SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Morphine 10mg/5ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of Oral Solution contains 10 mg of Morphine Sulfate

Excipients with known effect:

Each 5 ml also contains 2250 mg sucrose, 0.400 ml Ethanol, 10 mg Sodium methyl hydroxybenzoate (E219) and 1.250 mg Sodium propyl hydroxybenzoate (E217).
Total sodium content is 0.299mg/ml

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral Solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of severe pain.

4.2 Posology and method of administration

Posology

Adults: Recommended dose: 10-20 mg (5-10 ml) every 4 hours.
Maximum daily dose: 120 mg per day

Paediatric population:

Children 13 to 18 years: Recommended dose:5-20 mg (2.5-10 ml) every 4 hours.
Maximum daily dose: 120 mg per day

Children 6-12 years:	Recommended dose: 5-10 mg (2.5-5 ml) every 4 hours. Maximum daily dose: 60 mg per day
Children 1-5 years:	Recommended dose 5 mg (2.5 ml) every 4 hours. Maximum daily dose: 30 mg per day
Children under 1 year:	Not recommended.

Dosage can be increased under medical supervision according to the severity of the pain and the patient's previous history of analgesic requirements.

Special populations:
Reductions in dosage may be appropriate in the elderly, and in patients with chronic hepatic disease (for acute hepatic disease see section 4.3), renal impairment, severe hypothyroidism, adrenocortical insufficiency, prostatic hypertrophy, shock or where sedation is undesirable.

Treatment goals and discontinuation
Before initiating treatment with Morphine Oral solution, 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 Oral Solution, 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 Oral Solution should not be used longer than necessary.

Method of Administration For oral use.
When patients are transferred from other morphine preparations to Morphine Oral Solution dosage titration may be appropriate.

Morphine Sulfate is readily absorbed from the gastro-intestinal tract following oral administration. However, when Morphine Oral Solution 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.

4.3 Contraindications

Morphine Oral Solution is contraindicated in:

- patients known to be hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- respiratory depression
- obstructive airways disease
- acute hepatic disease,
- acute alcoholism,
- head injuries (see section 4.4)
- coma (see section 4.4)
- convulsive disorders
- increased intracranial pressure (see section 4.4)
- paralytic ileus (see section 4.4)
- patients with known morphine sensitivity
- concurrent administration with monoamine oxidase inhibitors or within two weeks of discontinuation of their use (see section 4.5)
- patients with phaeochromocytoma. Morphine and some other opioids can induce the release of endogenous histamine and thereby stimulate catecholamine release
- acute asthma exacerbations (see section 4.4 for information relating to use in controlled asthma)

4.4 Special warnings and precautions for use

Care should be exercised if morphine sulfate is given

- in the first 24 hours post-operatively,
- in hypothyroidism (see section 4.2), and where there is reduced respiratory function such as kyphoscoliosis, emphysema, cor pulmonale and severe obesity.

Asthma

It has been suggested that opioids can be used with caution in controlled asthma. However, opioids are contraindicated in acute asthma exacerbations (see section 4.3).

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.

Head injury and increased intracranial pressure

Morphine Oral Solution is contraindicated in patients with increased intracranial pressure; head injuries and coma (see section 4.3). The capacity of morphine to elevate cerebrospinal fluid pressure may be greatly increased in the presence of

already elevated intracranial pressure produced by trauma. Also, morphine may produce confusion, miosis, vomiting and other adverse reactions which may obscure the clinical course of patients with head injury.

Abdominal conditions

Morphine sulfate must not be given if paralytic ileus is likely to occur (see section 4.3) or if the patient has bowel or obstructive biliary disease. Should paralytic ileus be suspected or occur during use, Oral Morphine Solution should be discontinued immediately.

Caution should be exercised where there is an obstructive bowel disorder, biliary colic, operations on the biliary tract, acute pancreatitis or prostatic hyperplasia.
If constipation occurs, this may be treated with the appropriate laxatives. Care should be exercised in patients with inflammatory bowel disease.
Morphine may obscure the diagnosis or clinical course of patients with acute abdominal conditions and complications following abdominal surgery.

Hypotensive effect

The administration of morphine may result in severe hypotension in individuals whose ability to maintain homeostatic blood pressure has already been compromised by depleted blood volume or the concurrent administration of drugs such as phenothiazine or certain anaesthetics (see section 4.5).

