PRODUCT INFORMATION

DILAUDID® 2 mg in 1 mL injection ampoule
DILAUDID®-HP 10 mg in 1 mL injection ampoule
DILAUDID®-HP 50 mg in 1 mL concentrated injection ampoule

NAME OF THE MEDICINE

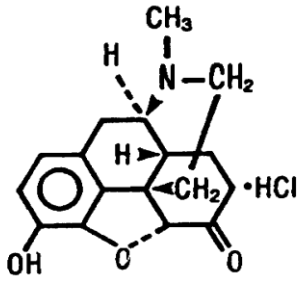
DILAUDID® preparations contain hydromorphone hydrochloride.

Chemical name: 4,5α-epoxy-3-hydroxy-17-methylmorphinan-6-one hydrochloride.

Molecular weight: 321.81.

CAS registration number: 71-68-1.

The structural formula of hydromorphone hydrochloride is:



DESCRIPTION

Hydromorphone hydrochloride, a hydrogenated ketone of morphine, is an opioid analgesic.

Hydromorphone hydrochloride is a fine, white or practically white, odourless, crystalline powder. It is freely soluble in water, sparingly soluble in ethanol and practically insoluble in ether.

The inactive ingredients in DILAUDID® 2 mg injection ampoule, DILAUDID®-HP 10 mg injection ampoule and DILAUDID®-HP 50 mg concentrated injection ampoule are sodium citrate dihydrate, citric acid, sodium chloride, hydrochloric acid or sodium hydroxide, and water for injections.

PHARMACOLOGY

Hydromorphone is an opioid agonist with no antagonist activity. Many of the effects described below for hydromorphone are common to the class of μ-opioid agonist analgesics (e.g. morphine). In some instances, data may not exist to distinguish the effects of hydromorphone from those observed with other opioid analgesics. However, in the absence of data to the contrary, it is assumed that hydromorphone would mirror the pharmacological effects of μ-agonist opioids.

Although estimates vary, hydromorphone is thought to be approximately eight times as potent (by weight) as morphine. It is estimated that 1.3 mg of intramuscular (IM) hydromorphone is equianalgesic to 10 mg of IM morphine. The relative potency, (based

on a single dose bioassay) of oral hydromorphone was found to be approximately one-fifth that of IM hydromorphone - this ratio being similar to that for morphine. However, clinical experience with morphine indicates that this 1:5 ratio changes to 1:2 with chronic oral dosing. Such a change in oral-parenteral relative potency may also occur with hydromorphone.

Opioid analgesics exert their primary effects on the central nervous system (CNS) and organs containing smooth muscle. The principal actions of therapeutic value are analgesia and sedation. A significant feature of the analgesia is that it can occur without loss of consciousness. Opioid analgesics also suppress the cough reflex and may cause respiratory depression, mood changes, mental clouding, euphoria, dysphoria, nausea, vomiting and electroencephalographic changes. The precise mode of analgesic action of opioid analgesics is unknown. However, specific CNS opiate receptors have been identified. Opioids are believed to express their pharmacological effects through interaction with these receptors.

Opioids depress the respiratory reflex by a direct effect on brain stem respiratory centres and reducing the responsiveness of these centres to increases in carbon dioxide.

Opioids can cause a marked increase in biliary tract pressure as a result of spasm of the sphincter of Oddi. Gastric, biliary and pancreatic secretions are decreased by opioids. Opioids cause a reduction in gastrointestinal motility. Digestion of food in the small intestine is delayed and propulsive contractions are decreased resulting in constipation.

Certain opioids produce peripheral vasodilation which may result in orthostatic hypotension. Release of histamine may occur with opioids and may contribute to drug-induced hypotension. Other manifestations of histamine release may include pruritus, flushing and red eyes.

Effects on the myocardium after intravenous (IV) administration of opioids are not significant in normal persons, vary with different opioid analgesic agents and vary with the haemodynamic state of the patient, state of hydration and sympathetic drive.

In vitro and animal studies indicate various effects of natural opioids, such as morphine, on components of the immune system; the clinical significance of these findings is unknown. Whether hydromorphone, a semisynthetic opioid, has immunological effects similar to morphine is unknown.

Pharmacokinetics

Adult

Hydromorphone (8 mg) is rapidly absorbed after oral administration and the plasma half-life ranges from 2.3-2.6 hours. Hydromorphone undergoes extensive first-pass metabolism resulting in oral bioavailability of about 25%. Dose proportionality between the 8 mg DILAUDID® tablets and other strengths of DILAUDID® tablets has not been established.

Following intravenous administration of hydromorphone to normal volunteers, the mean half-life of elimination was 2.64 $\pm$ 0.88 hours. The mean volume of distribution was 301 L, suggesting extensive tissue uptake. Hydromorphone is rapidly removed from the blood stream and distributed to skeletal muscle, kidneys, liver, intestinal tract, lungs, spleen and brain. Hydromorphone also crosses the placental membranes. Total plasma clearance following IV administration is approximately 1.85 L/min.

Hydromorphone metabolism is typical of that seen for the 5-ring morphinan derivatives - the primary pathway being glucuronidation in the liver. The major metabolite, hydromorphone-3-glucuronide (H3G), small amounts of parent drug and the minor 6-hydroxy reduction metabolites are excreted primarily in the urine.

The 3-glucuronide metabolite of hydromorphone (H3G) can be isolated in a ratio of roughly 25:1 to parent drug after oral administration of hydromorphone to patients with normal renal function. In patients with renal impairment, suspected of having adverse reactions due to the accumulation of metabolite, H3G levels were identified at levels more than four times higher than predicted. Such accumulation of H3G may be responsible for the psychomimetic reactions occasionally reported in patients taking high doses of hydromorphone. Accumulation of neuroexcitatory metabolites is also postulated as the aetiology of similar and occasionally severe dystonic reactions reported with high doses of morphine and semi-synthetic opioids.

INDICATIONS

DILAUDID® preparations are indicated for the relief of moderate to severe pain.

CONTRAINDICATIONS

DILAUDID® preparations are contraindicated in patients with: known hypersensitivity to hydromorphone or to any of the ingredients; respiratory depression with hypoxia or elevated carbon dioxide levels in the blood in the absence of resuscitative equipment, status asthmaticus, paralytic ileus, concurrent monoamine oxidase inhibitors (MAOIs) or within 14 days of such therapy, pregnancy; premature infants and children, or during labour for delivery of premature infants.

PRECAUTIONS

Hydromorphone must be administered with caution in patients taking CNS depressants (see INTERACTIONS WITH OTHER MEDICINES).

Opioids may influence the hypothalamic-pituitary-adrenal or -gonadal axes. Some changes that can be seen include an increase in serum prolactin, and decreases in plasma cortisol and testosterone. Clinical symptoms may manifest from these hormonal changes.

Special risk patients

In general, opioids should be given with caution and the initial dose should be reduced in the elderly or debilitated and those with renal impairment; hepatic impairment; severe impairment of pulmonary function; myxoedema or hypothyroidism; adrenocortical insufficiency (e.g. Addison's Disease); CNS depression or coma; toxic psychosis; prostatic hypertrophy or urethral stricture; gall bladder disease; acute alcoholism; *delirium tremens;* pancreatitis or following gastrointestinal surgery as opioids are known to impair intestinal motility and should not be used until the physician is assured of normal bowel function. Should paralytic ileus be suspected or occur during use, DILAUDID® preparations should be discontinued immediately. The administration of opioid analgesics including hydromorphone may obscure the diagnoses or clinical course in patients with acute abdominal conditions and may aggravate pre-existing convulsions in patients with convulsive disorders. Reports of mild to severe

seizures and myoclonus have been reported in severely compromised patients, administered high doses of parenteral hydromorphone, for cancer and severe pain.

Impaired respiration

The major risk of opioid excess is respiratory depression. Respiratory depression occurs most frequently in overdose situations, in the elderly, in the debilitated, and in those suffering from conditions accompanied by hypoxia or hypercapnia when even moderate therapeutic doses may dangerously decrease pulmonary ventilation.

Hydromorphone should be used with extreme caution in patients with chronic obstructive pulmonary disease or *cor pulmonale*, patients having a substantially decreased respiratory reserve (e.g. kyphoscoliosis), hypoxia, hypercapnia, or in patients with pre-existing respiratory depression. In such patients even usual therapeutic doses of opioid analgesics may decrease respiratory drive while simultaneously increasing airway resistance to the point of apnoea.

Head injury and increased intracranial pressure

The respiratory depressant effects of hydromorphone with carbon dioxide retention and secondary elevation of cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or pre-existing increase in intracranial pressure. Opioid analgesics, including hydromorphone, may produce effects which can obscure the clinical course and neurologic signs of further increase in intracranial pressure in patients with head injuries.

Hypotensive effect

Opioid analgesics, including hydromorphone, may cause severe hypotension in an individual whose ability to maintain blood pressure has already been compromised by depleted blood volume or a concurrent administration of drugs such as phenothiazines or general anaesthetics (see also **INTERACTIONS WITH OTHER MEDICINES**). Therefore, hydromorphone should be administered with caution to patients in circulatory shock, since vasodilation produced by the drug may further reduce cardiac output and blood pressure. Hydromorphone may produce orthostatic hypotension in ambulatory patients.

Driving and operating dangerous machinery

Hydromorphone may impair mental and/or physical ability required for the performance of potentially hazardous tasks (e.g. driving, operating machinery). Patients should be cautioned accordingly.

Use in surgery

DILAUDID® and DILAUDID®-HP injections should be used with caution pre- or intra-operatively and within the first 24 hours post-operatively.

Opioid analgesics including hydromorphone should also be used with caution in patients requiring biliary tract procedures since it may cause spasm of the sphincter of Oddi.

Drug abuse and dependence

Physical dependence and tolerance are expected to occur with chronic opioid therapy, but both are distinct entities from psychological (psychogenic) dependence. It is apparent from a review of pertinent medical literature that the risk of true psychological dependence or

addiction in patients appropriately treated with opioids is thought to be low. Unlike physical dependence and tolerance, psychological dependence to opioids is not considered a normal consequence of their continued use for medical purposes and is thought to occur only in susceptible individuals.

Like other opioids, continuing use of hydromorphone may result in physical dependence, tolerance, and, in susceptible individuals, psychological dependence.

Abrupt discontinuation of therapy with hydromorphone, or any opioid, can result in a constellation of symptoms known as abstinence syndrome or "withdrawal". This syndrome can also be precipitated in physically dependent patients by the concurrent administration of a drug with opioid antagonist properties such as naloxone (see **OVERDOSAGE**). Opioid abstinence syndrome has been well described in the literature and the severity of the syndrome in a particular patient can vary from mild discomfort to potential cardiovascular collapse. Without treatment most observable symptoms resolve in 5-14 days. A period of "subacute withdrawal" lasting up to 6 months has also been described in which previously dependent patients experience difficulty concentrating, insomnia, irritability, myalgias and autonomic instability.

For patients in whom physical dependence has become established and in whom it has become necessary to withdraw opioid therapy, a gradual reduction ("wean") of the dosage is recommended in order to avoid precipitation of an abstinence syndrome. Various regimens have been described for treatment of severe abstinence syndrome, including but not limited to methadone substitution, clonidine, benzodiazepines, and phenothiazines. Supportive care is essential and associated symptoms, such as dehydration and gastrointestinal (GI) disturbances, should be treated accordingly.

Use in drug and alcohol-dependent patients

Hydromorphone has an abuse profile similar to other strong opioids. Hydromorphone may be sought and abused by people with latent or manifest addiction disorders. Hydromorphone should be used with caution in patients with alcoholism and other drug dependencies due to the increased frequency of opioid tolerance, physical and psychological dependence observed in these patient populations. Abuse of hydromorphone in combination with other CNS depressant drugs can result in serious risks to the patient.

