration and treatment goals, and a plan for end of the treatment, should be agreed together with the patient, in accordance with pain management guidelines. During treatment, there should be frequent contact between the physician and the patient to evaluate the need for continued treatment, consider discontinuation and to adjust dosages if needed. When a patient no longer requires therapy with <Morphine hydrochloride trihydrate>, it may be advisable to taper the dose gradually to prevent symptoms of withdrawal. In absence of adequate pain control, the possibility of hyperalgesia, tolerance and progression of underlying disease should be considered (see section 4.4).

Duration of treatment

<Morphine hydrochloride trihydrate> should not be used longer than necessary.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Respiratory depression
- Impaired mucus secretion of the airways
- Obstructive airways disease
- Convulsive disorders or head injury
- Paralytic ileus
- Acute abdomen or delayed gastric emptying
- Acute hepatic disease
- Agitation states in patients affected by alcohol or hypnotics
- Children < 1 year

4.4 Special warnings and precautions for use

The major risk of opioid excess is respiratory depression.

<Morphine hydrochloride trihydrate> must be used with caution in elderly patients and patients with

- impaired respiratory function
- impaired hepatic and/or renal function
- heart failure
- opiate dependency
- increased intracranial pressure
- hypotension with hypovolaemia
- disorders of consciousness
- diseases of the biliary tract
- biliary or uretric colic
- pancreatitis
- obstructive and inflammatory bowel disorders
- prostatic hypertrophy
- pheochromocytoma (tumor of the adrenal medulla)

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 generalised 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.

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.

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.

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.

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 <Morphine hydrochloride trihydrate> 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 <Morphine hydrochloride trihydrate> 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).

Risk from concomitant use with monoamine oxidase inhibitors (MAOIs)

MAOIs are known to interact with certain narcotic opioid analgesics (in particular pethidine) producing CNS excitation or depression with hyper- or hypotensive crisis (see section 4.5).

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).

Opioid use disorder (abuse and dependence)

Tolerance and physical and/or psychological dependence may develop upon repeated administration of opioids such as <Morphine hydrochloride trihydrate>.

Repeated use of <Morphine hydrochloride trihydrate> 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 <Morphine hydrochloride trihydrate> 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 (e.g., major depression, anxiety and personality disorders).

Before initiating treatment with <Morphine hydrochloride trihydrate> 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 behaviour (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.

Duly administration in patients with chronic pain significantly reduces the risk of physical and psychic addiction. There is cross-tolerance with other opioids.

Morphine has an abuse potential similar to other strong agonist opioids.

Symptoms can be minimised with adjustments of dose or dosage form, and gradual withdrawal of morphine. For individual symptoms, see section 4.8.

A withdrawal syndrome may be precipitated when opioid administration is suddenly discontinued or opioid antagonists are administered.

The film-coated tablets must not be dissolved and must not be given parenteral. This may lead to serious, potentially fatal side effects such as respiratory depression, necrosis of local tissue and to granulomatous inflammation of organs (esp. lungs).

Not recommended use

Concomitant use of alcohol and <Morphine hydrochloride trihydrate> may increase the undesirable effects of <Morphine hydrochloride trihydrate>; concomitant use should be avoided.

Because of its mutagenic properties, men and women of procreative or child-bearing age should receive morphine, only if the use of effective contraceptive measures is ensured (see sections 4.6 and 5.3).

<Morphine hydrochloride trihydrate> prolonged-release tablets are not recommended during pregnancy or labour as well as for pre-operative use or the first 24 hours post-operative.

24 hours before a chordotomy or other pain relieving surgery, patients should be switched to an immediate-release, more controllable analgesic. In the event of further treatment with prolonged-release morphine after the procedure, the dose should be adjusted.

Should paralytic ileus be suspected or occur during use, <Morphine hydrochloride trihydrate> prolonged-release tablets should be discontinued immediately.

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.

Dose titration

A reduction in dosage may be advisable in the elderly, in hypothyroidism and in patients with significantly impaired renal or hepatic function.

Patients titrated to an effective dose of a certain opioid drug, should not be changed to other slow-, prolonged- or controlled-release morphine or other narcotic analgesic preparations without re-titration and clinical assessment.

Otherwise a continuing analgesic action is not ensured.

Excipients

This medicine contains lactose.

Patients with the rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

<Morphine hydrochloride trihydrate> 60 mg and 100 mg prolonged-release tablets contain the colouring agent Sunset Yellow (E 110) which can cause allergic reactions including asthma.