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 Morphine Oral Solution.

Repeated use of Morphine Oral Solution 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 Oral Solution 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 Morphine Oral Solution 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.

Additional support and monitoring may be necessary when prescribing for patients at risk of opioid misuse.

A comprehensive patient history should be taken to document concomitant medications, including over- the-counter medicines and medicines obtained on-line, and past and present medical and psychiatric conditions.
Patients may find that treatment is less effective with chronic use and express a need to increase the dose to obtain the same level of pain control as initially experienced. Patients may also supplement their treatment with additional pain relievers. These could be signs that the patient is developing tolerance. The risks of developing tolerance should be explained to the patient.

Overuse or misuse may result in overdose and/or death. It is important that patients only use medicines that are prescribed for them at the dose they have been prescribed and do not give this medicine to anyone else.

Patients should be closely monitored for signs of misuse, abuse, or addiction. The clinical need for analgesic treatment should be reviewed regularly.

Drug withdrawal syndrome
Prior to starting treatment with any opioids, a discussion should be held with patients to put in place a withdrawal strategy for ending treatment with Morphine Oral Solution.

Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. When a patient no longer requires therapy, it is advisable to taper the dose gradually to minimise symptoms of withdrawal. Tapering from a high dose may take weeks to months.

The opioid drug withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms may also develop including irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate.

If women take this drug during pregnancy, there is a risk that their newborn infants will experience neonatal withdrawal syndrome.

Hyperalgesia

Hyperalgesia may be diagnosed if the patient on long-term opioid therapy presents with increased pain. This might be qualitatively and anatomically distinct from pain related to disease progression or to breakthrough pain resulting from development of opioid tolerance. Pain associated with hyperalgesia tends to be more diffuse than the pre-existing pain and less defined in quality. Symptoms of hyperalgesia may resolve with a reduction of opioid dose.

Hypersensitivity

Hypersensitivity and anaphylactic reactions have both occurred with the use of Morphine Oral Solution. Care should be taken to elicit any history of allergic reactions to opiates. Morphine Oral Solution is contraindicated in patients known to be hypersensitive to morphine sulfate (see section 4.3).

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).

Risk in special populations

Morphine is metabolised by the liver and should be used with caution in patients with hepatic disease as oral bioavailability may be increased. It is wise to reduce dosage in chronic hepatic and renal disease, severe hypothyroidism, adrenocortical insufficiency, prostatic hypertrophy or shock (see section 4.2).

The active metabolite Morphine-6-glucoranide may accumulate in patients with renal failure, leading to CNS and respiratory depression.

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

Concomitant use of Morphine Sulfate Injection 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 Sulfate Oral 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).

Acute chest syndrome (ACS) in patients with sickle cell disease (SCD)
ACS symptoms is warranted. 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.

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.

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.

Excipient related warnings
Contains the excipients Sodium propyl hydroxybenzoate (E217) and sodium methyl hydroxybenzoate (E219) which are preservatives and may cause an allergic reaction (possibly delayed).

Patients with rare hereditary problems of fructose intolerance, glucosegalactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

This medicinal product contains less than 1mmol sodium (23mg) per 1ml. ie to say essentially 'sodium-free'.

Morphine Oral solution contains alcohol, which is harmful for those suffering from alcoholism. To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease, or epilepsy.

4.5 Interaction with other medicinal products and other forms of interaction

Monoamine oxidase inhibitors

Monoamine oxidase inhibitors are known to interact with narcotic analgesics producing CNS excitation or depression with hyper- or hypotensive crisis, therefore their concomitant use with Morphine Oral Solution in contraindicated (please see section 4.3).

Gabapentin

Interactions have been reported in those taking morphine and gabapentin. Reported interactions suggest an increase in opioid adverse events when co-prescribed, the mechanism of which is not known. Caution should be taken where these medicines are co-prescribed.

In a study involving healthy volunteers (N=12), when a 60 mg controlled-release morphine capsule was administered 2 hours prior to a 600 mg gabapentin capsule, mean gabapentin AUC increased by 44% compared to gabapentin administered without morphine. Therefore, patients should be carefully observed for signs of CNS depression, such as somnolence, and the dose of gabapentin or morphine should be reduced appropriately.

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.

