Ibuprofen is a nonsteroidal anti-inflammatory agent [non-selective COX inhibitor] with analgesic and antipyretic properties.

Serious, life-threatening, or fatal respiratory depression may occur with use of hydrocodone bitartrate and ibuprofen tablets. The risk of respiratory depression is greatest in patients receiving concomitant opioids and benzodiazepines or other sedatives, including alcohol. Hydrocodone bitartrate and ibuprofen tablets expose patients and other users to the risks of opioid addiction, abuse, or misuse, which can be fatal.

The Coxib and Traditional NSAID Trialists’ Collaboration meta-analysis of randomized controlled trials demonstrated an increased risk of GI bleeding, ulceration, and perforation with the use of any NSAID compared to placebo. These events occurred at any time during treatment, with or without warning symptoms, in patients treated with aspirin-sensitive asthma and aspirin-desensitized subjects. The Coxib and Traditional NSAID Trialists’ Collaboration meta-analysis indicated that the risk of GI bleeding related to COX-2 selective NSAIDs was not greater than the risk of GI bleeding related to traditional NSAIDs.

Protein Binding:
Opioids bind plasma protein to a similar degree (range 19% [hydromorphone] to 45% [oxycodone]), hydrocodone is expected to displace other highly protein-bound drugs. This elutes slowly from the plasma protein binding sites, resulting in extended drug exposure and possible toxicity.

Concomitant Use of MAOIs or Other Serotonin-Monamine Oxidase Inhibitors (MAOIs):
If urgent use of an opioid is necessary with MAOIs such as phenelzine, tranylcypromine, linezolid, use test doses and frequent medical monitoring. The concurrent use of opioids with MAOIs may increase the risk of serotonin syndrome, manifested by confusion, agitation, hallucinations, paranoia, excitation, myoclonus, hyperreflexia, and in extreme cases, death.

Concomitant Use of Other CNS Depressants:
Patients should be advised to avoid concurrent use of hydrocodone bitartrate and ibuprofen tablets with CNS depressants (e.g., benzodiazepines, general anesthetics, ketamine, morphine, propofol, or theophylline) or other medications that produce CNS depression, particularly if they take a higher than recommended dose of hydrocodone bitartrate and ibuprofen tablets. Concurrent use with CNS depressants increases the risk of respiratory depression and death.

Concomitant Use of Opioids with Anticoagulants:
The concomitant use of opioids with anticoagulants has an increased risk of serious bleeding compared to the use of either drug alone.

Laboratory Monitoring:
Routine laboratory monitoring of patients taking opioid analgesics is not indicated. However, patients who are being considered for opioid therapy should have baseline laboratory tests performed prior to initiation of therapy. Monitoring includes an assessment of renal function, hepatic function, hematopoietic function, and coagulation studies. Laboratory monitoring should be performed at intervals appropriate to the clinical situation. In patients already receiving an opioid, baseline laboratory data may be less relevant. When appropriate, laboratory monitoring may be performed in response to changes in clinical status or changes in the concomitant use of medications that may influence the clearance of hydrocodone bitartrate and ibuprofen tablets.

Opioid-Induced Constipation:
Opioid-induced constipation is a common adverse reaction associated with opioid therapy. A trial of laxatives for opioid-induced constipation is recommended for all patients who are receiving opioids for more than 10 days. