PRODUCT INFORMATION

DILAUDID® TABLETS (2 mg, 4 mg and 8 mg)
DILAUDID® ORAL LIQUID (1 mg/mL)
DILAUDID® AMPOULE (2 mg/1 mL)
DILAUDID-HP® AMPOULES (10 mg/1 mL and 50 mg/5 mL)
DILAUDID-HP® VIAL (500 mg/50 mL)

NAME OF THE MEDICINE
DILAUDID® preparations contain hydromorphone hydrochloride. The structural formula of hydromorphone hydrochloride is:

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\text{\includegraphics[width=0.5\textwidth]{structure.png}}
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DESCRIPTION
Hydromorphone hydrochloride, a hydrogenated ketone of morphine, is an opioid analgesic. Chemical name: 4,5α-epoxy-3-hydroxy-17-methylmorphinan-6-one hydrochloride. Molecular weight: 321.81. 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. CAS registration number: 71-68-1.

The inactive ingredients in DILAUDID® tablets are lactose anhydrous and magnesium stearate. Additionally, the 2 mg tablet contains vat red 1 aluminium lake (CI73360) and quinoline yellow aluminium lake (CI47005) as colourant and the 4 mg tablet contains quinoline yellow aluminium lake (CI47005) as colourant.

The inactive ingredients in DILAUDID® oral liquid are sucrose, glycerol, propyl hydroxybenzoate, methyl hydroxybenzoate and purified water.

The inactive ingredients in DILAUDID® ampoules and DILAUDID-HP® ampoules and vials are sodium citrate, citric acid monohydrate and Water for Injections.

PHARMACOLOGY
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 i.m. hydromorphone is equianalgesic
to 10 mg of i.m. morphine. The relative potency, (based on single dose bioassay) of oral hydromorphone was found to be approximately one-fifth that of i.m. hydromorphone\(^1\) - 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 may influence the hypothalamic-pituitary-adrenal or –gonadal axes. Some changes that can be seen include an increase in serum prolactin, and decrease in plasma cortisol and testosterone. Clinical symptoms may be manifest from these hormonal changes.

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 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.

**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\(^\text{®}\) tablets and other strengths of DILAUDID\(^\text{®}\) tablets has not been established.

Following intravenous administration of hydromorphone to normal volunteers, the mean half-life of elimination was 2.64 ± 0.88 hours. The mean volume of distribution was 301 litres, 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 litres per minute.
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 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 MAO inhibitors (or within 14 days of such therapy); pregnancy; premature infants and children, or during labour for delivery of premature infants.

PRECAUTIONS
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 preexisting 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
Respiratory depression is the chief hazard of hydromorphone. 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 preexisting 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 a depleted blood volume or a concurrent administration of drugs such as phenothiazines or general anaesthetics (see also PRECAUTIONS - 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.

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.

Hydromorphone may produce orthostatic hypotension in ambulatory patients.

Use in surgery
DILAUDID® tablets and oral liquid should be used with caution pre-operatively and within the first 24 hours post-operatively.

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

Use in biliary surgery
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 very low. Unlike physical
dependence and tolerance, psychological dependence to opioids is not 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 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 risk 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, in high doses. A hydromorphone dose reduction or change in opioid may be
required.

Carcinogenicity
Studies in animals to evaluate the drug’s carcinogenic potential have not been done.

Genotoxicity
There was no evidence of mutagenic potential in a limited Ames test.
Effects on fertility
Studies in animals on the effect of hydromorphone on fertility have not been conducted.

Use in pregnancy
Pregnancy Category C. Literature reports of hydromorphone hydrochloride administered to pregnant Golden hamsters show that hydromorphone is teratogenic at doses greater than 14 mg/kg s.c. The relevance of this finding to humans is unknown since adequate reproductive toxicity studies have not been done.

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, nursing 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 and PRECAUTIONS).

Interactions with other medicines
The concomitant use of other central nervous system depressants including sedatives or hypnotics, general anaesthetics (e.g. barbiturates), phenothiazines, tranquillisers, antiemetics, antidepressants, neuroleptics, other opioids and alcohol may produce additive depressant effects. Respiratory depression, hypotension and profound sedation or coma 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 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.

Most frequently observed with opioid analgesics (common > 1%)
The most frequently observed adverse effects are asthenic conditions, confusional state, dizziness, dry mouth, dysphoria, euphoria, light-headedness, nausea, pruritus, rash, sedation, somnolence, sweating and vomiting. These effects 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.