Abuse of oral dosage forms

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

Hyperalgesia

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

Carcinogenicity

Long term carcinogenicity studies have not been performed.

Genotoxicity

Hydromorphone was non-genotoxic in the Ames test and the *in vivo* mouse micronucleus

assay but positive in mouse lymphoma assay with metabolic activation. Similar findings have been reported with other opioid analgesics such as codeine and oxycodone.

Effects on fertility

No effects have been observed on male or female fertility or sperm parameters in rats.

Use in pregnancy

Australian Categorisation of Medicines in Pregnancy: Category C. Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details.

Literature reports of hydromorphone hydrochloride administered to pregnant Golden hamsters showed that hydromorphone is teratogenic at subcutaneous (SC) doses greater than 14 mg/kg. Evidence of a teratogenic effect has also been reported in the literature in mice and hamsters but was not observed in rat and rabbit studies conducted by the sponsor. The relevance of these findings to humans is unknown since there are no well-controlled studies of hydromorphone in pregnant women.

A pre- and post-natal study in rats showed that there was an increase in pup mortality and reduced body weight gain in the early postnatal period, associated with maternal toxicity. No effects on continued pup development or reproductive performance were observed.

Like other opioid analgesics, hydromorphone may cause respiratory depression in the newborn infant. Hydromorphone should only be used during labour after considering the needs of the mother against the risk to the foetus. In long-term treatment during pregnancy, the risk of neonatal withdrawal should be considered.

Use in lactation

Low levels of opioid analgesics have been detected in human milk. As a general rule, breast feeding should not be undertaken while a patient is receiving hydromorphone since it, and other drugs in this class, may be excreted in the milk.

Use in the elderly

Elderly subjects have been shown to have at least twice the sensitivity (as measured by EEG changes) of young adults to some opioids. When administering DILAUDID® preparations to the elderly, the initial dose should be reduced (see **DOSAGE AND ADMINISTRATION**).

INTERACTIONS WITH OTHER MEDICINES

The concomitant use of other central nervous system depressants which include, but are not limited to sedatives (including benzodiazepines), anxiolytics, hypnotics, general anaesthetics (e.g. barbiturates), phenothiazines, tranquillisers, antiemetics, antidepressants (including tricyclic antidepressants), neuroleptics, opioids or alcohol may produce additive depressant effects. Respiratory depression, hypotension and profound sedation, coma or death may occur. When such combined therapy is contemplated, the dose of one or both agents should be reduced however, hydromorphone should not be taken with alcohol.

Hydromorphone should not be given to patients taking non-selective MAOIs or within 14 days

of stopping such treatment.

Opioid analgesics including hydromorphone may enhance the action of neuromuscular blocking agents and produce an extensive degree of respiratory depression.

Pharmaceutical incompatibility

DILAUDID® injection is physically compatible and chemically stable for at least 24 hours at 25°C protected from light in most common large volume parenteral solutions which do not have a pH > 7.

Hydromorphone hydrochloride injection is incompatible with soluble barbiturates.

ADVERSE EFFECTS

The adverse effects of hydromorphone are similar to those of other opioid agonist analgesics, and represent established pharmacological effects of the drug class. The major hazards include respiratory depression and apnoea. To a lesser degree, circulatory depression, respiratory arrest, shock and cardiac arrest have occurred.

Adverse effects reported commonly (frequency > 1%) seem to be more prominent in ambulatory patients and in those not experiencing severe pain. Syncopal reactions and related symptoms in ambulatory patients may be alleviated if the patient lies down.