<Morphine hydrochloride trihydrate> 200 mg prolonged-release tablets contain the colouring agents Sunset Yellow (E 110) and Ponceau 4R (E 124) which can cause allergic reactions including asthma.

4.5 Interaction with other medicinal products and other forms of interaction

Alcohol may enhance the pharmacodynamic effects of <Morphine hydrochloride trihydrate> prolonged-release tablets; concomitant use should be avoided.

Other central nervous system depressants

Morphine should be used with caution in patients who are concurrently receiving other central nervous system depressants, including

- general anaesthetics
- phenothiazines or other tranquilisers
- hypnotics and sedatives, such as benzodiazepines or related drugs
- neuroleptics
- antidepressants
- muscle relaxants
- antihypertensives
- antiemetics
- antihistamines
- other opioids
- gabapentin or pregabalin
- alcohol

Interactive effects resulting in respiratory depression, hypotension, profound sedation, or coma may result and may be enhanced by <Morphine hydrochloride trihydrate> prolonged-release tablets if these drugs are taken in combination with the usual doses of morphine.

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

In case of possible misuse, patients should be informed, that concomitant abuse of alcohol, and also uncontrolled combination with other centrally depressant pharmaceuticals may lead to respiratory depression with possible lethal outcome.

The effects of <Morphine hydrochloride trihydrate> prolonged-release tablets are affected by

- antacids. The concomitant use may result in a more rapid release of morphine than otherwise expected. An at least two-hours interval is recommended between the intakes.
- cimetidine inhibits the metabolism of morphine and may therefore potentiate its effects.
- monoamine oxidase inhibitors (MAOIs) are known to interact with certain opioid analgesics producing CNS excitation or depression with hyper- or hypotensive crisis. Serotonergic syndrome has been reported in patients treated concomitantly with pethidine and MAOIs, and can therefore not be excluded with the combination of morphine and MAOIs. Co-administration of MAOIs or administration within two weeks discontinuation of MAOIs should be avoided or given with special caution.
- rifampicin induces the metabolism of orally administered morphine to a high degree, and therefore higher doses may be needed.
- clomipramine and amitriptyline increase the analgesic effects of morphine, which may partly be due to an increased bioavailability.
- anticholinergics may increase opioid side effects such as constipation, dry mouth or urination problems.

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.

The combination with morphine agonists/antagonists (buprenorphine, nalbuphine, pentazocine) is contraindicated due to the competitive receptor block leading to a reduction of the analgesic effect, with a risk of occurrence of a withdrawal syndrome.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are insufficient data in humans to permit evaluation of the teratogenic risks. There have been reports of a possible connection with increased incidence of hernias. Morphine passes the placental barrier. Animal studies showed damaging potential for the offspring during the entire duration of pregnancy (see section 5.3). Morphine may therefore only be used during pregnancy, if the benefit for the mother clearly outweighs the risk for the child; other therapeutic options should be taken into account before. Because of its mutagenic properties, it is recommended that men and women of procreative or child bearing age use morphine only when the use of effective contraceptive measures is ensured.

The administration of morphine is not recommended during labour due to the risk of neonatal respiratory depression.

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.

Breast-feeding

The administration in breast-feeding mothers is not recommended as morphine is excreted into breast milk. Withdrawal symptoms may be observed in the newborns of mothers undergoing chronic treatment.

Fertility

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

4.7 Effects on ability to drive and use machines

Morphine has major influence on the ability to drive and use machines. It may change attention, influence concentration and the ability to react in such manner that the ability to actively participate in traffic or to operate machines is impaired or not provided anymore.

4.8 Undesirable effects

Undesirable effects are classified according to their severity and frequency:

Very common ($\geq 1/10$)

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1\ 000$ to $< 1/100$)

Rare ($\geq 1/10\ 000$ to $< 1/1\ 000$)

Very rare ($< 1/10\ 000$)

Not known (cannot be estimated from the available data).

The most common side effects are nausea, vomiting, constipation, miosis, and drowsiness.

Immune system disorders

Uncommon: hypersensitivity

Not known: anaphylactic/anaphylactoid reactions

Endocrine disorders

Very rare: syndrome of inadequate ADH secretion (SIADH; leading symptom: hyponatraemia)

Psychiatric disorders

Common: confusion, sleeping disorders

Uncommon: agitation, euphoria, mood swings, hallucinations

Rare: insomnia

Not known: cognitive disorders, dependence, dysphoria

Nervous system disorders

Common: dizziness, headache, drowsiness, somnolence, myoclonus
Uncommon: convulsions, paraesthesia, syncope, increased muscle tone. Overdose may lead to respiratory depression.