Less frequently observed with opioid analgesics (uncommon < 1%)

Cardiovascular disorders
bradycardia, hypertension, hypotension, palpitation, tachycardia

Eye disorders
blurred vision, diplopia, miosis, nystagmus, visual disturbances

Gastrointestinal disorders
anorexia, constipation, cramps, diarrhoea, paralytic ileus

General disorders and administration site conditions
chills, drug tolerance, drug withdrawal syndrome, peripheral oedema

Hepatobiliary disorders
biliary tract spasm, increased hepatic enzymes

Immune system disorders
hypersensitivity reactions (including oropharyngeal swelling)

Nervous system disorders
convulsions, dyskinesia, faintness, headache, hyperalgesia, increased intracranial pressure, uncoordinated muscle movements, muscle rigidity, muscle tremor, paraesthesia, syncope, taste alteration, tremor, weakness

Psychiatric disorders
agitation, drug dependence, insomnia, alterations of mood (nervousness, apprehension, depression, floating feelings, dreams), transient hallucinations and disorientation

Renal and urinary disorders
antidiuretic effects, urinary retention or hesitancy

Respiratory, thoracic and mediastinal disorders
bronchospasm, laryngospasm, respiratory depression

Skin and subcutaneous tissue disorders
diaphoresis, urticaria, and other skin rashes
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 NARCOTIC-TOLERANT PATIENTS. DO NOT CONFUSE DILAUDID-HP® INJECTION WITH STANDARD PARENTERAL FORMULATIONS OF DILAUDID OR OTHER NARCOTICS. 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:
Oral: 2 to 4 mg every four hours
There are no data available on the effects of food on the absorption of orally administered hydromorphone. Patients taking the drug chronically should take their oral doses consistently either with food or on an empty stomach.

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 minute 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 (see below). For opioids not in the table, first estimate the equivalent total daily dose of morphine, then use the table below to determine the equivalent total daily dose of hydromorphone.

**EQUIANALGESIC TABLE**

<table>
<thead>
<tr>
<th>Nonproprietary Name</th>
<th>Equianalgesic IM or SC Dose</th>
<th>Comparable Oral Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine Sulfate</td>
<td>10 mg</td>
<td>30 mg</td>
</tr>
<tr>
<td>Hydromorphone HCl</td>
<td>1.3-2.0 mg</td>
<td>6.5-7.5 mg</td>
</tr>
<tr>
<td>(DILAUDID® preparations)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pethidine HCl</td>
<td>75-100 mg</td>
<td>300-400 mg</td>
</tr>
<tr>
<td>Methadone HCl</td>
<td>10 mg</td>
<td>10-20 mg</td>
</tr>
<tr>
<td>Papaveretum</td>
<td>20 mg</td>
<td>-</td>
</tr>
</tbody>
</table>

* Dosages, and ranges of dosages represented in the 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 **PRESENTATIONS**) provides total flexibility in respect of dose and route of administration. Hence, the appropriate DILAUDID® dose 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 the 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 in 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 more by the need for analgesia than the absolute dose of opioid employed.

DILAUDID-HP® Injection (HP = High Potency) is usually administered to 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).

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 or coma, 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; 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.

Naloxone, a specific opioid antagonist, is the mainstay of pharmacologic therapy in overdose and unusual sensitivity to opioids, including hydromorphone. In patients in whom physical dependence is NOT suspected and in whom a modest degree of respiratory depression is the chief symptom of overdose, the usual initial dose of naloxone is 0.1 to 0.2 mg, given intravenously when possible, in conjunction with respiratory support. This may be repeated
at two to three minute intervals in doses up to 2.0 mg, titrated to the desired response (appropriate ventilation and level of consciousness without significant pain or discomfort). Profound respiratory depression and decreased responsiveness are usually treated with an initial I.V. dose of 0.4 mg of naloxone, with repeat doses of up to 0.1 mg/kg given every two to three minutes as needed to maintain responsiveness.

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.

Please phone the Poisons information Centre on 131126 for advice on managing overdose.

**STORAGE CONDITIONS**

Store below 25°C. Protect from light.

**PRESENTATIONS**

*DILAUDID® tablets, 2 mg*: packs of 20’s. Light orange, round, flat-faced tablets, with bevelled edges, with the number “2” on one side and a “D” on the other side.

*DILAUDID® tablets, 4 mg*: packs of 20’s. Light yellow, round, flat-faced tablets, with bevelled edges with the number “4” on one side and either a “D” on the other side.

*DILAUDID® tablets, 8 mg*: packs of 20’s. White, triangular shaped tablet, bisected on one face, with a “D” on each side of the bisecting line, and with the number “8” on the other face.  
*DILAUDID® oral liquid (1 mg/1 mL): 473 mL.*

*DILAUDID® ampoules, 2 mg/1 mL*: packs of 5’s.

*DILAUDID-HP® ampoules 10 mg/1 mL and 50 mg/5 mL*: packs of 5’s.

*DILAUDID-HP® vials 500 mg/50 mL*: pack of 1. Note: The packaging (vial stopper) of this product contains rubber latex which may cause allergic reactions.
NAME AND ADDRESS OF THE SPONSOR
Mundipharma Pty Limited
ABN 087 081 322 509
50 Bridge Street
SYDNEY NSW 2000

POISON SCHEDULE OF THE MEDICINE S8

Reference

TGA APPROVAL DATE 20 November 2000

DATE OF LAST AMENDMENT
9 July 2004
14 August 2008
24 September 2008
12 March 2009
19 November 2009 (minor editorial changes)
22 February 2010 (safety-related notification)

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