Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Oramorph Oral Solution 10 mg/5 ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Morphine Sulfate 10 mg per 5 ml.

Excipient(s) with known effect
Each 5 ml also contains 1500 mg Sucrose, 500 mg corn syrup (contains glucose), 0.525 ml Ethanol (96%), 9 mg Methyl parahydroxybenzoate (E218) and 1 mg Propyl parahydroxybenzoate (E216).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution

A clear, colourless oral solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of severe pain in adults, adolescents (aged 13-18 years) and children (aged 1-12 years).

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 13-18 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.

Discontinuation of therapy
Prior to starting treatment with opioids, a discussion should be held with patients to put in place a strategy for ending treatment with Oramorph in order to minimise the risk of addiction and drug withdrawal syndrome (see section 4.4).

Method of Administration
For oral use.

When patients are transferred from other morphine preparations to Oramorph preparations dosage titration may be appropriate.

Morphine sulfate is readily absorbed from the gastro-intestinal tract following oral administration. However, when oral Oramorph preparations are 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.

Treatment goals and discontinuation
Before initiating treatment with Oramorph, 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 Oramorph 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
Oramorph 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
- obstructive airways disease
- paralytic ileus (see section 4.4)
- acute hepatic disease
- acute alcoholism
- head injuries (see section 4.4)
- coma (see section 4.4)
- increased intracranial pressure (see section 4.4)
- convulsive disorders
- 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. AsthmaIt 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). Head injury and increased intracranial pressureOramorph 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 conditionsMorphine 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, Oramorph 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 effectThe 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).Drug dependence, tolerance and potential for abuseMorphine sulfate is an opioid agonist and controlled drug. For all patients, prolonged use of this product may lead to drug dependence (addiction), even at therapeutic doses. The risks are increased in individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g., major depression). 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. Morphine sulfate may be abused by inhaling or injecting the product. These practices pose a significant risk to the abuser that could result in overdose and death. Patients should be closely monitored for signs of misuse, abuse, or addiction. The clinical need for analgesic treatment should be reviewed regularly.Drug withdrawal syndromePrior to starting treatment with any opioids, a discussion should be held with patients to put in place a withdrawal strategy for ending treatment with Oramorph. 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.HyperalgesiaHyperalgesia 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. HypersensitivityHypersensitivity and anaphylactic reactions have both occurred with the use of Oramorph. Care should be taken to elicit any history of allergic reactions to opiates. Oramorph is contraindicated in patients known to be hypersensitive to morphine sulfate (see section 4.3).

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 amenorrhoea.

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 Oramorph.
Repeated use of Oramorph 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 Oramorph 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 Oramorph 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.

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-glucuronide may accumulate in patients with renal failure, leading to CNS and respiratory depression.

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.

Concomitant use of sedative medicines
Concomitant use of Oramorph and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death.

Because of these risks, concomitant use of Oramorph and sedative medicines should be reserved for patients for whom alternative treatment options are not possible.

Oramorph particularly when prescribed concomitantly with sedative medicines, should be used at the lowest effective dose for the shortest period of time.

Patients should be monitored closely for signs and symptoms of respiratory depression and sedation (see also section 4.5).

Concomitant use of 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 related warnings
This product contains 3 g sucrose in each 10 ml dose. This product also contains 1 g corn syrup, which contains glucose, in each 10 ml dose. This should be taken into account in patients with diabetes mellitus. May be harmful to the teeth. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Oramorph Oral Solution contains the excipients methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E216) which may cause allergic reactions (possibly delayed).

Oramorph Oral Solution contains ethanol (alcohol). Each 10 ml dose contains contains up to 810 mg of alcohol, which is equivalent to 81 mg/ml (10%v/v). The amount of alcohol in 10 ml of this medicine is equivalent to 20 ml beer or 8 ml wine. To be taken into account in pregnant or breast-feeding women, children and those addicted to alcohol.

Adults

A dose of 10 ml of this medicine administered to an adult weighing 70 kg would result in exposure to 11.6 mg/kg of ethanol, which may cause a rise in blood alcohol concentration (BAC) of about 1.9 mg/100ml.

For comparison, for an adult drinking a glass of wine or 500ml beer, the BAC is likely to be about 50 mg/100 ml.

Paediatric population
Children 13-18 years: A dose of 10 ml of this medicine administered to a 13 year old child weighing 41 kg would result in exposure to 19.8mg/kg of ethanol, which may cause a rise in BAC of about 3.3 mg/100 ml

Children 6-12 years: A dose of 5 ml of this medicine administered to a 6 year old child weighing 21 kg would result in exposure to 19.3 mg/kg of ethanol, which may cause a rise in BAC of about 3.2 mg/100 ml

Children 1-5 years: A dose of 2.5 ml of this medicine administered to a 1 year old child weighing 9 kg would result in exposure to 22.5 mg/kg of ethanol, which may cause a rise in blood alcohol concentration (BAC) of about 3.7 mg/100ml.

