AUSTRALIAN PRODUCT INFORMATION – ORDINE® (MORPHINE HYDROCHLORIDE TRIHYDRATE) ORAL SOLUTION

1 NAME OF THE MEDICINE

Morphine hydrochloride trihydrate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

ORDINE oral solution (1 mg/mL) contains morphine hydrochloride trihydrate 1 mg/mL.

ORDINE oral solution (2 mg/mL) contains morphine hydrochloride trihydrate 2 mg/mL.

ORDINE oral solution (5 mg/mL) contains morphine hydrochloride trihydrate 5mg/mL.

ORDINE oral solution (10 mg/mL) contains morphine hydrochloride trihydrate 10mg/mL.

ORDINE oral solution (20 mg/mL) contains morphine hydrochloride trihydrate 20mg/mL.*

ORDINE oral solution (40 mg/mL) contains morphine hydrochloride trihydrate 40mg/mL.*

* Not currently distributed in Australia

Excipients of known effect: sodium methyl hydroxybenzoate. For the full list of excipients, see Section 6.1 – List of excipients

3 PHARMACEUTICAL FORM

ORDINE oral solution is a clear, colourless or pale yellow aqueous solution available in bottles of 200 mL.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Relief of severe pain in patients not responding to non-opioid analgesics; to produce sleep where sleeplessness is due to pain.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dosage must be titrated to the patient's needs because of the wide inter-individual variability in plasma concentration required to achieve analgesia. The usual adult dosage is 5-20 mg (2.5-10 mL of the 2 mg/mL mixture) every 4 hours. The initial dose will depend largely on the patient's previous treatment and should be the lowest compatible with pain control. Treatment should start at a dosage of 5 mg every 4 hours, with further increments as required. With repeated administration, tolerance may develop and the dose may need to be increased gradually in order to control the pain.

Dosage should be lower in elderly patients, those with respiratory, hepatic or renal impairment and in patients receiving CNS depressants.

Dosage in children should be adjusted according to body weight, 0.1-0.2 mg/kg every 4 hours.

4.3 CONTRAINDICATIONS

Morphine is contraindicated in patients hypersensitive to opioids; known hypersensitivity to any of the excipients; in children under one year of age including premature infants or during labour or delivery of premature infants; following biliary tract surgery or surgical anastomosis; paralytic ileus; concomitant monoamine oxidase inhibitors (MAOIs), or within 14 days of such therapy (see Section 4.5 – Interactions with other medicines and other forms of interactions).

Morphine is contraindicated in respiratory depression especially in the presence of cyanosis and excessive bronchial secretion.

It should be used with extreme caution, if benefits outweigh risks, in patients with decreased respiratory reserve, acute bronchial asthma or other obstructive airway disease, heart failure secondary to chronic pulmonary disease (*cor pulmonale*), cardiac arrhythmias, severe CNS depression, acute alcoholism, *delirium tremens*, head injuries, brain tumour, raised cerebrospinal or intracranial pressure, suspected surgical and acute abdomen, paralytic ileus, delayed gastric emptying, severe liver and renal dysfunction, incipient hepatic encephalopathy and convulsive states such as status epilepticus, tetanus due to stimulatory effects on the spinal cord or strychnine poisoning.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Head injury and increased intracranial pressure

Morphine should be used with extreme caution and only if it is judged essential, in patients with head injuries, brain tumour, and raised cerebrospinal or intracranial pressure. The respiratory depressant effects of morphine, and the capacity to elevate cerebrospinal fluid pressure, may be greatly increased in the presence of already elevated intracranial pressure. Also, morphine may produce confusion, miosis, vomiting and other side effects which obscure the clinical course of such patients.

Respiratory depression

The major risk of opioid excess is respiratory depression. Morphine should be used with extreme caution in patients with substantially decreased respiratory reserve, pre-existing respiratory depression, hypoxia or hypercapnia, acute bronchial asthma, chronic obstructive pulmonary disease or *cor pulmonale*. Such patients are often less sensitive to the stimulatory effects of carbon dioxide on the respiratory centre and the respiratory depressant effects of morphine may reduce respiratory drive to the point of apnoea. Resuscitative equipment and opioid antagonists must be readily available.

