

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Hydromorphone Hydrochloride 20 mg/ml Solution for Injection / Concentrate for Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml ampoule contains 20mg Hydromorphone Hydrochloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Injection
Concentrate for solution for infusion
A clear colourless solution for injection in Type I glass ampoules.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Treatment of severe pain associated with palliative care.

4.2 Posology and method of administration

In those patients with severe chronic pain associated with cancer, dosage should be individualised based on the response and tolerance of the patient, higher than usual dosages of hydromorphone are often required.

Usual dose:

Age	Bolus	Infusion
Adults and adolescents (>12 years)		
subcutaneous (s.c.) use	1-2 mg s.c. every 3-4 hours	0.15-0.45 mg/h 0.004 mg/kg bodyweight/h
intravenous (i.v.) use	1-1.5 mg i.v. every 3-4 hours to be injected slowly over at least 2-3 minutes	0.15-0.45 mg/h 0.004 mg/kg bodyweight/h
PCA (s.c. and i.v.)	0.2 mg bolus, stop interval 5-10 min.	
Children (<12 years)	Not recommended	

Intramuscular administration [Adult dose and adolescents (>12 years)]

Dosage by intramuscular injection is 1-2mg every 3 – 6 hours.

Elderly: The initial dose should be reduced in the elderly.

4.3 Contraindications

Known hypersensitivity to hydromorphone. The presence of increased intracranial pressure or head injury, acute alcoholism and respiratory depression (chronic obstructive airways disease, cor pulmonale, emphysema, status asthmaticus). Avoid injection in phaeochromocytoma. Current use of monoamine oxidase inhibitor (MAOI) drugs or within 2 weeks of discontinuing their use.

4.4 Special warnings and precautions for use

Use with caution and reduce the initial dose in the elderly or debilitated and those with severely impaired renal, hepatic or pulmonary function. Also those suffering from prostatic hypertrophy, hypothyroidism, hypotension, adrenocortical insufficiency (Addison's disease), CNS depression or coma, toxic psychosis, gallbladder disease, delirium tremens or kyphoscoliosis.

Hydromorphone may obscure diagnosis of acute abdominal conditions and may aggravate convulsions in those patients with existing convulsive disorders.

Hydromorphone may cause spasm of the sphincter of Oddi.

There is a risk of physical dependence developing after several weeks of continued use. Dependence and tolerance will be indicated by a decrease in duration and intensity of analgesia.

4.5 Interaction with other medicinal products and other forms of interaction

Those patients receiving other narcotic analgesics, general anaesthetics, phenothiazines, tranquilizers, anxiolytics and hypnotics, alcohol, tricyclic antidepressants and antipsychotics concomitantly with Hydromorphone may enhance hypotensive and sedative effects. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Cimetidine inhibits the metabolism of opioids. The gastrointestinal effect of opioids can delay absorption of other drugs or may be counteractive as with metoclopramide and domperidone. Opioids can reduce ciprofloxacin levels when used concomitantly. Possible CNS excitation or depression when hydromorphone is given with MAOIs and moclobemide. Opioid analgesics delay the absorption of mexiletine.

Plasma concentration of opioid analgesics elevated by ritonavir, increasing the likelihood of toxicity.

4.6 Fertility, pregnancy and lactation

There have been no reports of congenital birth defects following the use of hydromorphone during pregnancy. Prolonged use of hydromorphone during pregnancy can result in neonatal withdrawal syndrome. Clinical use during pregnancy is principally confined to use during labour. Respiratory depression, as seen with pethidine and morphine, can occur in the neonate, if used during labour.

Opioids have been detected in breast milk, although at extremely low levels, and are unlikely to have a significant clinical effect. In the absence of clinical data, the patient should not breast feed whilst using hydromorphone.

4.7 Effects on ability to drive and use machines

May cause drowsiness, patients being discharged to the home environment should be warned not to drive or operate machinery if affected.

4.8 Undesirable effects

Central Nervous System: Sedation, drowsiness, dry mouth, sweating, headache, facial flushing, hypothermia, hallucinations, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, dizziness, psychological dependence, mood changes.

