

PRESCRIBING INFORMATION

^NDILAUDID-HP[®] (10 mg/mL, 1 mL and 5 mL ampoules, 50 mL vial)

^NDILAUDID-HP-PLUS[®] (20 mg/mL, 50 mL vial)

^NDILAUDID-XP[®] (50 mg/mL, 50 mL vial)

^NDILAUDID[®] STERILE POWDER (250 mg vial)

(hydromorphone hydrochloride)

Opioid Analgesic

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DATE OF PREPARATION:
August 8, 2008

Control No.: 123554

PRESCRIBING INFORMATION

NAME OF DRUG

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(hydromorphone hydrochloride)

THERAPEUTIC CLASSIFICATION

Opioid Analgesic

DILAUDID-HP[®], **DILAUDID-HP-Plus**[®], **DILAUDID-XP**[®] and Reconstituted **DILAUDID**[®] Sterile Powder are highly concentrated solutions of hydromorphone hydrochloride. They should be used only in opioid tolerant patients requiring high doses or high concentrations of opioid agonists. Do not confuse **DILAUDID-HP**[®], **DILAUDID-HP-Plus**[®], **DILAUDID-XP**[®] and Reconstituted **DILAUDID**[®] Sterile Powder with the lower concentration of the **DILAUDID**[®] 2 mg/mL ampoules since overdose and death could result.

CLINICAL PHARMACOLOGY

DILAUDID[®] (hydromorphone hydrochloride) is a hydrogenated ketone of morphine. It is an opioid analgesic with many of the effects common to the class of drugs.

Opioid analgesics have multiple actions but exert their primary effects on the central nervous system and organs containing smooth muscle. The principal actions of therapeutic value are analgesia and sedation. Opioid analgesics also suppress the cough reflex and cause respiratory depression, mood

changes, mental clouding, euphoria, dysphoria, nausea, vomiting, increased cerebrospinal fluid pressure, pinpoint constriction of the pupils, increased biliary tract pressure, increased parasympathetic activity and transient hyperglycemia.

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 by combining with these receptors.

The relationship between plasma concentration of hydromorphone and analgesic effect has not been well established. In patients with chronic pain, hydromorphone should be titrated to the dose required to adequately relieve pain without unmanageable side effects. There is no intrinsic limit to the analgesic effect of hydromorphone; adequate doses will relieve even the most severe pain. Clinically, however, dosage limitations are imposed by the adverse effects, primarily respiratory depression; nausea and vomiting which can result from high doses.

Pharmacokinetics

In normal human volunteers hydromorphone is metabolized primarily in the liver. It is excreted predominantly as the glucuronidated conjugate, with small amounts of parent drug and minor amounts of 6-hydroxy reduction metabolites.

Following intravenous administration of hydromorphone to normal volunteers, the mean $t_{1/2}$ of elimination was 2.65 +/- 0.88 hours. The mean volume of distribution was 91.5 liters, suggesting extensive tissue uptake. Hydromorphone is rapidly removed from the bloodstream and distributed to skeletal muscle, kidneys, liver, intestinal tract, lungs, spleen and brain. It also crosses the placental membranes.

Hydromorphone is approximately 5 to 7 times more potent than morphine (i.e. 1.5 to 2 mg of hydromorphone produces analgesia equal to that produced by 10 mg of morphine). After intramuscular administration, hydromorphone has a slightly more rapid onset and slightly shorter

duration of action than morphine. The duration of analgesia in the non-tolerant patient with usual doses may be up to 4 to 5 hours. However, in opioid tolerant subjects, duration of analgesia will vary substantially depending on tolerance and dose. Dose should be adjusted so that 3 to 4 hours of pain relief may be achieved.

INDICATIONS AND CLINICAL USE

DILAUDID-HP[®], **DILAUDID-HP-PLUS[®]**, **DILAUDID-XP[®]** and Reconstituted **DILAUDID[®]** Sterile Powder (hydromorphone hydrochloride) are indicated exclusively for the relief of severe pain in patients who require subcutaneously, intravenously or intramuscularly administered opioids in doses or concentrations higher than those usually needed. Because hydromorphone is highly soluble, a smaller injection volume can be used and discomfort associated with the intramuscular or subcutaneous injection of larger volumes of solution can be minimized.