Hypotensive effect

Morphine administration may result in severe hypotension in patients whose ability to maintain adequate blood pressure is compromised by reduced blood volume, impaired myocardial function or concurrent administration of drugs such as sympatholytics, phenothiazines or

certain anaesthetics. Morphine should be used with caution and these patients should be carefully observed for orthostatic hypotension.

Abdominal conditions

Morphine may obscure the diagnosis or clinical course of patients with acute abdominal conditions. Morphine should be used with extreme caution in suspected surgical and acute abdomen, and in patients with obstructive bowel disorders. Where there is a possibility of paralytic ileus occurring, morphine should not be used. Should paralytic ileus be suspected or occur during use, ORDINE oral solution should be discontinued immediately. As with all oral morphine preparations, ORDINE oral solution should be used with caution post-operatively including, but not limited to, following abdominal surgery, as morphine impairs intestinal motility and should not be used until the physician is assured of normal bowel function.

Decreased gastric emptying associated with morphine may be expected to increase the risks of aspiration either associated with morphine-induced CNS depression/coma, or during or after general anaesthesia.

Biliary tract and sphincter of Oddi conditions

Because of the spasmogenic properties of morphine in the biliary tract and sphincter of Oddi, it should be used only when necessary, and with caution in biliary colic, diseases of the biliary tract and acute pancreatitis.

Acute ulcerative colitis

ORDINE oral solution should be used with caution in patients with inflammatory bowel disorders. Morphine may cause toxic dilation in patients with acute ulcerative colitis.

Cordotomy

Severe pain antagonises the subjective and respiratory depressant actions of morphine. Should pain suddenly subside, these effects may rapidly become manifest. Patients who are scheduled for cordotomy or other pain-relieving surgical procedures should not receive ORDINE oral solution within 24 hours of the procedure. Pain in the immediate pre-operative period, and any symptoms of opioid withdrawal, should be managed with short-acting analgesic agents. If further treatment with ORDINE oral solution is then indicated, the dosage should be adjusted to the new post-operative requirement.

Hyperalgesia

Hyperalgesia that will not respond to a further dose increase of morphine may occur in particular at high doses. A morphine dose reduction or change in opioid may be required.

Special risk groups

Morphine should be administered with caution and in reduced dosages to patients with adrenocortical insufficiency, hypothyroidism, prostatic hypertrophy or urethral stricture.

Seizures may result from high doses. Morphine may lower the seizure threshold in patients with a history of seizure. Patients with known seizure disorders should be carefully observed, especially when doses are increased in response to tolerance.

Morphine should be used with extreme caution, if benefits outweigh risks, in convulsive states such as status epilepticus.

Morphine should be used with caution pre-operatively or within the first 24 hours post-operatively.

Drug dependence

Except in patients with terminal conditions, morphine should be restricted to short-term administration for the relief of severe pain not responding to non-opioid analgesics. As with other opioids, tolerance and physical dependence tend to develop upon repeated administration of morphine and there is a potential for abuse of the drug and for development of strong psychological dependence. Morphine should therefore be prescribed and handled with the high degree of caution appropriate to the use of a drug with strong abuse potential.

In the absence of a clear indication for a strong opioid analgesic, drug-seeking behaviour must be suspected and resisted, particularly in individuals with a history of, or propensity for, drug abuse.

Morphine should be used with caution and under close supervision in patients with pain not due to malignancy who have a prior history of substance abuse or opioid dependency. In such cases, prior psychological assessment is essential and the prescribing doctor should consider whether the benefit of treatment outweighs the risk of abuse.

Withdrawal symptoms (including convulsions) may occur in those physically dependent following abrupt discontinuation of morphine therapy or upon administration of an opioid antagonist. Therefore, patients on prolonged therapy should be withdrawn gradually from the drug if it is no longer required for pain control.

Abuse of oral dosage forms

Abuse of oral dosage forms by parenteral administration can be expected to result in serious adverse events, which may be fatal.

Use during labour/delivery

Morphine may prolong labour by reducing the strength and frequency of uterine contractions. Morphine crosses the placental barrier and its administration during labour may cause respiratory depression in the newborn infant.