Very rare: tremor

Not known: allodynia, hyperalgesia (see section 4.4), hyperhidrosis

Eye disorders

Uncommon: visual disturbances, blurred vision, diplopia, nystagmus

Not known: miosis

Ear and labyrinth disorders

Uncommon: vertigo

Cardiac disorders

Uncommon: palpitations, increased or decreased heart rate

Vascular disorders

Uncommon: increase or decrease of blood pressure

Respiratory, thoracic and mediastinal disorders

Uncommon: pulmonary oedema, bronchospasm, respiratory depression

Rare: attacks of asthma in predisposed patients

Not known: central sleep apnoea syndrome

Gastrointestinal disorders

Very common: nausea, constipation

Common: abdominal pain, anorexia, dry mouth, vomiting

Uncommon: ileus, dysgeusia, dyspepsia, colic

Rare: increased pancreatic enzymes, pancreatitis

Hepatobiliary disorders

Uncommon: increased hepatic enzymes, bile tract spasms

Not known: spasm of sphincter of Oddi

Skin and subcutaneous tissue disorders

Common: flush

Uncommon: urticaria, pruritus

Very rare: exanthema

Not known: acute generalised exanthematous pustulosis (AGEP)

Renal and urinary disorders

Uncommon: problems passing urine, urinary tract spasms

Rare: renal colic

Reproductive system and breast disorders

Not known: Amenorrhoea, decreased libido, erectile dysfunction

General disorders and administration site conditions

Common: asthenia, fatigue, malaise

Uncommon: peripheral oedema (reversible after stopping the treatment), general asthenia up to syncope, feeling cold

Very rare: chills

Not known: tolerance development, drug withdrawal (abstinence) syndrome, neonatal withdrawal syndrome

Drug dependence and withdrawal (abstinence) syndrome

Repeated use of <Morphine hydrochloride trihydrate> can lead to drug dependence or tolerance, 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.

If nausea and vomiting occur with <Morphine hydrochloride trihydrate> prolonged-release tablets, the tablets can be combined with an antiemetic if required. Constipation may be treated with appropriate laxatives.

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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system:

[according to Appendix V - to be completed nationally].

4.9 Overdose

Symptoms

Signs of morphine toxicity and overdose are drowsiness, somnolence up to stupor and coma, pin-point pupils, respiratory depression, bradycardia and hypotension. Death may occur from respiratory failure. Circulatory failure and deepening coma with a fatal outcome may occur in more severe cases. In addition pneumonia aspiration, tachycardia, vertigo, decrease of body temperature, relaxation of skeletal muscles have been reported. In children general convulsions were observed. Rhabdomyolysis and renal failure due to opioid overdose have been reported.

Management

Primary attention should be given to establishing a patent airway and assisted or controlled ventilation. In the case of massive overdosage, the intravenous administration of naloxone is recommended. The infusion should be run at a rate related to the previous bolus doses administered and should be in accordance with the patient's response. However, because the duration of action of naloxone is relatively short, the patient must be carefully monitored until spontaneous respiration is reliably re-established. <Morphine hydrochloride trihydrate> prolonged-release film-coated tablets will continue to release morphine for up to 12 hours after administration and the management of morphine overdosage should be modified accordingly.

Naloxone should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to morphine overdosage. Naloxone should be administered cautiously to persons who are known, or suspected, to be physically dependent on morphine. In such cases, an abrupt or complete reversal of opioid effects may precipitate an acute withdrawal syndrome.

Gastric contents may need to be emptied as this can be useful in removing unabsorbed drug, up to 4 hours after a modified release formulation has been taken.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Natural opium alkaloids.

ATC-Code: N02AA01

Morphine acts as an agonist at opiate receptors in the CNS, particularly μ and, to a lesser extent, κ receptors. μ receptors are thought to mediate supraspinal analgesia, respiratory depression and euphoria, and κ receptors spinal analgesia, miosis and sedation. Morphine also directly affects the nerve plexuses in the intestinal wall, causing constipation.

In elderly patients, the analgesic effect of morphine is increased.

Other effects of morphine on the central nervous system are nausea, vomiting and release of antidiuretic hormone.

