SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Kaolin and Morphine Mixture

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Kaolin Light (Grade A1) 1g
Sodium Hydrogen Carbonate Powder 250mg
Morphine Hydrochloride 0.458mg per 5ml dose.

Excipients with known effects
Each 5ml dose contains 0.46%vol ethanol (alcohol)
Each 5ml dose contains 3.2mmol (74mg) sodium
Each 5ml dose contains 0.08g sucrose
Each 5ml dose contains 0.000025mg benzyl alcohol
Each 5ml dose contains 32.5mg sodium methyl hydroxybenzoate (E219)
Each 5ml dose contains 3.4mg sodium propyl hydroxybenzoate (E217)
Each 5ml dose contains 0.0875mg benzyl benzoate (equivalent to 0.00175% w/v)
Each 5ml dose contains 35mg fructose

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral suspension.

A buff coloured suspension which separates on standing to give a buff coloured sediment and a brown supematant liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For relief of the symptoms of diarrhoea and upset stomachs in adults and children over 12 years.

4.2 Posology and method of administration

Oral.

Recommended doses:

Adults and children over 12 years: Two 5ml spoonfuls.

Children under 12 years: Not recommended for children under 12 years.

Directions for use: Shake the bottle.

Dosage schedule:

The dose may be repeated 3 times daily or as directed.

4.3 Contra-indications

Kaolin is contraindicated in intestinal obstruction. Whilst this product only contains a small amount of morphine, theoretically it should be contraindicated in the same conditions as other morphine-containing preparations. These conditions include respiratory depression, obstructive airways disease, known morphine sensitivity, acute hepatic disease, acute alcoholism, head injuries, coma, convulsive disorders, where intracranial pressure is raised, and in concurrent administration with monoamine oxidase inhibitors or within 2 weeks of discontinuation of their use.

Hypersensitivity to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

As this product contains sodium hydrogen carbonate, it should not be administered to patients with metabolic or respiratory alkalosis, hypocalcaemia or hypochlorhydria, and should be administered with caution in patients with congestive heart failure, renal impairment, cirrhosis of the liver, hypertension and to patients receiving corticosteroids.

Whilst this product only contains a small amount of morphine, it should (as with other morphine-containing preparations) be used with care in the elderly or debilitated (when the dose should be reduced), in prostatic hypertrophy, in hypotension, in hypothyroidism and where there is reduced respiratory reserve (avoid use during an asthma attack), and should not be given if paralytic ileus is likely to occur.

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.

Opioid Use Disorder (abuse and dependence)

Tolerance and physical and/or psychological dependence may develop upon repeated administration of opioids such as Kaolin and Morphine Mixture.

Repeated use of Kaolin and Morphine Mixture 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 Kaolin and Morphine Mixture 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 and during treatment with Kaolin and Morphine Mixture the patient should be informed about the risks and signs of OUD. If these signs occur, patients should be advised to contact their physician or pharmacist.

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.

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

Concomitant use of morphine 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 this medicine 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).

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).

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption should not take this medicine. This product contains 70mg fructose in each 10ml dose. The additive effect of concomitantly administered products containing fructose (or sorbitol) and dietary intake of fructose (or sorbitol) should be taken into account.

This medicine contains 0.175mg benzyl benzoate in each 10ml dose, which is equivalent to 0.00175% w/v.

This product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

This medicine contains 38mg ethanol per 10ml dose which is equivalent to 0.38% w/v. The amount in 10ml is equivalent to less than 1ml of beer and 1ml of wine. The small amount of alcohol in this medicine will have no noticeable effects.

This product contains 6.4mmol (or 148mg) of sodium (main component of cooking/table salt) per 10ml dose, equivalent to 7.4% of the WHO recommended maximum daily intake of 2g sodium for an adult.

This product contains 0.05µg benzyl alcohol per 10ml dose, which may cause allergic reactions. High volumes should be used with caution and only if necessary, especially in subjects with liver or kidney impairment because of the risk of accumulation and toxicity (metabolic acidosis). This product contains sodium methyl and sodium propyl parahydroxybenzoates (E219 and E217 respectively) which may cause allergic reactions (possibly delayed).

The following warnings and precautions appear on the labels:
Do not take more medicine than the label tells you to.
Keep out of the sight and reach of children
Do not take with alcoholic or hot drinks.

4.5 Interaction with other medicinal products and other forms of interaction

As kaolin is adsorbent, the absorption of other drugs from the gastro-intestinal tract administered concomitantly may be reduced. Kaolin possibly reduces absorption of aspirin, tetracycline, chloroquine and hydroxychloroquine, and phenothiazines.

Sodium hydrogen carbonate may also reduce or delay absorption of other drugs as a result of its antacid effect.

Morphine should be used with caution in patients who are concurrently receiving other central nervous system depressants including sedatives or hypnotics, general anaesthetics, phenothiazines, other tranquilisers, muscle relaxants, antihypertensives, gabapentin or pregabalin and alcohol. Interactive effects resulting in respiratory depression, hypotension, profound sedation, or coma may result if these drugs are taken in combination with the usual doses of morphine.

Morphine, whilst only present in a very low concentration, theoretically may potentiate the effects of tranquillisers such as barbiturates, anaesthetics, anxiolytics and hypnotics, sedatives and alcohol. The reduction in intestinal motility caused by morphine may delay the absorption

or antagonise the gastrointestinal effects of other drugs. The effects of domperidone and metoclopramide on gastrointestinal activity are antagonised by opioid analgesics. Metabolism of opioid analgesics is inhibited by cimetidine leading to increased plasma concentration.