Use in hepatic impairment

Morphine should be administered with caution and in reduced dosages to patients with severely reduced hepatic function.

Use in renal impairment

Morphine should be administered with caution and in reduced dosages to patients with severely reduced renal function.

Use in the elderly

Morphine should be administered with extreme caution and in reduced dosages, to elderly or debilitated patients.

Paediatric use

Safety and effectiveness in neonates have not been established.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Acidifying or alkalising agents

The clearance of morphine may be increased by acidifying agents and decreased by alkalising agents. Morphine's actions on gastrointestinal motility may influence the absorption of other drugs.

Amphetamines, chlorpromazine and methocarbamol

The analgesic effect of morphine is potentiated by amphetamines, chlorpromazine and methocarbamol.

Anticholinergics

Medicinal products that block the action of acetylcholine, for example antihistamines, anti-parkinsonian drugs and anti-emetics, may interact with morphine to potentiate anti-cholinergic adverse events.

Cimetidine

Cimetidine inhibits the metabolism of morphine. A potentially lethal interaction between morphine and cimetidine has been reported. The patient exhibited apnoea, significantly reduced respiratory rate and suffered a grand mal seizure. Naloxone increased the respiratory rate; however, confusion, disorientation, generalised twitching and periods of apnoea persisted for 80 hours.

CNS depressants

Morphine should be used only with caution and in reduced dosage in patients who are concurrently receiving other CNS depressants including other opioids, anaesthetics, sedatives (including benzodiazepines), hypnotics, barbiturates, phenothiazines, tricyclic antidepressants, chloral hydrate, glutethimide, tranquilisers, muscle relaxants, antihypertensives, gabapentin and alcohol as they may enhance the depressant effects of morphine. Pyrazolidone antihistamines, cimetidine, beta-blockers and alcohol may also enhance the depressant effect of morphine. Interactive effects resulting in respiratory depression, hypotension, profound sedation and/ or coma may result if these drugs are taken in combination with the usual doses of morphine.

Coumarin and other anticoagulants

Morphine may increase the anticoagulant activity of coumarin and other anticoagulants.

Mixed agonist/antagonist opioid analgesics

Mixed agonist/antagonist opioid analgesics (e.g. buprenorphine, nalbuphine, pentazocine) should not be administered to a patient who has received a course of therapy with a pure opioid agonist analgesic.

Monoamine Oxidase Inhibitors (MAOIs)

Non-selective MAOIs (including procarbazine hydrochloride) intensify the effects of morphine and other opioid drugs which can cause anxiety, confusion and significant respiratory depression, sometimes leading to coma. Morphine should not be given to patients taking non-

selective MAOIs or within 14 days of stopping such treatment. It is unknown whether there is an interaction between the selective MAOIs (e.g. moclobemide, selegiline) and morphine, therefore caution is advised with this drug combination.

Propranolol

The combination of morphine and propranolol is potentially lethal. Propranolol increases the acute CNS toxicity of morphine.

Rifampicin

Plasma concentrations of morphine may be reduced by rifampicin.

Ritonavir

Available data indicate that 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.

Zidovudine

Morphine may alter the metabolism of zidovudine by competitively inhibiting glucuronidation or directly inhibiting hepatic microsomal metabolism; therefore this combination should be used with caution.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Prolonged use of opioid drugs may result in impairment of reproductive function, including infertility and sexual dysfunction in both sexes and irregular menses in women.

Use in pregnancy – Pregnancy Category C

Australian Pregnancy Categorisation C: Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible.

Opioid analgesics may cause respiratory depression in the newborn infant. Morphine has been associated with foetal CNS defects in rodent studies.

In humans it is not known whether morphine can cause foetal harm when administered during pregnancy. Use of ORDINE should be avoided to the extent possible in patients who are pregnant.

Infants born of mothers who have been taking morphine chronically may exhibit withdrawal symptoms.

Use in lactation

Morphine has been detected in human breastmilk. Morphine administration to nursing mothers is not recommended.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Morphine may impair the mental and/or physical abilities needed for certain potentially hazardous activities, such as driving a car or operating machinery. Patients should be cautioned accordingly.