Ritonavir

Although there are no pharmacokinetic data available for concomitant use of ritonavir with morphine, ritonavir may increase the activity of glucuronyl transferases. Consequently, co-administration of ritonavir and morphine may result in decreased serum concentrations of morphine with possible loss of analgesic effectiveness.

Rifampicin

Rifampicin can reduce the serum concentration of morphine and decrease its analgesic effect, the mechanism of which is not known.

Oral P2Y12 inhibitor antiplatelet therapy

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.

Cimetidine
Cimetidine inhibits the metabolism of morphine.

CNS depressants
It should be noted that morphine potentiates the effects of CNS depressants such as tranquillisers, anaesthetics (see section 4.4), hypnotics, sedatives, antipsychotics, tricyclic antidepressants and alcohol.

Esmolol
Morphine may increase plasma concentrations of esmolol.

Domperidone/ metoclopramide
Opioid analgesics including morphine may antagonise the actions of domperidone and metoclopramide on gastro-intestinal activity.

Mexiletine
The absorption of mexiletine may be delayed by concurrent use of morphine.

Phenothiazine antiemetics
Phenothiazine antiemetics may be given with morphine. However, hypotensive effects have to be considered (see section 4.4).

Voriconazole
Interactions have been reported in those subjects taking Morphine Oral Solution and voriconazole.

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).

4.6 Fertility, pregnancy and lactation

Pregnancy
Regular use during pregnancy may cause drug dependence in the foetus, leading to withdrawal symptoms in the neonate.
If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.
Administration during labour may depress respiration in the neonate and an antidote for the child should be readily available.

Breast feeding

Administration to nursing women is not recommended as Morphine may be secreted in breast milk and may cause respiratory depression in the infant.

Fertility

Long term use of opioid analgesics can cause hypogonadism and adrenal insufficiency in both men and women. This is thought to be dose related and can lead to amenorrhoea, reduced libido, infertility and erectile dysfunction.

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

4.7 Effects on ability to drive and use machines

Morphine sulfate is likely to impair ability to drive and to use machinery. This effect is even more enhanced, when used in combination with alcohol or CNS depressants. Patients should be warned not to drive or operate dangerous machinery after taking Morphine Oral Solution.

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

In normal doses the commonest side effects of morphine sulfate are respiratory depression, nausea, vomiting, constipation, drowsiness and confusion. If constipation occurs, this may be treated with appropriate laxatives. The effects of morphine have led to its abuse and misuse. Dependence and addiction may develop with regular, inappropriate use.

Adverse effects can be listed in terms of their frequency of occurrence:

- Very common (>1/10)
- Common (>1/100 to <1/10)
- Uncommon (>1/1,000 to <1/100)
- Not known (cannot be estimated from available data)

Data from clinical trials are not available. Therefore, it is not possible to provide information on the frequencies of undesirable effects. A full list of currently known adverse reactions is presented below.

SOC Category	**Adverse effect and frequency of occurrence:**
	Not known
Immune system disorders	Hypersensitivity
	Anaphylactic reaction (see section 4.4)
	Anaphylactoid reactions
Psychiatric disorders	Confusional state
	Restlessness
	Altered mood
	Hallucination
	Drug Dependence (see section 4.4)
Nervous System Disorders	Somnolence
	Headache
	Increased intracranial pressure (see section 4.4)
	Allodynia, hyperalgesia (see section 4.4)
	Hyperhidrosis
Eye disorders	Miosis
Ear and labyrinth disorders	Vertigo
Respiratory, thoratic and mediastinal disorders	Respiratory depression (see section 4.4 and section 6.6)
	Central sleep apnoea syndrome
Cardiac disorders	Bradycardia
	Tachycardia
	Palpitations
Vascular disorders	Hypotension
	Flushing
Gastrointestinal disorders	Nausea
	Vomiting
	Constipation (see section 4.4)
	Dry mouth
	Pancreatitis
General disorders and administration site conditions	Hypothermia
	Drug tolerance (see section 4.4)
	Uncommon: Drug withdrawal syndrome (see section 4.4 and section 4.6)
Hepatobiliary disorders	Biliary colic

	Spasm of sphincter of Oddi
Skin and subcutaneous tissue disorders	Urticaria
	Pruritus
	Hyperhidrosis
	Acute generalised exanthematous pustulosis (AGEP)
Musculoskeletal and connective tissue disorders	Muscle rigidity
Renal and urinary disorders	Dysuria
	Utereral spasm
	Oliguria
Reproductive system and breast disorders	Decreased libido
	Erectile dysfunction

These effects are more common in ambulant patients than in those who are bedridden.

Description of selected adverse reactions

Drug dependence and withdrawal (abstinence) syndrome

Repeated use of Morphine Oral Solution 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).

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, restlessness, diarrhoea, abdominal cramps, nausea, 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 reaction 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

Symptoms:
Patients should be informed of the signs and symptoms of overdose and to ensure that family and friends are also aware of these signs and to seek immediate medical help if they occur.

Signs of morphine toxicity and overdosage are likely to consist of pin-point pupils, respiratory depression and hypotension. Aspiration pneumonia may also occur. Circulatory failure and deepening coma may occur in more severe cases. Convulsions may occur in infants and children. Death may occur from respiratory failure. Death may occur from respiratory failure.

Treatment:
Adults: Administer 0.4-2 mg of naloxone intravenously. Repeat at 2-3-minute intervals as necessary to a maximum of 10 mg, or by an infusion of 2 mg in 500 ml of normal saline or 5 % dextrose (4 micrograms/ml).
Children: 5-10 micrograms per kilogram body weight of naloxone intravenously. If this does not result in the desired degree of clinical improvement, a subsequent dose of 100 mcg/kg body weight may be administered.

Care should always be taken to ensure that the airway is maintained. Assist respiration if necessary. Maintain fluid and electrolyte levels Oxygen, i.v. fluids, vasopressors and other supportive measures should be employed as indicated. Peak plasma concentrations of morphine are expected to occur within 15 minutes of oral ingestion. Therefore, gastric lavage and activated charcoal are unlikely to be beneficial.

Caution: the duration of the effect of naloxone (2-3 hours) may be shorter than the duration of the effect of the morphine overdose. It is recommended that a patient who has regained consciousness after naloxone treatment should be observed for at least 6 hours after the last dose of naloxone.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Natural opium alkaloids
ATC Code: N02A A01

Morphine binds to specific receptors, which are located at various levels of the central nervous system and also in various peripheral organs. The pain sensation and the affective reaction to pain is relieved by interaction with the receptors in the central nervous system.

5.2 Pharmacokinetic properties

Absorption

Morphine is modestly absorbed from the gastrointestinal tract following oral administration. Following oral administration of radiolabelled morphine to humans, peak plasma levels were reached after approximately 15 minutes. Morphine undergoes significant first pass metabolism in the liver resulting in a systemic bioavailability of approximately 25%.

Distribution

Approximately one third of morphine in the plasma is protein bound after a therapeutic dose.

Biotransformation

Metabolism of morphine principally involves conjugation to morphine 3- and 6- glucuronides. Small amounts are also metabolised by N-demethylation and N-dealkylation. Morphine-6-glucuronide has pharmacological effects indistinguishable from those of morphine. The half-life of morphine is approximately 2 hours. The t1/2 of morphine-6- glucuronide is somewhat longer.

Elimination

A small amount of a dose of morphine is excreted through the bowel into the faeces. The remainder is excreted in the urine, mainly in the form of conjugates. Approximately 90 % of a single dose of morphine is excreted in the first 24 hours. Enterohepatic circulation of morphine and its metabolites can occur, and may result in small quantities of morphine to be present in the urine or faeces for several days after the last dose.

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose, ethanol, sodium methyl hydroxybenzoate (E219), sodium propyl hydroxybenzoate (E217), disodium edetate, raspberry flavour, hydrochloric acid and purified water.

6.2. Incompatibilities

None stated.

6.3 Shelf life

3 years (36 months) unopened
Discard Morphine Oral Solution 90 days after first opening.

6.4 Special precautions for storage

Do not store above 25°C
Keep container in the outer container.

6.5 Nature and contents of container

Round amber glass bottles with child proof and tamper evident caps. The bottles are packed in a cardboard carton along with a patient information leaflet.

Pack sizes: 100ml, 250ml, 300ml or 500ml.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None stated.

7 MARKETING AUTHORISATION HOLDER

Martindale Pharmaceuticals Ltd
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8 MARKETING AUTHORISATION NUMBER(S)

PL 00156/0036

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10 DATE OF REVISION OF THE TEXT

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