CONTRAINDICATIONS

High concentration **DILAUDID[®]** preparations (hydromorphone hydrochloride) are contraindicated in patients who are not already receiving high doses or high concentrations of opioids; patients with known hypersensitivity to the drug; patients with respiratory depression in the absence of resuscitative equipment; in patients with severe CNS depression; and in patients with status asthmaticus. High concentration hydromorphone preparations are also contraindicated for use obstetrical analgesia and are not intended for use except in patients with severe pain.

WARNINGS

Drug Dependence

All opioids, like morphine and **DILAUDID[®]** (hydromorphone hydrochloride) can produce drug dependence and therefore have the potential for being abused. As with other opioid drugs, psychic dependence, physical dependence and tolerance are likely to develop upon repeated administration of hydromorphone, and it should be prescribed and administered with the same degree of caution appropriate for the use of morphine. Abrupt discontinuation of the administration of hydromorphone is likely to result in a withdrawal syndrome - (See **PRECAUTIONS** - Dependence **Liability**).

Infants born to mothers physically dependent on hydromorphone will also be physically dependent and may exhibit respiratory difficulties and withdrawal symptoms (See **PRECAUTIONS** - Dependence **Liability**).

Impaired Respiration

Respiratory depression is the chief hazard of hydromorphone. It occurs most frequently in overdose, 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. This effect may be lessened by careful dose titration as severe pain can antagonize the respiratory depressant action of hydromorphone.

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

As mentioned above, severe pain antagonizes the subjective and respiratory depressant actions of hydromorphone. However, should pain suddenly subside, these effects may rapidly become manifest. Patients who are scheduled for cordotomy or other interruptions of pain transmission pathways should not receive hydromorphone within 24 hours of the procedure.

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 individuals whose ability to maintain normal blood pressure has already been compromised by depleted blood volume, or the concurrent administration of drugs such as phenothiazines and other tranquilizers, sedative/hypnotics, tricyclic antidepressants or general anesthetics (see also **PRECAUTIONS - Drug Interactions**). Hydromorphone may produce orthostatic hypotension in ambulatory patients.

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.

Rapid intravenous injection of opioid analgesics increases the possibility of hypotension and respiratory depression and should be avoided (see **DOSAGE AND ADMINISTRATION**).

Use in Pregnancy (see **WARNINGS - Drug Dependence**)

Animals: Adequate animal studies on reproduction have not been performed to determine whether hydromorphone affects fertility in males or females. However, animal studies with both morphine and hydromorphone have indicated the possibility of teratogenic effects.

Humans: There are no well-controlled studies in women. Reports based on marketing experience do not identify any specific teratogenic risks following routine (short-term) clinical use. Although there is no clearly defined risk, such reports do not exclude the possibility of infrequent or subtle damage to the human fetus. Hydromorphone should be used in pregnant women only when clearly needed (see **Labor and Delivery** and **Dependence Liability**).

Labor and Delivery

High concentration hydromorphone preparations are contraindicated in labor and delivery (see **CONTRAINDICATIONS**).

PRECAUTIONS

General

When used at high concentrations, the delivery of precise lower doses of **DILAUDID**[®] (hydromorphone hydrochloride) may be difficult. Therefore, high concentration hydromorphone preparations should be used only if the amount of hydromorphone required can be delivered accurately.

Where high concentration hydromorphone preparations are indicated; the patient is presumed to be receiving an opioid to which tolerance has developed and the initial dose of hydromorphone selected, should therefore be estimated on the basis of the relative potency of hydromorphone and the opioid previously used by the patient (See **DOSAGE AND ADMINISTRATION**).

In diseases, such as malignant cancers, where pain control is the primary focus opioid administration at very high doses is associated with seizures and myoclonus.

Special Risks Groups

In general, opioids should be given with caution and the initial dose should be reduced for the elderly or debilitated, and those with severe impairment of hepatic, pulmonary or renal function; myxedema or hypothyroidism; adrenocortical insufficiency (i.e. Addison's disease); CNS depression or coma; elevated intracranial pressure; toxic psychosis; prostatic hypertrophy or urethral stricture; gallbladder disease; acute alcoholism; delirium tremens; or kyphoscoliosis.

The administration of opioid analgesics including hydromorphone may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Opioid analgesics including hydromorphone should also be used with caution in patients about to undergo surgery of the biliary tract, since it may cause spasm of the sphincter of Oddi.

Dependence Liability

Opioid analgesics may cause psychological and physical dependence (see **WARNINGS**). Physical dependence results in withdrawal symptoms in patients who abruptly discontinue the drug. Withdrawal symptoms may also be precipitated in the patient with physical dependency by the administration of a drug with opioid antagonist activity, i.e. naloxone or mixed agonist antagonists i.e. pentazocine (see also **SYMPTOMS AND TREATMENT OF OVERDOSAGE**). Physical dependence usually does not occur to a clinically significant degree until after several weeks of continued opioid usage. Tolerance, in which increasingly large doses are required in order to produce the same degree of analgesia, is initially manifested by a shortened duration of analgesic effect and subsequently, by decreases in the intensity of analgesia. The dose required to produce analgesia is, therefore, related to the degree of tolerance.

In chronic pain patients in whom opioid analgesics are abruptly discontinued, a severe abstinence syndrome should be anticipated. This may be similar to the abstinence syndrome noted in patients withdrawing from heroin.

The latter abstinence syndrome may be characterized by restlessness, lacrimation, rhinorrhea, yawning, perspiration, gooseflesh, restless sleep or "y'en", and a mydriasis during the first 24 hours. Those symptoms may increase in severity and over the next 72 hours may be accompanied by increasing irritability, anxiety, weakness, twitching and spasms of muscles, kicking movements, severe backache, abdominal and leg pains, abdominal and muscle cramps, hot and cold flashes, insomnia, nausea, anorexia, vomiting, intestinal spasm, diarrhea, coryza and repetitive sneezing, increase in body temperature, blood pressure, respiratory rate and heart rate.

Because of the excessive loss of fluids through sweating, or vomiting and diarrhea, there is usually marked weight loss, dehydration, ketosis, and disturbances in acid-base balance. Cardiovascular collapse can occur. Without treatment, most observable symptoms disappear in 5 to 14 days; however, there appears to be a phase of secondary or chronic abstinence which may last for 2 to 6 months and is characterized by insomnia, irritability, muscular aches, and autonomic instability.

In the treatment of physical dependence on hydromorphone, the patient may be detoxified by gradual reduction of the dosage, although this is unlikely to be necessary in the terminal cancer patient. If abstinence symptoms become severe, the patient may be given methadone. Temporary administration of tranquilizers and sedatives may aid in reducing patient anxiety. Gastrointestinal disturbances or dehydration should be treated accordingly.

Hydromorphone hydrochloride should be used with caution in patients with alcoholism and other drug dependencies due to increased frequency of opioid tolerance and psychological dependence observed in these patient populations.

Drug Interactions

The concomitant use of other central nervous system depressants including sedatives or hypnotics, general anesthetics, phenothiazines, tranquilizers 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. Opioid analgesics, including hydromorphone may enhance the action of neuromuscular blocking agents and produce an increased degree of respiratory depression.

Pregnancy

During pregnancy, hydromorphone hydrochloride should be administered with caution and after the need of the mother has been considered against the risk of the child. In long-term treatment during pregnancy, the risk of neonatal withdrawal should be considered.

Nursing Mothers

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.

Pediatric Use

Safety and effectiveness in children have not been established.

Geriatric Use

In general, dose selection for elderly patients should be cautious and the initial dose should be reduced due to the greater frequency of decreased hepatic, renal or cardiac functions and of concomitant disease or other drug therapy in these patients.

Cough Reflex

Hydromorphone hydrochloride suppresses the cough reflex; as with all opioid analgesics, caution should be exercised when hydromorphone hydrochloride is used post-operatively in patients with pulmonary disease.

Ability to Drive and Use Machines

Hydromorphone hydrochloride may impair mental and/or physical ability required for the performance of potentially hazardous tasks such as driving and operating machinery.

ADVERSE REACTIONS

The adverse effects of **DILAUDID**[®] (hydromorphone hydrochloride) are similar to those of other opioid analgesics and represent an extension of pharmacological effects of the drug class. The major hazards include respiratory depression and apnea. To a lesser degree, circulatory depression, respiratory arrest, shock and cardiac arrest have occurred.

The most frequently observed adverse effects are constipation, lightheadedness, dizziness, sedation, nausea, vomiting, and sweating. All of these effects, except constipation seem to be more prominent in ambulatory patients and in those not experiencing severe pain. Some adverse reactions in ambulatory patients may be alleviated if the patient lies down. When instituting prolonged therapy with an opioid for chronic pain, the prescription of antiemetics for nausea and vomiting and an

appropriate regimen of bowel management for constipation (stool softeners, laxatives etc.) should be considered.

Sedation

Some degree of sedation is experienced by most patients upon initiation of therapy. This may be at least partly because patients often recuperate from prolonged fatigue after the relief of persistent pain. Most patients develop tolerance to the sedative effects of opioids within three to five days and, if the sedation is not severe, will not require any treatment except reassurance. If excessive sedation persists beyond a few days, the dose of the opioid should be reduced and alternate causes investigated. Some of these are: concurrent CNS depressant medication, hepatic or renal dysfunction, brain metastases, hypercalcemia and respiratory failure. 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 and may be alleviated if the patient lies down.

Nausea and Vomiting

Nausea is a common side effect on initiation of therapy with opioid analgesics and is thought to occur by activation of the chemoreceptor trigger zone, stimulation of the vestibular apparatus and through delayed gastric emptying. The prevalence of nausea declines following continued treatment with opioid analgesics. When instituting prolonged therapy with an opioid for chronic pain, the routine prescription of an antiemetic should be considered. In the cancer patient, investigation of nausea should include such causes as constipation, bowel obstruction, uremia, hypercalcemia, hepatomegaly, tumor invasion of celiac plexus and concurrent use of drugs with emetogenic properties. Persistent nausea which does not respond to dosage reduction may be caused by opioid-induced gastric stasis and may be accompanied by other symptoms including anorexia, early satiety, vomiting and abdominal fullness. These symptoms respond to chronic treatment with gastrointestinal prokinetic agents.

Constipation

Practically all patients become constipated while taking opioids on a persistent basis. In some patients, particularly the elderly or bedridden, fecal impaction may result. It is essential to caution the patients in this regard and to institute an appropriate regimen of bowel management at the start of prolonged opioid analgesic therapy. Stool softeners, stimulant laxatives and other appropriate measures should be used as required.

Less Frequently Observed with Opioid Analgesics

General and CNS: Dysphoria, euphoria, weakness, headache, agitation, tremor, uncoordinated muscle movements, alterations of mood (nervousness, apprehension, depression, floating feelings, dreams), muscle rigidity, paresthesia, muscle tremor, blurred vision, nystagmus, diplopia and miosis, hallucinations and disorientation, visual disturbances, insomnia and increased intracranial pressure may occur.

Cardiovascular: Flushing of the face, chills, tachycardia, bradycardia, palpitation, faintness, syncope, hypotension and hypertension have been reported.

Respiratory: Bronchospasm and laryngospasm have been known to occur.

Gastrointestinal: Dry mouth, constipation, biliary tract spasm, anorexia, diarrhea, cramps, ileus and taste alterations have been reported.

Genitourinary: Urinary retention or hesitancy, and antidiuretic effects have been reported.

Dermatologic: Pruritus, urticaria, other skin rashes, wheal and flare over the vein with intravenous injection, and diaphoresis have been reported with opioid analgesics.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms

Serious overdose with **DILAUDID**[®] (hydromorphone hydrochloride) is characterized by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils and sometimes bradycardia and hypotension. In serious overdose, particularly following intravenous injection, apnea, circulatory collapse, cardiac arrest and death may occur.

Treatment

In the treatment of overdose, primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. It should be borne in mind that for individuals who are physically dependent on opioids and are receiving large doses of these drugs, the administration of the usual dose of opioid antagonist will precipitate an acute withdrawal syndrome. The severity will depend on the degree of physical dependence and the dose of the antagonist administered. Use of an opioid antagonist in such persons should be avoided. If necessary to treat serious respiratory depression in the physically dependent patient, the antagonist should be administered with extreme care and by titration, commencing with 10 to 20% of the usual recommended initial dose.

Respiratory depression which may result from overdose, or unusual sensitivity to hydromorphone in a non-opioid-tolerant patient, can be managed with the opioid antagonist naloxone. A dose of naloxone (usually 0.4 to 2.0 mg) should be administered intravenously, if possible, simultaneously with respiratory resuscitation. The dose can be repeated in 3 minutes. Naloxone should not be administered in the absence of clinically significant respiratory or circulatory depression. Naloxone should be administered cautiously to persons who are known or suspected to be physically dependent on hydromorphone. In such cases, an abrupt or complete reversal of opioid effects may precipitate an acute abstinence syndrome.

Since the duration of action of hydromorphone may exceed that of the antagonist, the patient should be kept under continued surveillance; repeated doses of the antagonist may be required to maintain adequate respiration. Other supportive measures should be applied when indicated.