Patients should also be cautioned about the combined effects of morphine with other CNS depressants, including other opioids, phenothiazines, sedative/hypnotics and alcohol.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The following frequencies are the basis for assessing adverse effects.

Very common	(≥ 1/10)
Common	(≥ 1/100 to < 1/10)
Uncommon	(≥ 1/1,000 to < 1/100)
Rare	(≥ 1/10,000 to < 1/1,000)
Very rare	(< 1/10,000)
Not known	(cannot be estimated from the available data)

The major hazards associated with morphine, as with other opioid analgesics, are respiratory depression and, to a lesser degree, circulatory depression. Respiratory arrest, shock and cardiac arrest have occurred following oral and parenteral use of morphine.

Very common adverse reactions requiring medical attention

Frequently observed adverse reactions of opioid analgesics such as morphine are sedation, nausea and vomiting, constipation and sweating.

Sedation

Most patients experience initial drowsiness partly for pharmacokinetic reasons and partly because patients often recuperate from prolonged fatigue after the relief of persistent pain. Drowsiness usually clears in three to five days and is usually not a reason for concern providing that it is not excessive, or associated with unsteadiness or confusional symptoms. If excessive sedation persists, the reason for it must be sought. Some of these are: concomitant sedative medications, hepatic or renal failure, exacerbated respiratory failure, higher doses than tolerated in an older patient, or the patient is actually more severely ill than realised. If it is necessary to reduce the dose, it can be carefully increased again after three or four days if it is obvious that the pain is not being well controlled. Dizziness and unsteadiness may be caused by postural hypotension particularly in elderly or debilitated patients. It can be alleviated if the patient lies down. Because of the slower clearance in patients over 50 years of age, an appropriate dose in this age group may be as low as half or less the usual dose in the younger age group.

Nausea and Vomiting

Nausea and vomiting occur frequently after single doses of opioids or as an early unwanted effect of regular opioid therapy. When instituting prolonged therapy for chronic pain, the

routine prescribing of an anti-emetic should be considered. Patients taking the equivalent of a single dose of 20 mg or more of morphine usually require an anti-emetic during early therapy. Small doses of prochlorperazine or haloperidol are frequently prescribed anti-emetics. Nausea and vomiting tend to lessen in a week or so but may persist due to opioid-induced gastric stasis. In such patients, metoclopramide is often useful.

Constipation

As with all opioid analgesics, constipation is very common. In some instances, particularly the elderly or bedridden, patients may become impacted. It is essential to caution patients in this regard and to institute an appropriate regimen of bowel management at the start of prolonged opioid therapy. Dietary modification, suitable exercise, softeners, laxatives and other appropriate measures should be used as required.

Other adverse reactions include:

Cardiac disorders

Not known: bradycardia, palpitations, supra-ventricular tachycardia

Ear and labyrinth disorders

Uncommon: vertigo

Endocrine disorders

Uncommon: syndrome of inappropriate antidiuretic hormone secretion characterised by hyponatraemia secondary to decreased free-water excretion may be prominent (monitoring of electrolytes may be necessary)