Gastrointestinal System: Nausea and vomiting occur infrequently; they are more frequent in ambulatory than in recumbent patients. Prolonged administration of Hydromorphone may produce constipation. Opiate agonist-induced increase in intraluminal pressure may endanger surgical anastomosis.

Cardiovascular System: Circulatory depression, peripheral circulatory collapse and cardiac arrest have occurred after rapid intravenous injection. Orthostatic hypotension and fainting may occur if a patient stands up suddenly after receiving an injection of Hydromorphone. Bradycardia, tachycardia and palpitations may also occur.

Genitourinary System: Urethral spasm of vesical sphincters and urinary retention have been reported.

Respiratory Depression: Hydromorphone produces a dose-related respiratory depression by acting directly on brain stem respiratory centres. Hydromorphone also affects centres that control respiratory rhythm, and may produce irregular and periodic breathing.

Other side effects include; miosis, decreased libido, rashes, urticaria and pruritus. Pain at injection site and local tissue irritation following subcutaneous administration when repeated in the same area.

Drug abuse and Dependence: Hydromorphone is a narcotic. Psychological dependence, physical dependence, and tolerance may develop upon repeated administration. However, dependence is unlikely to develop when Hydromorphone is used for a short time for the treatment of pain. The rate of development of tolerance varies among patients.

Hydromorphone has the potential for withdrawal symptoms.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms

Serious over-dosage is characterised by respiratory depression, extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. Particularly by the intravenous route, apnoea, circulatory collapse, cardiac arrest, and death may occur.

Treatment

Attention should be given to the re-establishment of a patent airway and institution of assisted or controlled ventilation. The narcotic antagonist naloxone hydrochloride is a specific antidote against respiratory depression.

Since the duration of action of Hydromorphone may exceed that of the naloxone, the patient should be kept under continued surveillance; repeated doses of naloxone may be required to maintain adequate respiration. Naloxone should not be administered in the absence of any clinically significant respiratory or cardiovascular depression. Rather oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Hydromorphone is an opioid analgesic similar to morphine, with a longer duration of action. It is a strong agonist with actions predominantly at the μ receptor. These actions result in analgesia, respiratory depression, suppression of cough, nausea, vomiting and constipation. An effect on the nucleus of the oculomotor nerve, and perhaps on opioid receptors in the pupillary muscles, cause pupillary constriction. It causes a dependence syndrome of the morphine type. The greater lipid solubility and affinity for the μ receptor compared to morphine result in a greater analgesic effect with reduced nausea, vomiting and constipation compared to morphine.

5.2 Pharmacokinetic properties

Hydromorphone is rapidly but incompletely absorbed from the gastrointestinal tract following oral administration, oral bioavailability being about 50%. Following oral or intravenous administration, the plasma half life is about 2.5 hours.

Hydromorphone is widely distributed in tissues and crosses the placenta. Hydromorphone is metabolised in the liver and excreted in the urine as conjugated hydromorphone, dihydromorphine and dihydroisomorphine.

5.3 Preclinical safety data

No additional data of relevance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium citrate
Citric acid monohydrate
Water for injections

6.2 Incompatibilities

Incompatible with minocycline and tetracycline solutions resulting in a colour change to light green, whilst cloudiness and precipitation result when hydromorphone is mixed with sodium thiopental. Mixtures with dexamethasone sodium phosphate, sodium bicarbonate and thiopental sodium exhibit a concentration dependent incompatibility and instability.

6.3 Shelf life

Unopened: 3 years.
The product should be used immediately after opening.

6.4 Special precautions for storage

Do not store above 25°C. Keep container in the outer carton in order to protect from light.

6.5 Nature and contents of container

Clear colourless Type 1 glass ampoules packed in cardboard cartons.
Pack size: 10 x 1ml ampoules.

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

Hydromorphone Injection must be diluted prior to administration by intravenous infusion. The following infusion fluids may be used: 5 % Dextrose in Water, 0.9% Sodium Chloride, Ringers Solution and Water for Injections.

For single use only.
Discard any unused contents.

7 MARKETING AUTHORISATION HOLDER

Martindale Pharmaceuticals Ltd.
Bampton Road
Romford, RM3 8UG
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA0361/018/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 October 2005

Date of last renewal: 28 October 2010

10 DATE OF REVISION OF THE TEXT

March 2017