

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

J Collis Browne's Mixture.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains:

Morphine hydrochloride equivalent to 1.0mg anhydrous Morphine

Peppermint Oil 1.5 microlitre

Excipient(s) with known effect:

Each 5ml contains:

Ethanol (96%) 122.667mg

Benzoic acid (E 210) 5.000mg

Sorbitol (E 420) 835.000mg

Treacle (Contains Sucrose & Fructose) 400mg

3 PHARMACEUTICAL FORM

Aqueous based mixture.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the alleviation of coughs and the symptoms of diarrhoea.

4.2 Posology and Method of Administration

Oral

Adults and Children over 12 years of age.

For coughs: One to two 5 ml medicinal teaspoonsful. May be repeated every four hours.

For diarrhoea: Two to three 5 ml medicinal teaspoonsful. May be repeated once or twice at four hourly intervals if required.

Elderly and debilitated patients; use with caution; a reduced dose can be recommended by a doctor.

Children under 12 years old: Not recommended

4.3 Contraindications

Hypersensitivity to the active substances, to any of the excipients or to menthol.

Children under the age of 12 years.

Acute respiratory depression, chronic obstructive pulmonary disease, acute alcoholism, risk of paralytic ileus, acute ulcerative colitis, acute abdomen, delayed gastric emptying, raised intra-cranial pressure and head injury, and phaeochromocytoma. It should not be given during an attack of asthma or to patients with heart failure secondary to chronic lung disease.

Concurrent administration with monoamine oxidase inhibitors (MAOIs) or within 2 weeks of discontinuation of their use.

Acute hepatic disease

Obstructive bowel disorders

Pancreatitis

Coma

Convulsive disorders

Administration of some opioid analgesics to patients taking a monoamine oxidase inhibitor (MAOI) has been associated with very severe and sometimes fatal reactions. If the use of J Collis Browne's Mixture is considered essential, then great care should be taken in patients taking MAOIs or within 14 days of stopping MAOIs (see section 4.5).

4.4. Special Warnings and Precautions for Use

Use with care in hypotension, shock, myasthenia gravis, prostatic hypertrophy, diseases of the biliary tract, and cardiac arrhythmias. Caution is advised in patients with asthma or other respiratory disorders, hepatic and renal disease, and a history of drug abuse.

Cough suppressants may cause sputum retention and this may be harmful in patients with chronic bronchitis, bronchiectasis and chronic obstructive pulmonary disease.

A reduced dose is recommended in elderly or debilitated patients, in hepatic and renal impairment (but avoid if severe), in hypothyroidism, and in adrenocortical insufficiency.

J Collis Browne's Mixture is not intended as a substitute for rehydration therapy in the treatment of diarrhoea; patients should take plenty of fluids.

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 J Collis Browne's Mixture.

Repeated use of J Collis Browne's 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 J Collis Browne's 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 J Collis Browne's 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 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.

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).

Labels state: Do not take more medicine than the leaflet tells you to.
If symptoms persist consult your doctor.
The elderly and debilitated patients. Ask your doctor for advice; a lower dose might be more suitable.
Do not give to children under 12 years old.
Keep out of the sight and reach of children.
Shake the bottle.

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).

Excipient warnings:

This medicine contains 119mg of alcohol (ethanol) in each 5ml dose which is equivalent to 3% v/v. The amount in 5ml of this medicine is equivalent to less than 3ml of beer and 2ml of wine. The small amount of alcohol in this medicine will not have any noticeable effects.

This medicine contains 585mg sorbitol in each 5ml dose. Sorbitol is a source of fructose. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product. The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.

This medicine contains Treacle (Contains Sucrose & Fructose). Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

This medicine contains 5mg benzoic acid in each 5ml dose.

4.5 Interactions with other medicinal products and other forms of Interaction

Morphine should be used with caution in patients who are concurrently receiving other CNS 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.

The depressant effects of opioid analgesics are enhanced by other CNS depressants such as alcohol, anxiolytics, hypnotics, antidepressants including tricyclic antidepressants, anticoagulants such as warfarin, antiepileptics and antipsychotics.

The sedative effect of morphine are increased by baclofen. The hypotensive and sedative effects of opioid analgesics are enhanced when given with alcohol or antipsychotics, and sedative effects enhanced when given with tricyclic antidepressants, sedating antihistamines, anxiolytics or hypnotics.

Possible CNS excitation or depression (hypertension or hypotension) can occur when opioid analgesics are given with antidepressants such as MAOIs, including moclobemide, rasagiline and selegiline (avoid concomitant use and for 2 weeks after stopping MAOIs).