Cardiovascular disorders

Common	hypotension
Uncommon	bradycardia, hypertension, palpitation, tachycardia
Unknown	flushing

Eye disorders

Uncommon	blurred vision, diplopia, miosis, visual impairment

Gastrointestinal disorders

Very common	constipation, nausea
Common	abdominal pain, dry mouth, vomiting
Uncommon	cramps, diarrhoea, dysgeusia (taste alteration), paralytic ileus

General disorders and administration site conditions

Common	asthenia, injection site reactions (following parenteral administration only)
Uncommon	chills, drug tolerance, drug withdrawal syndrome, drug withdrawal syndrome neonatal, peripheral oedema, fatigue, malaise

Hepatobiliary disorders

Uncommon	biliary colic, increased hepatic enzymes

Immune system disorders

Uncommon	anaphylactic reactions, hypersensitivity reactions (including oropharyngeal swelling)

Metabolism and nutrition disorders

Common	anorexia

Nervous system disorders

Very common	dizziness, somnolence
Common	headache, light-headedness, sedation
Uncommon	convulsions, dyskinesia, faintness, hyperalgesia, increased intracranial pressure, myoclonus, uncoordinated muscle movement, muscle rigidity, paraesthesia, syncope, tremor, weakness
Rare	lethargy

Psychiatric disorders

Common	anxiety, confusional state, dysphoria, euphoria, insomnia, nervousness
Uncommon	agitation, drug dependence, alterations of mood (apprehension, depression, floating feelings), transient hallucinations, disorientation, nightmares

Renal and urinary disorders

Common	urinary retention
Uncommon	antidiuretic effects, urinary hesitancy

Reproductive system and breast disorders

Uncommon	erectile dysfunction

Respiratory, thoracic and mediastinal disorders

Uncommon	bronchospasm, dyspnoea, laryngospasm, respiratory depression

Skin and subcutaneous tissue disorders

Common	hyperhidrosis (sweating), pruritus, rash
Uncommon	urticaria and other skin rashes

Key:

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)

Other

In clinical trials, neither local tissue irritation nor induration was observed at the site of subcutaneous injection of DILAUDID®-HP injection; pain at the injection site was rarely observed.

DOSAGE AND ADMINISTRATION

WARNING: DILAUDID®-HP INJECTION (HIGH POTENCY) IS A HIGHLY CONCENTRATED SOLUTION OF HYDROMORPHONE INTENDED FOR USE IN OPIOID-TOLERANT PATIENTS. DO NOT CONFUSE DILAUDID®-HP INJECTION WITH STANDARD PARENTERAL FORMULATIONS OF DILAUDID® OR OTHER OPIOIDS. OVERDOSE AND DEATH COULD RESULT.

General

Hydromorphone, like other opioids, may cause clinically significant physical dependence usually after several weeks of continued opioid therapy, but in some patients it may be clinically relevant after a shorter treatment period (see **PRECAUTIONS** - Drug abuse and dependence). Tolerance, i.e. when increasingly larger doses are required to produce a given clinical effect, is initially manifested as a shortened duration of action followed by a decrease in the intensity of analgesic effect. Tolerance is a normal and expected sequela of continued opioid therapy and, in chronic pain patients and in patients with cancer, it may become a significant consideration. DILAUDID® dosage, in these patients, should be titrated to the desired analgesic effect.

Adult

Individualisation of dosage

As with other opioid analgesics, safe and effective administration of DILAUDID® preparations to patients with acute or chronic pain depends upon a comprehensive assessment of the patient. The nature of the pain (severity, frequency, aetiology and pathophysiology) as well as the concurrent medical status of the patient will affect selection of the starting dosage.

Owing to the varied response observed to opioids between individuals, it is recommended that all patients be started at a conservative dose of hydromorphone and titrated to an adequate level of analgesia, balanced with an acceptable level of adverse effect(s). The relatively short half-life of hydromorphone usually allows for rapid titration.

Non opioid-tolerant patients

The recommended initial dose is as follows:

Intramuscular or subcutaneous: 1 to 2 mg every four to six hours.

Intravenous: 0.5 to 1.0 mg (given slowly over 2 to 3 minutes)
Intravenous or subcutaneous administration is usually not painful.

