Hydromorphone is a semisynthetic morphine derivative. Each hydromorphone (Jurnista) 16 mg prolonged-release tablet contains 16.35 mg and delivers 16 mg hydromorphone HCl, equivalent to 7.12 mg hydromorphone base. Each hydromorphone (Jurnista) 8 mg prolonged-release tablet contains 8.72 mg and delivers 8 mg hydromorphone HCl, equivalent to 3.56 mg hydromorphone base. Each 4 mg extended-release tablet contains 4.36 mg and delivers 4 mg hydromorphone HCl, equivalent to 1.74 mg hydromorphone base.

Pharmacokinetic Properties
Pharmacokinetics of Hydromorphone
Hydromorphone is a weak acidic metabolite and demonstrates that, as intended, hydromorphone is released in a controlled manner, consistent with orally administered tablets. Steady-state plasma concentrations are achieved within 24-48 hours after chronic administration of 240 mg/day. Steady state plasma concentrations are approximately twice those observed following the first dose, and time to reach peak concentration is 1.5-2 hours. Hydromorphone in plasma is not metabolized, unlike morphine, no active 6-glucuronide metabolite is produced. Linear pharmacokinetics were demonstrated for hydromorphone over the dose range of 4 to 64 mg. Hydromorphone is rapidly absorbed after oral administration and is well distributed in body tissues. Hydromorphone is 97% protein bound. Glucuronidation is the main metabolic pathway and the principal route of elimination. The plasma half-life of hydromorphone is 8 hours after intravenous administration. The systemic clearance is 11.5 mL/min/kg body weight. Hydromorphone (Jurnista) 16 mg prolonged-release tablet contains 16.35 mg and delivers 16 mg hydromorphone HCl, equivalent to 7.12 mg hydromorphone base.

Special Warnings and Precautions for Use
Drug dependence: Drug dependence may occur with hydromorphone. Patients prescribed hydromorphone for an extended period of time should be slowly tapered to prevent symptoms of withdrawal. Patients should be advised not to abruptly discontinue hydromorphone. Use of alcohol while on hydromorphone therapy may result in excessive sedation and confusion. Patients who are scheduled for regional anesthetic procedures or other interruptions of pain transmission should not receive hydromorphone (Jurnista) within 24 hours of the procedure. Concomitant administration of hydromorphone with other opioid analgesics is associated with an increased risk of respiratory failure. It is important to reduce the dose of hydromorphone when other analgesics are given concomitantly.

Head Injury and increased intracranial pressure:
Respiratory depression of opioids with carbon dioxide retention and secondary elevation of intracranial pressure may be exacerbated in the presence of raised intracranial pressure. Opioids produce effects that may obscure neurologic signs of further increases in intracranial pressure in patients with head injuries. Hydromorphone (Jurnista) should only be administered under such circumstances when considered essential and then with extreme caution.

Gastrointestinal tract and other smooth muscle:
Hydromorphone causes a reduction in gastrointestinal motility associated with an increase in smooth muscle tone. Consequently, constipation is a frequent side effect reported with use of hydromorphone. Patients should be advised on measures to prevent constipation and prophylactic laxative use should be considered. Extra caution should be used in patients with chronic constipation.

Clinical conditions or medicinal products that can cause a sudden and significant shortening of gastrointestinal transit time may result in decreased hydromorphone absorption with hydromorphone (Jurnista) and it may potentially lead to withdrawal symptoms in patients with a physical dependence on opioids. The administration of opioids may obscure the diagnosis or clinical course of acute abdominal conditions. Therefore, it is important to make sure that the patient is not suffering from intestinal obstruction, especially in the elderly, before initiation of treatment. Hydromorphone also can cause an increase in bilirubin test result as a result of spasm in the sphincter of Oddi. Caution should therefore be exercised in the treatment of patients with jaundice, acute cholecystitis, or any other disorders that can cause biliary obstruction, acute pancreatitis secondary to biliary tract disease and in patients about to undergo biliary surgery.

The hydromorphone (Jurnista) tablet is nonformable and does not appreciably change in shape in the GI tract. Hydromorphone (Jurnista) 8 mg may produce a larger number of obstructive symptoms in patients with increased gastric motility in association with ingestion of medicinal products in nonformable controlled-release formulations (see Contraindications and Precautions for Use). Patients should be advised not to be alarmed if they notice what appears to be the hydromorphone (Jurnista) tablet unchanged in the stools, as it is simply the nonformable shell.

Special risk patients:
Hydromorphone (Jurnista), like all opioid analgesics, should be administered with caution and in reduced dosage to patients with impaired renal or hepatic insufficiency, adrenocortical insufficiency, myelomalacia, hypothyroidism, prostatic hypertrophy or urethral stricture. Caution should be used in patients with these conditions, as hydromorphone (Jurnista) can cause ileus, delirium, hallucinations, mydriasis, tachycardia, urinary retention, myxedema, hypothyroidism, prostatic hypertrophy or urethral stricture. Caution should therefore be exercised in the treatment of these patients, as these conditions may precipitate acute renal failure. Pre-existing renal impairment increases the risk of developing neurotoxicity of the hydromorphone base.