Supportive measures, including oxygen and vasopressors, should be employed in the management of circulatory shock and pulmonary edema accompanying overdose, as indicated. Cardiac arrest or arrhythmias may require cardiac massage or defibrillation.

DOSAGE AND ADMINISTRATION

DILAUDID-HP[®], **DILAUDID-HP-Plus[®]**, **DILAUDID-XP[®]** and Reconstituted **DILAUDID[®]** Sterile Powder are highly concentrated solutions of hydromorphone hydrochloride. They should be used only in opioid tolerant patients requiring high doses or high concentrations of opioid agonists. Do not confuse **DILAUDID-HP[®]**, **DILAUDID-HP-Plus[®]**, **DILAUDID-XP[®]** and Reconstituted **DILAUDID[®]** Sterile Powder with the lower concentration of the **DILAUDID[®]** 2 mg/mL ampoules since overdosage and death could result.

High concentration hydromorphone preparations are indicated for relief of severe pain in opioid tolerant patients. Thus, these patients will already have received opioid analgesics. If the patient is being changed from one injectable form of hydromorphone to higher concentration hydromorphone preparations, similar doses should be used, depending on the patient's clinical response to the drug. If high concentration hydromorphone preparations are substituted for a different opioid analgesic, Table 1 is provided as a guide to determine the approximate equivalent dose of hydromorphone.

**DILAUDID-HP
DILAUDID-HP-PLUS
DILAUDID-XP
DILAUDID STERILE POWDER**

Prescribing Information

In open clinical trials with hydromorphone in patients with terminal cancer, both subcutaneous and intramuscular injections of hydromorphone were well-tolerated, with minimal pain and/or burning at the injection site. Mild erythema was rarely noted after intramuscular injection. Subcutaneous injections of hydromorphone were particularly well tolerated when administered with a short, 30 gauge needle. In addition, continuous subcutaneous infusions of hydromorphone have been shown to be well tolerated. The most common adverse reaction is local tissue redness which can be relieved with more frequent site changes. Experience with administration of hydromorphone by the intravenous route is limited. Should intravenous administration be necessary, the injection should be given slowly, over at least 2 to 3 minutes. Rapid intravenous injection of opioid analgesics increases the possibility of hypotension and respiratory depression. The intravenous route is usually painless.

A gradual increase in dose may be required if analgesia is inadequate, tolerance occurs, or if pain severity increases. The first sign of tolerance is usually a reduced duration of effect.

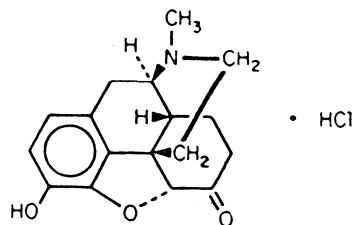
PHARMACEUTICAL INFORMATION

Drug Substance

Proper Name: Hydromorphone Hydrochloride

Chemical Name: 4,5 α -Epoxy-3-hydroxy-17-methylmorphinan-6-one hydrochloride

Structural Formula:



**DILAUDID-HP
DILAUDID-HP-PLUS
DILAUDID-XP
DILAUDID STERILE POWDER**

Prescribing Information

Molecular Formula: $C_{17}H_{20}ClNO_3$

Molecular Weight: 321.8

pH: 1.0 mg/mL solution in water has a pH between 4.5 - 6.5.
10.0 mg/mL solution in water has a pH between 3.5 - 5.5.
100.0 mg/mL solution in water has a pH between 3.5 - 5.5.
250.0 mg/mL solution in water has a pH between 3.0 - 5.0.

Melting Point: 305 to 315°C

pKa: 8.2 (20°C)

Solubility: 1 in 3 of water
1 in 100 of Ethanol (90%)
Practically insoluble in chloroform and ether

Composition

DILAUDID-HP[®] - Each 1 mL of sterile solution contains 10.0 mg of hydromorphone hydrochloride, 2.0 mg of citric acid, 2.0 mg of sodium citrate in water for injection; no added preservative.

DILAUDID-HP-PLUS[®] - Each 1 mL of sterile solution contains 20.0 mg of hydromorphone hydrochloride, 2.0 mg of citric acid, 2.0 mg of sodium citrate in water for injection; no added preservative.

DILAUDID-XP[®] - Each 1 mL of sterile solution contains 50.0 mg of hydromorphone hydrochloride, 2.0 mg of citric acid, 2.0 mg of sodium citrate in water for injection; no added preservative.