Opioid analgesics should be avoided when ciprofloxacin is to be used for antibacterial surgical prophylaxis as concomitant use can lead to decreased plasma concentration of ciprofloxacin. The opioid analgesics enhance effects of sodium oxybate, used to treat symptoms of narcolepsy and concomitant use should be avoided.

Possible CNS excitation or depression (hypertension or hypotension) can occur when opioid analgesics are given with antidepressants such as moclobemide and MAOIs (avoid concomitant use and for 2 weeks after stopping MAOIs). The sedative effects of morphine can possibly be increased when given with tricyclic antidepressants, with anxiolytics or hypnotics, or with sedating antihistamines. Antipsychotic medicines can enhance hypotensive and sedative effects when opioid analgesics are given with antipsychotics.

Morphine also has the following specific interaction information. Morphine possibly increases plasma concentration of the beta-blocker esmolol which may be used as an anti-arrythmic. The plasma concentration of morphine is possibly reduced by the antiviral ritonavir. Morphine increases the bioavailability of the anticonvulsant medication gabapentin.

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).

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 mobility 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

This product should not be used in pregnancy or whilst breastfeeding unless recommended by a doctor.

4.7 Effects on Ability to Drive and Use Machines

Although it is not considered that the product will have any effect, morphine may cause drowsiness, patients should not drive or operate machinery if affected.

4.8 Undesirable effects

The sodium hydrogen carbonate in this product may cause stomach cramps and flatulence. Morphine, whilst only present in a low concentration, may theoretically cause nausea, vomiting, constipation, drowsiness and confusion. Prolonged use may lead to tolerance and dependence.

Although there are qualitative and quantitative differences in side effects for the opioid analgesics, other recognised possible side effects include:
difficulty with micturition; ureteric or biliary spasm; dry mouth; sweating; headache; facial flushing; vertigo; bradycardia, tachycardia or palpitation; postural hypotension; hypothermia; hallucinations, dysphoria or mood changes; miosis; decreased libido or potency; rashes, urticaria, pruritis and opioid-induced hyperalgesia (OIH).

Skin and subcutaneous tissue disorders: Acute generalised exanthematous pustulosis (AGEP).

Respiratory disorders: Central sleep apnoea syndrome.

Gastrointestinal disorders: Pancreatitis.

Hepatobiliary disorders: Spasm of sphincter of Oddi.

Drug dependence
Repeated use of Kaolin and Morphine Mixture 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).

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for “MHRA Yellow Card” in the Google Play or Apple App Store.

4.9 Overdose

In the unlikely event of overdosage with this product, signs of morphine toxicity and overdosage include pin-point pupils, respiratory depression and hypotension. Circulatory failure and deepening coma may occur in more severe cases.

Treatment should consist of naloxone administration, aspiration and gastric lavage with assisted respiration (if necessary), and maintenance of fluid and electrolytes.

Excessive administration of sodium hydrogen carbonate may lead to metabolic alkalosis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

A07 DA52 - Antipropulsives

Kaolin is an adsorbent, it adsorbs toxic and other substances from the alimentary tract and increases the bulk of the faeces.

Sodium hydrogen carbonate is an alkalising agent and antacid.

Morphine reduces the peristaltic activity of the intestines.

5.2 Pharmacokinetic Properties

Kaolin is not absorbed following oral administration. It remains unchanged throughout transit of the gastrointestinal tract.

Sodium hydrogen carbonate is neutralised in the stomach with the formation of carbon dioxide. Any remaining is absorbed and excreted as bicarbonate and sodium ions in the urine in the absence of a plasma deficit.

Morphine is well absorbed from the gastrointestinal tract but has poor bioavailability due to extensive first pass metabolism in the liver. It is distributed throughout the body but mainly in the kidneys, liver, lungs and spleen, with lower concentrations in the brain and muscles. Morphine diffuses across the placenta and traces appear in milk and sweat. About 35% is protein bound. Conjugation to 3- and 6- glucuronides occurs in the liver and gut. Up to 10% of morphine is excreted as conjugates in the bile and faeces and the remainder is excreted in the urine. About 90% of total morphine is excreted in 24 hours with traces in the urine up to 48 hours or more.

5.3 Preclinical Safety Data

No data of relevance to the prescriber, which is additional to that included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol (96%)
Peppermint Oil
Anise oil
Saccharin sodium
Sodium methyl hydroxybenzoate (E219)
Sodium propyl hydroxybenzoate (E217)
Treacle black commercial (contains fructose)
Liquorice Flavour (contains E1518 glyceryl triacetate, E1520 propylene glycol, E1505 triethyl citrate & E1529 benzyl alcohol and benzyl benzoate)
Syrup (sucrose)
Purified water

6.2 Incompatibilities

None.

6.3 Shelf Life

200ml: 18 months unopened.

6.4 Special Precautions for Storage

Store below 25°C. Keep tightly closed.

6.5 Nature and Contents of Container

200ml: Glass bottle with polypropylene cap.

6.6 Instructions for Use, Handling and Disposal

None.

7. MARKETING AUTHORISATION HOLDER

L.C.M. Ltd.
Linthwaite Laboratories
Huddersfield
HD7 5QH

8. MARKETING AUTHORISATION NUMBER(S)

PL 12965/0021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25th October 1993

10 DATE OF REVISION OF THE TEXT

03/10/2023