Patient-controlled analgesia (PCA): There are limited data available on the use of intravenous hydromorphone administered as PCA. One regimen described in the literature is as follows: Adequate analgesia should be established prior to commencement of the PCA. A background continuous intravenous infusion of 0.1 mg per hour should be used together with patient-administered bolus doses of 0.2 mg at no more than 5 minutely intervals and up to a maximum of 1.2 mg per hour.

Continuous intravenous infusion: Limited data are available. An infusion of up to 0.3 mg per hour has been used in a small number of patients.

In general, and irrespective of route of administration, elderly patients may require lower doses of DILAUDID® preparations (see **PRECAUTIONS** - Use in the elderly).

Patients currently receiving opioids

When converting patients currently receiving opioids to a DILAUDID® preparation, both the dose of hydromorphone and the duration of its analgesic effect will vary substantially depending on the patient's opioid tolerance. A hydromorphone dose should be selected and adjusted so that at least 3-4 hours of pain relief is achieved. In patients taking opioid

analgesics, the starting dose of hydromorphone should be based on the prior daily opioid dose. This should be done by converting the total daily dose of the previous opioid to an equivalent total daily dose of hydromorphone using the Equianalgesic Table. For opioids not in the table, first estimate the equivalent total daily dose of morphine, then use the table to determine the equivalent total daily dose of hydromorphone.

EQUIANALGESIC TABLE*
Opioid Analgesic Equivalents with Approximately Equianalgesic Potency

Nonproprietary Name	**Equianalgesic IM or SC Dose**	**Comparable Oral Dose**
morphine sulfate	10 mg	30 mg
hydromorphone HCl (DILAUDID® preparations)	1.3-2.0 mg	6.5-7.5 mg
pethidine HCl	75-100 mg	300-400 mg
methadone HCl	10 mg	10-20 mg

***** Dosages and ranges of dosages represented in the above table are a compilation of estimated equipotent dosages from published references comparing opioid analgesics in cancer and severe pain.

Once the total daily dosage of hydromorphone has been estimated, it should be divided into the desired number of doses. Since there is individual variation in response to different opioid drugs, only 1/2 to 2/3 of the estimated dose of hydromorphone calculated from the Equianalgesic Table should be given for the first few doses, then increased as needed according to the patient's response to its analgesic effect.

The DILAUDID® range of products (see **PRESENTATION AND STORAGE CONDITIONS**) provides total flexibility in respect of dose and route of administration. Hence, the appropriate DILAUDID® dosage form should be carefully considered, consistent with the route of administration, to achieve the pain relief sought for the patient.

In chronic pain, doses should be administered around-the-clock. A supplemental dose of 5-15% of the total daily usage may be administered every two hours on an "as-needed" basis.

Periodic reassessment after initial dosing is always required. If pain management is not satisfactory and, in the absence of significant opioid-induced adverse events, the hydromorphone dose may be increased gradually. If excessive opioid side effects are observed early during the dosing interval, the hydromorphone dose should be reduced. If this results in breakthrough pain at the end of the dosing interval, the dosing interval may need to be shortened. Dose titration should be guided by the need for analgesia rather than the absolute dose of opioid employed.

DILAUDID®-HP Injection (HP = *H*igh *P*otency) is only recommended for patients who are already receiving high doses of parenteral opioids where the volume required for parenteral administration (to achieve the high dose) becomes unacceptably large for the chosen route of administration (e.g. subcutaneous).

DILAUDID®-HP 50 mg concentrated injection must be diluted with an appropriate sterile diluent (e.g. 0.9% saline, 5% dextrose, water for injections) to a suitable concentration that can

be tolerated by the patient.

Continuous subcutaneous infusion has also been used as a method of delivering large daily doses of hydromorphone in opioid-tolerant patients with severe pain.

Children

Safety and efficacy have not been established in children.