Eye disorders

Uncommon: visual disturbance

Not known: miosis

Gastrointestinal disorders

Common: abdominal pain, anorexia, dry mouth

Uncommon: dyspepsia, ileus, taste perversion

Not known: cramps, gastrointestinal disorders

General disorders

Common: asthenia, fatigue, malaise, pruritus

Uncommon: peripheral oedema

Not known: drug tolerance, oedema, drug withdrawal syndrome

Hepato-biliary disorders

Uncommon: increased hepatic enzyme

Not known: biliary pain, biliary spasm, biliary tract cramps

Immune system disorders

Uncommon: hypersensitivity

Not known: anaphylactic reaction, anaphylactoid reaction

Nervous system disorders

Common: dizziness, headache, involuntary muscle contractions, somnolence

Uncommon: convulsions, hypertonia, paraesthesia, syncope

Not known: hyperalgesia, weakness

Psychiatric disorders

Common: confusion, insomnia

Uncommon: agitation, euphoria, hallucinations, malaise, mood altered

Not known: drug dependence, dysphoria, thinking disturbances

Renal and urinary disorders

Uncommon: uretic spasm, urinary retention or hesitance

Not known: oliguria

Reproductive system and breast disorders

Not known: amenorrhoea, erectile dysfunction, reduced libido or potency

Respiratory, thoracic and mediastinal disorders

Uncommon: bronchospasm, pulmonary oedema, respiratory depression

Not known: cough decreased

Skin and subcutaneous tissue disorders

Common: hyperhidrosis, other skin rashes including contact dermatitis

Uncommon: urticaria

Vascular disorders

Uncommon: facial flushing, hypotension

Not known: faintness, postural hypotension

Withdrawal (abstinence) syndrome

Physical dependence with or without psychological dependence tends to occur with chronic administration. An abstinence syndrome may be precipitated when opioid administration is discontinued or opioid antagonists administered.

The following withdrawal symptoms may be observed after opioids are discontinued: body aches, diarrhoea, gooseflesh, loss of appetite, nervousness or restlessness, runny nose, sneezing, chills, tremors or shivering, stomach cramps, nausea, trouble with sleeping, unusual increase in sweating and yawning, weakness, tachycardia and unexplained fever. With appropriate medical use of opioids and gradual withdrawal from the drug, these symptoms are usually mild.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

Symptoms and Signs

Serious morphine overdosage is characterised by respiratory depression (reduced respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, miotic pupils (dilated if hypoxia is severe), rhabdomyolysis progressing to renal failure, flaccidity of skeletal muscle, cold or clammy skin, and sometimes hypotension and bradycardia. Severe overdosage may result in apnoea, pulmonary oedema, circulatory collapse, cardiac arrest and death.

Treatment

Primary attention should be given to the establishment of adequate respiratory exchange through the provision of a patent airway and controlled or assisted ventilation. The opioid antagonist naloxone hydrochloride is a specific antidote against respiratory depression due to overdosage or as a result of unusual sensitivity to morphine. (Please refer naloxone product information). An appropriate dose of one of the antagonists should therefore be administered, preferably by the intravenous route. The usual initial intravenous (I.V.) adult dose of naloxone is 0.4 mg or higher. Concomitant efforts at respiratory resuscitation should be carried out. Since the duration of action of morphine may exceed that of the antagonist, the patient should be under continued surveillance and doses of the antagonists should be repeated as needed to maintain adequate respiration.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression. Oxygen, intravenous fluids, vasopressors and other supportive measures should be used as indicated to manage circulatory shock accompanying an overdose. Cardiac arrest or arrhythmias may require cardiac massage or defibrillation. Artificial ventilation should be applied if necessary and fluid and electrolyte metabolism maintained.

In an individual physically dependent on opioids, the administration of the usual dose of opioid antagonist will precipitate an acute withdrawal syndrome. The severity of this syndrome will depend on the degree of physical dependence and the dose of antagonist administered. The use of opioid antagonists in such individuals should be avoided if possible. If an opioid antagonist must be used to treat serious respiratory depression in the physically dependent patient, the antagonist should be administered with extreme care by using dosage titration, commencing with 10 to 20% of the usual recommended initial dose.

Evacuation of gastric contents may be useful in removing unabsorbed drug.

Toxicity

Morphine toxicity may result from overdosage but because of the great inter-individual variation in sensitivity to opioids it is difficult to determine an exact dose of any opioid that is toxic or lethal.

The presence of pain or tolerance tends to diminish the toxic effects of morphine. Published data suggest that in a morphine-naive, pain-free individual, the lethal dose would be in excess of 120 mg. Patients on chronic oral morphine therapy have been known to take in excess of 3000 mg/day with no apparent toxicity.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Morphine is the principal alkaloid of opium and is a phenanthrene derivative.

Morphine, like other opioids, acts as an agonist interacting with stereo-specific and saturable binding sites/receptors in the brain, spinal cord and other tissues. These sites have been classified as μ receptors and are widely distributed throughout the central nervous system being present in highest concentration in the limbic system (frontal and temporal cortex, amygdala and hippocampus), thalamus, striatum, hypothalamus, midbrain and laminae I, II, IV and V of the dorsal horn in the spinal cord. It has been postulated that exogenously administered morphine exerts its analgesic effect, in part, by altering the central release of neurotransmitter from afferent nerves sensitive to noxious stimuli. Peripheral threshold or responsiveness to noxious stimuli is unaffected leaving monosynaptic reflexes such as the patella or the Achilles tendon reflex intact.

Morphine exerts its primary effects on the central nervous system and organs containing smooth muscle. Pharmacological effects include analgesia, drowsiness, alteration in mood (euphoria), reduction in body temperature, dose-related depression of respiration, interference with adrenocortical response to stress (at high doses), reduction in peripheral resistance with little or no effect on cardiac index, cough suppressions mediated through a direct effect on the medullary centre and miosis.

Direct stimulation of the chemoreceptor trigger zone may cause emesis and spasmogenic effects on the gastrointestinal tract resulting in decreased peristaltic activity. Urinary retention may occur due to increased bladder sphincter tone.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Morphine is readily absorbed from the gastrointestinal tract. Significant first-pass metabolism occurs in the liver following oral administration; hence, the bioavailability of oral morphine is low and variable.

With repeated regular dosing, oral morphine is about 1/3 as potent as when given by intramuscular injection.

Distribution

Morphine is distributed throughout the body, but particularly to parenchymatous tissue such as kidney, lung, liver and spleen. Lower concentrations are found in skeletal muscle and brain tissue. Morphine diffuses across the placenta and trace amounts are found in sweat and breast milk. About 35% is protein bound, mainly to albumin.

Metabolism

Morphine is metabolised principally in the liver by conjunction with glucuronic acid at the 3-hydroxyl group, and to a much lesser extent to the 3,6-diglucuronide.

Excretion

Elimination half-life is approximately 1.5-2 hours in healthy subjects and 90% of the dose is recovered in urine within 24 hours. Approximately 7-10% of the dose is recovered in faeces, the majority after conjugation and excretion via bile.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No regulatory studies to assess the mutagenic potential of morphine have been conducted.

Carcinogenicity

Regulatory studies in animals to evaluate the carcinogenic potential of morphine have not been conducted.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The sugar and alcohol free vehicle contains the excipients anhydrous citric acid, sodium citrate, glycerol and disodium edetate with sodium methyl hydroxybenzoate 0.23% w/v as preservative and water for injections.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

Discard 6 months after opening. Do not exceed the stated expiry date printed on the label.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C. Do not refrigerate. Protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

Polyethylene terephthalate bottle, 200 mL

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

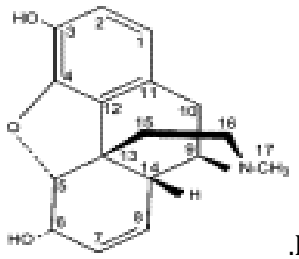
Morphine hydrochloride is a white, crystalline powder or colourless, silky crystals. It is soluble 1:21 in water and 1:10 in boiling alcohol. It is practically insoluble in chloroform or ether.

Morphine is liable to precipitate out of solution in an alkaline environment.

Chemical structure

Morphine hydrochloride is 7,8-didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol hydrochloride trihydrate (molecular weight 375.8).

The structural formula of morphine hydrochloride is:



.HCl.3H2O

CAS number

52-26-6 (anhydrous).

7 MEDICINE SCHEDULE (POISONS STANDARD)

S8

8 SPONSOR

Mundipharma Pty Limited
ABN 87 081 322 509
88 Phillip Street
SYDNEY NSW 2000
Further information may be obtained from Mundipharma's Medical Information Department 1800 188 009.

9 DATE OF FIRST APPROVAL

09 July 1991 (20mg/mL, 40mg/mL)

26 August 2008 (1mg/mL, 2mg/mL, 5mg/mL, 10mg/mL)

10 DATE OF REVISION

21 December 2018

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	The PI has been reformatted to comply with the revised TGA form for providing product information format.
4.5	Addition of 'benzodiazepines' as a potential class interaction.
4.8	Addition of 'Oliguria' under 'Adverse Effects (Undesirable effects); Renal and urinary disorders'.
6.5	Information on the container included

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