Use in renal and hepatic impaired:
Patients with either moderate hepatic or renal insufficiency should be started on a reduced dose and closely monitored for possible increased adverse effects. As renal function decreases, the dosage interval should also be considered and these patients should in addition be monitored during maintenance therapy for development of opioid-related adverse reactions (see Dosage and method of administration).

Use in the elderly:
Elderly patients may be more sensitive to the CNS depressant effects of opioid analgesics. The concomitant use of alcohol should be avoided. Alcohol increases the sedative effect of hydromorphone on the CNS. In the elderly, the use of other CNS depressants, such as sedative hypnotics, muscle relaxants and some of the anticonvulsants, may cause respiratory depression and coma. The concomitant use of alcohol with opioids, including hydromorphone, should be avoided. Alcohol increases the risk of respiratory depression and coma. The concomitant use of alcohol with opioids, including hydromorphone, should be avoided. Alcohol increases the risk of respiratory depression and coma. In the elderly, the use of other CNS depressants, such as sedative hypnotics, muscle relaxants and some of the anticonvulsants, may cause respiratory depression and coma. The concomitant use of alcohol with opioids, including hydromorphone, should be avoided. Alcohol increases the risk of respiratory depression and coma.

Drug dependence:
Physical dependence is a state of adaptation that is manifested by an opioid specific withdrawal syndrome when the drug is discontinued or the dose is reduced. The severity of physical dependence varies directly with the duration of opioid therapy and the dose of opioid required to maintain adequate analgesia. Opioids with a high potential for abuse are associated with a high risk of physical dependence. Physical dependence may diminish or disappear with continued administration of the opioid. However, if a opioid is abruptly discontinued after long-term administration, physical dependence may be indicated, the dose of one or both agents should be reduced.

The concomitant use of alcohol should be avoided. Alcohol increases the incidence of opioid withdrawal symptoms when used concomitantly with opioids. The concomitant use of alcohol with opioids, including hydromorphone, should be avoided. Alcohol increases the risk of respiratory depression and coma. The concomitant use of alcohol with opioids, including hydromorphone, should be avoided. Alcohol increases the incidence of opioid withdrawal symptoms when used concomitantly with opioids.

Hydromorphone (Jurnista) should be used with caution in patients with alcoholism and other drug dependencies due to the increased frequency of opioid tolerance and psychological dependence observed. The concomitant use of alcohol with opioids, including hydromorphone, should be avoided. Alcohol increases the incidence of opioid withdrawal symptoms when used concomitantly with opioids.

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controlled-release, and hydromorphone immediate-release. One study was placebo-controlled. The three active-controlled studies included a titration phase where patients had their dose of adjusted hydromorphone titrated after they obtained the same stabilization phase. In another study, patients were assigned a fixed dose of hydromorphone (Jurnista) and no dose adjustments were allowed. (b) The end-of-study studies, two studies were of identical study design, one in patients with cancer pain and one in patients with non-cancer pain. One study was in patients with low back pain. The steady-state PK and PD measures of hydromorphone (Jurnista) were characterized in patients with chronic pain. A pilot study in patients with acute pain was also performed. Three studies evaluated the long-term safety of hydromorphone (Jurnista) in patients who continued treatment from prior short-term studies.

Adverse Events

The following adverse drug reactions (ADRs) were identified progressing on the basis of data from the 12 studies. The ADR frequency was calculated based on the total reported cases in this period of time. The ADR frequency was calculated based on the total reported cases in this period of time.

In patients with moderate hepatic insufficiency, the dose should be initiated cautiously at a reduced initial dose.

In the treatment of overdose, primary attention should be given to the reestablishment of adequate respiratory exchange keeping the airway open and instituting assisted or controlled ventilation. If the patient is not intubated, maintenance of oxygen saturation is desirable. Additional measures such as oxygen and vasopressors should be used to manage the shock and hypotension associated with opioid overdose. A wide array of cardiovascular adverse events may be expected to be enhanced by naloxone. Withdrawing doses of hydromorphone (Jurnista) should be used to gradually taper the dose before reinitiation of narcotic antagonist. Of the eight uncontrolled studies, two studies were of identical study design, one in patients with cancer pain and one in patients with non-cancer pain. One study was in patients with low back pain. The steady-state PK and PD measures of hydromorphone (Jurnista) were characterized in patients with chronic pain. A pilot study in patients with acute pain was also performed. Three studies evaluated the long-term safety of hydromorphone (Jurnista) in patients who continued treatment from prior short-term studies.

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