Co-administration with medicines containing e.g. propylene glycol or ethanol may lead to accumulation of ethanol and induce adverse effects, in particular in young children with low or immature metabolic capacity.

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 Oramorph is contraindicated (see section 4.3).

Gabapentin and Pregabalin
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.

Cimetidine
Cimetidine inhibits the metabolism of morphine.

CNS depressants
It should be noted that morphine potentiates the effects of other CNS depressants such as tranquillisers, anaesthetics (see section 4.4), sedatives (e.g. benzodiazepines), antipsychotics, tricyclic antidepressants and alcohol, which might lead to respiratory depression, coma and death. The dose and duration of concomitant use should be limited (see section 4.4).
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.

Oral P2Y12 inhibitors
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

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).

4.6 Fertility, pregnancy and lactation

Pregnancy
Although morphine sulfate has been in general use for many years, there is inadequate evidence of safety in human pregnancy.

Morphine is known to cross the placenta. Therefore, Oramorph should not be used in pregnancy, especially the first trimester unless the expected benefit is thought to outweigh any possible risk to the foetus.

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.

The risk of gastric stasis and inhalation pneumonia is increased in the mother during labour. Since morphine rapidly crosses the placental barrier it should not be used during the second stage of labour or in premature delivery because of the risk of secondary respiratory depression in the newborn infant.
The quantity of ethanol contained in Oramorph Oral Solution should be considered in pregnant women (See section 4.4).

Breast-feeding
Although morphine sulfate has been in general use for many years, there is inadequate evidence of safety during lactation.

Administration to nursing women is not recommended as morphine sulfate 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 5.3. preclinical safety data).

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 Oramorph.

4.8 Undesirable effects

In normal doses, the commonest side effects of morphine sulfate are 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 use.

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

SOC Category	Side effect
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)
Eye Disorders	Miosis
Ear and labyrinth disorders	Vertigo
Respiratory, thoracic and mediastinal disorders	Respiratory depression (see section 4.4 and section 4.6) 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) 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 Ureteral spasm Oliguria
Reproductive system and breast disorders	Decreased libido Erectile dysfunction

*Frequency uncommon (≥ 1/1,000 to < 1/100)

Drug dependence

Repeated use of Oramorph 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:

HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

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.

Symptoms
Signs of morphine toxicity and overdosage are likely to consist of pin-point pupils, respiratory depression and hypotension. Circulatory failure, pneumonia aspiration and deepening coma may occur in more severe cases. Convulsions may occur in infants and children. 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 2 mg in 500 ml of normal saline or 5 % dextrose (4 micrograms/ml). Children: 5-10 micrograms per kilogram body weight 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: NO2AA01

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 sulfate is readily absorbed from the gastrointestinal tract following oral administration. Following oral administration of radiolabelled morphine sulfate 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% (range 15-49%).

Distribution
Morphine is distributed throughout the body but found mainly in the kidneys, liver, lung and spleen with lower concentrations being found in the brain and muscles. Approximately one third of morphine in the plasma is protein bound after a therapeutic dose. Morphine diffuses across the placenta and traces of the drug appear in breast milk.

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

Elimination
About 10 % 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. About
90 % of a single dose of morphine is excreted in 24 hours. Enterohepatic circulation of morphine and its metabolites can occur, and may result in small quantities of morphine being present in the urine or faeces 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
Corn syrup
Methyl Parahydroxybenzoate (E218)
Propyl Parahydroxybenzoate (E216)
Ethanol 96 %
Purified Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened: 3 years.
Opened: 3 months after first opening.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container in order to protect from light.

6.5 Nature and contents of container

Registered Packs:

Type III, amber glass bottles with a tamper-evident, child-resistant closure with an outer cap of polypropylene and expanded PE liner are available in packs of 100 ml, 250 ml, 300 ml or 500 ml.
Not all pack sizes may be marketed.
Marketed Packs:

Oramorph Oral Solution is available in 100 ml, 300 ml and 500 ml bottles with a tamper-evident, child-resistant closure with an outer cap of polypropylene and expanded PE liner.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Glenwood GmbH
Pharmazeutische Erzeugnisse
Arabellastr. 17
81925 Munich
Germany

8 MARKETING AUTHORISATION NUMBER

PA2256/004/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 July 1990

Date of last renewal: 31 January 2009

10 DATE OF REVISION OF THE TEXT

November 2020