The CNS effects of opioid analgesics are possibly increased by barbiturates. The plasma concentration of opioid analgesics is increased (metabolism inhibited) by cimetidine

Morphine increases the bioavailability of gabapentin and may increase the plasma concentration of esmolol. Opioid analgesics may enhance the effects of general anaesthetics (intravenous and volatile gases), and enhance the effects of sodium oxybate (avoid concomitant use).

Opioid analgesics reduce the plasma concentration of ciprofloxacin and antagonise the effects of domperidone and metoclopramide.

The effect of morphine is reduced (metabolism increased) by rifampicin, and plasma concentration possibly reduced by ritonavir.

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.

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).

Peppermint oil can inhibit CYP3A4 and may affect the clearance of drugs whose metabolism is mediated by this enzyme, including warfarin.

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

This medicine may cause drowsiness. If affected, patients should not drive or operate machinery.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

- The medicine is likely to affect your ability to drive
- Do not drive until you know how the medicine affects you
- It is an offence to drive while under the influence of this medicine
- However, you would not be committing an offence (called "statutory defence") if:
 - The medicine has been prescribed to treat a medical or dental problem and
 - You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
 - It was not affecting your ability to drive safely

4.8 Undesirable Effects

The following undesirable effects have been reported for use of morphine or opioid analgesics and may arise from use of J. Collis Browne's Mixture. Allergic reactions and dyspepsia may also be attributable to peppermint oil. The frequency of adverse effects cannot be estimated from available data.

Psychiatric disorders: hallucinations, dysphoria, euphoria, mood changes, confusion, dependence, restlessness, agitation, delirium, disorientation, excitation

Nervous system disorders: dizziness, drowsiness, sleep disturbances, headache, vertigo, raised intracranial pressure, malaise, seizures, paraesthesia, opioid-induced hyperalgesia (OIH)

Eye disorders: miosis, visual disturbances, nystagmus

Cardiac disorders: palpitations, bradychardia, tachycardia

Vascular disorders: postural hypotension, hypotension, hypothermia, facial flushing, oedema, hypertension, syncope

Respiratory, thoracic and mediastinal disorders: respiratory depression (with larger doses), bronchospasm, inhibition of cough reflex, central sleep apnoea syndrome.

Gastrointestinal disorders: nausea, vomiting, constipation, abdominal pain, anorexia, pancreatitis, exacerbation of pancreatitis, dry mouth, paralytic ileus, dyspepsia, taste disturbances

Hepatobiliary disorders: biliary spasm, spasm of sphincter of Oddi.

Skin and subcutaneous tissue disorders: rashes, urticaria, pruritis, sweating, acute generalised exanthematous pustulosis (AGEP).

Musculoskeletal and connective tissue disorders: muscular rigidity (with higher doses), muscle fasciculation, myoclonus, weakness.

Renal and urinary disorders: difficulty with micturition, urinary retention, ureteric spasm

Reproductive system and breast disorders: decreased libido or potency, amenorrhoea.

Drug dependence

Repeated use of J Collis Browne's 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

Large doses of opioids can lead to muscle rigidity, pinpoint pupils, respiratory depression, hypotension, circulatory failure and coma. Rhabdomyolysis has also been reported.

Gastric lavage and symptomatic treatment as for morphine is recommended.

In acute opioid poisoning the stomach should be emptied by aspiration and lavage, intensive supportive therapy may be required to correct respiratory failure and shock. Activated charcoal may be given orally in conscious patients if a substantial overdose has been ingested within 1 hour provided that the airway can be protected.

Severe respiratory depression and coma produced by excessive doses of opioids can be counteracted by the administration of naloxone given intravenously at a dose of 0.4 to 2 mg, repeated at 2-3 minute intervals if necessary, up to 10 mg.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Morphine, among other actions, diminishes propulsive peristalsis in the intestinal tract. It is an effective agent for treating diarrhoea. Peppermint Oil is a carminative which relieves flatulence and intestinal griping.

5.2 Pharmacokinetic properties

No information available.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol (96%)

Benzoic Acid (E 210)

Capsicum Tincture

Caramel (E150)

Levomenthol

Citric Acid (E 330)

Hypromellose

Sorbitol Solution (E 420)

Treacle (Contains Sucrose & Fructose)

Purified Water

6.2 Incompatibilities

None stated.

6.3 Shelf life

Five years unopened.

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and contents of container

Amber glass bottle with 28mm white polypropylene cap with tamper evident band and EPE/Aluminium/Melinex/ liner in packs of 45ml and 100ml quantities.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Thornton & Ross Limited

Linthwaite

Huddersfield

West Yorkshire

HD7 5QH

United Kingdom

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