**DILAUDID-HP
DILAUDID-HP-PLUS
DILAUDID-XP
DILAUDID STERILE POWDER**

Prescribing Information

DILAUDID[®] STERILE POWDER - Each vial contains 250 mg of sterile lyophilized hydromorphone hydrochloride, no added preservatives.

Stability and Storage Recommendation

Store between 15 and 25°C. Protect from light. Do not use beyond the expiry date indicated on the label.

Reconstitution Information

DILAUDID[®] STERILE POWDER is provided sterile as 250 mg of hydromorphone HCl in a 30 mL vial. It can be reconstituted to desired concentration with sterile water for injection, 0.9% sodium chloride, or 5% dextrose. The table below provides information on the amount of diluent to be added in order to prepare a variety of concentrations.

Volume of Diluent to be added to Vial	Resulting Volume	Nominal Concentration per mL
24.8 mL	25.0 mL	10 mg/mL
12.4 mL	12.5 mL	20 mg/mL
4.9 mL	5.0 mL	50 mg/mL
2.4 mL	2.5 mL	100 mg/mL
1.6 mL	1.67 mL	150 mg/mL
1.1 mL	1.25 mL	200 mg/mL
0.9 mL	1.0 mL	250 mg/mL

The information provided below is only for physical compatibility and chemical stability of the reconstituted solutions. Continued sterility of the reconstituted solution is dependent on the procedures and equipment used during the preparation of the solution. Each pharmacist must address these factors in determining the duration of use of the solution prepared. The usual recommendation for reconstituted solutions is 24 hours at room temperature or 72 hours under refrigeration.

**DILAUDID-HP
DILAUDID-HP-PLUS
DILAUDID-XP
DILAUDID STERILE POWDER**

Prescribing Information

DILAUDID[®] STERILE POWDER for injection is physically compatible and chemically stable in the following diluents and containers:

DILUENT	FINAL CONC.mg HYDROMORPHONE HCl/mL	STORAGE CONDITION	TYPE OF CONTAINER	*PHYSICAL AND CHEMICAL STABILITY (IN DAYS)
Sterile Water for Injection	10,100,250	Room Temperature	Amber Glass	42
		Refrigerated (Fridge)	Amber Glass	42
Sterile Water for Injection	10,100,250	Room Temperature	Pharmacia Cassettes	42
		Refrigerated (Fridge)	Pharmacia Cassettes	42
Sterile Water for Injection	10,100,250	37° dry heat incubator (after storage in Fridge)	Pharmacia Cassettes	10 days after 42 days storage in fridge
0.9% Sodium Chloride Solution	10,100	Room Temperature	Amber Glass	28
5% Dextrose Solution	10,100	Room Temperature	Amber Glass	28
* This information does not address sterility. Please see the previous paragraph for further comments.				

Solutions made from **DILAUDID STERILE POWDER** (as well as **DILAUDID-HP**, **-HP-Plus** and **-XP**) can be administered by i.v., i.m. or s.c. routes including i.v. and s.c. continuous infusion.

AVAILABILITY OF DOSAGE FORMS

DILAUDID-HP[®] (10 mg/mL) ampoules are amber in colour. **DILAUDID-HP**[®] single-use vials are amber and have a white flip-off cap. 1 mL and 5 mL ampoules - boxes of 10. 50 mL single-use vials - boxes of 2.

DILAUDID-HP-PLUS[®] (20 mg/mL) single-use vials are amber in colour and have a brown flip-off cap - 50 mL single-use vials, boxes of 2.

DILAUDID-HP
DILAUDID-HP-PLUS
DILAUDID-XP
DILAUDID STERILE POWDER

Prescribing Information

DILAUDID-XP[®] (50 mg/mL) single-use vials are amber in colour and have a yellow flip-off cap - 50 mL single-use vials, boxes of 2.

DILAUDID[®] STERILE POWDER (250 mg/vial) vials are amber in colour and have a black flip-off cap - boxes of 4.

NOTE: Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. A slight yellowish discoloration may develop in hydromorphone solutions. This yellowish colouration is proportional to hydromorphone concentration and has a tendency to increase over time. The colouration is of an aesthetic nature and not a result of chemical degradation. No loss of potency has been demonstrated. Also, note that **DILAUDID[®]** does not contain any preservatives; therefore, unused portions of the remaining drug in the vial should be discarded.