The respiratory depressive effect of morphine can lead to respiratory insufficiency in patients with decreased ventilation capacity due to pulmonary disease or due to effects of other drugs.

The effects of morphine may be increased in patients with encephalitis.

5.2 Pharmacokinetic properties

Absorption and distribution

Orally administered morphine is well absorbed and undergoes extensive and variable first-pass metabolism in the liver.

The bioavailability of morphine is 30%, with a range between 10% and 50%. The bioavailability may increase in patients with liver cancer. Morphine has dose-linear pharmacokinetics.

In <Morphine hydrochloride trihydrate> prolonged-release tablets morphine hydrochloride is present as a prolonged-release formulation, which extends the dosing interval up to 12 hours, whereas non-prolonged-release formulations have a dosing interval of 4-6 hours.

Under fed conditions T_{max} increases from 2.4 (fasted) to 3.4 hours.

Morphine passes the placental barrier and is excreted into breast milk.

Biotransformation

A large amount of the active substance is metabolised to glucuronides, which undergo enterohepatic recirculation.

Elimination

Morphine, 90 % of which is excreted as metabolites (morphine-3-glucuronide and morphine-6-glucuronide), is excreted mainly renal, and only to a small extent biliary. Morphine-6-glucuronide is more active than the parent compound.

5.3 Preclinical safety data

There are clear positive findings on mutagenicity, which indicate that morphine has a clastogenic effect and performs this effect also in germ cells. Therefore morphine is to be regarded as a mutagenic effective substance; such an effect must also be assumed in humans. Morphine should only be used with safe contraceptive measures.

Long-term animal studies on the carcinogenic potential of morphine have not been conducted. Several studies show that morphine can enhance tumour growth.

In animal studies, morphine showed a teratogenic potential and neurobehavioural deficiencies in the developing organism, while data in humans do not show evidence of malformations or fetotoxic effects of morphine.

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

10 mg:

Lactose monohydrate, polyacrylate dispersion 30 per cent, methacrylic acid-ethyl acrylate copolymer (1:1), ammonio methacrylate copolymer type B, hypromellose 4000, colloidal anhydrous silica, magnesium stearate, macrogol 6000, talc, titanium dioxide (E 171), hypromellose 5.

30 mg:

Lactose monohydrate, polyacrylate dispersion 30 per cent, methacrylic acid-ethyl acrylate copolymer (1:1), ammonio methacrylate copolymer type B, hypromellose 4000, magnesium stearate, macrogol 6000, talc, titanium dioxide (E 171), hypromellose 5, Indigo carmine aluminium lake (E 132), quinoline yellow aluminium lake (E 104).

60 mg:

Lactose monohydrate, polyacrylate dispersion 30 per cent, methacrylic acid-ethyl acrylate copolymer (1:1), ammonio methacrylate copolymer type B, hypromellose 4000, magnesium stearate, macrogol 6000, talc, titanium dioxide (E 171), hypromellose 5, quinoline yellow aluminium lake (E 104), Sunset yellow aluminium lake (E 110).

100 mg:

Lactose monohydrate, polyacrylate dispersion 30 per cent, methacrylic acid-ethyl acrylate copolymer (1:1), ammonio methacrylate copolymer type B, hypromellose 4000, magnesium stearate, macrogol 6000, talc, titanium dioxide (E 171), hypromellose 5, quinoline yellow aluminium lake (E 104), Sunset yellow aluminium lake (E 110).

200 mg:

Lactose monohydrate, polyacrylate dispersion 30 per cent, methacrylic acid-ethyl acrylate copolymer (1:1), ammonio methacrylate copolymer type B, hypromellose 4000, magnesium stearate, macrogol 6000, talc, hypromellose 5, Ponceau 4 R aluminium lake (E 124), Sunset yellow aluminium lake (E 110).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

10 mg: 3 years

30 mg, 60 mg, 100 mg, 200 mg: 5 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

10, 14, 20, 30, 50, 60, 100, and 100x1 tablets in PCV/aluminium blisters.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

G.L. Pharma GmbH, 8502 Lannach

8. MARKETING AUTHORISATION NUMBER(S)

10 mg: 1-19834

30 mg: 1-19837

60 mg: 1-19833

100 mg: 1-19835

200 mg: 1-19836

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: November 2nd 1992

Date of latest renewal: July 28th 2008

10. DATE OF REVISION OF THE TEXT

March 2024

PRESCRIPTION/PHARMACY ONLY

Narcotic drug, dispensed only on prescription, pharmacy-only