OVERDOSAGE

Symptoms

Serious overdosage with hydromorphone is characterised by respiratory depression (reduced respiratory rate and/or tidal volume, cyanosis), extreme somnolence, progressing to stupor, coma or pneumonia aspiration, skeletal muscle flaccidity, cold and/or clammy skin, pupillary constriction, and possibly bradycardia, hypotension and death. Severe overdose may result in apnoea, pulmonary oedema, circulatory collapse and death.

Treatment

The primary concern in the treatment of opioid overdose is immediate supportive therapy with the establishment of adequate respiratory exchanges through the provision of, and maintenance of, adequate ventilation - patients may need ventilatory support up to and including endotracheal intubation and controlled ventilation. Adequate body temperature and fluid balance should be maintained. Oxygen, intravenous fluids, vasopressors and other supportive measures should be used as indicated.

Tolerance to the respiratory and CNS-depressant effects of opioids develops concomitantly with tolerance to the analgesic effects, therefore making respiratory depression unlikely in an opioid-tolerant patient taking the usual therapeutic doses of hydromorphone. Activated charcoal may reduce absorption of the drug if given within one to two hours after ingestion. A potentially serious recent oral ingestion of hydromorphone, if suspected, may be treated with activated charcoal in a patient who is fully conscious with an intact gag reflex or a secured airway. Initial dose of charcoal is 30 to 100 g in adults and 1 - 2 g/kg in children and is given as a slurry via nasogastric tube. In patients who are not fully conscious or have an impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube, once the airway is protected.

If there are signs of clinically significant respiratory or cardiovascular depression, the use of an opioid antagonist such as naloxone should be considered (please refer to naloxone Product Information for further information).

Caution should always be observed when using an opioid antagonist for the treatment of suspected hydromorphone overdose as the duration of action of hydromorphone may exceed that of the antagonist. Continuing surveillance is mandatory to prevent recurrence of respiratory depression and supportive care - including ventilatory and circulatory resuscitation/support when indicated - should always be provided. Additional doses of antagonist may be given as indicated by the clinical situation.

Opioid antagonists such as naloxone may precipitate an acute abstinence syndrome in opioid-dependent patients and should be carefully titrated to the desired degree of reversal. The severity of an abstinence syndrome precipitated by administration of an opioid antagonist is

contingent upon the degree of dependence and the dose of antagonist given. Too rapid or complete reversal may induce nausea, vomiting, sweating and circulatory stress and may reverse the desirable therapeutic effects (analgesia) as well.

Toxicity

Toxicity may result from overdosage but because of the great interindividual variation in sensitivity to opioids it is difficult to determine an exact dose of any opioid that is toxic or lethal. The toxic effects and signs of overdosage may be less pronounced than expected, when pain and /or tolerance are manifest.

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

PRESENTATION AND STORAGE CONDITIONS

DILAUDID® 2 mg injection contains 2 mg hydromorphone hydrochloride in 1 mL solution. Clear, colourless to pale yellow solution in a clear glass ampoule.
Packs of 5 x 1 mL ampoules. Store below 30°C. Protect from light.

DILAUDID®-HP 10 mg injection contains 10 mg hydromorphone hydrochloride in 1 mL solution. Clear, colourless to pale yellow solution in a clear glass ampoule. Packs of 5 x 1 mL ampoules. Store below 30°C. Protect from light.

DILAUDID®-HP 50 mg concentrated injection contains 50 mg hydromorphone hydrochloride in 1 mL solution. Clear, colourless to pale yellow solution in a clear glass ampoule.
Packs of 5 x 1 mL ampoules. Store below 30°C. Protect from light.

NAME AND ADDRESS OF THE SPONSOR

Mundipharma Pty Limited
ABN 087 081 322 509
88 Phillip Street
SYDNEY NSW 2000

Further information may be obtained from Mundipharma's Medical Information Department 1800 188 009.

POISON SCHEDULE OF THE MEDICINE

S8

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)

9th September 2016

DATE OF MOST RECENT AMENDMENT

3rd October 2017

® DILAUDID is a registered trade mark.
Orbis RA-0131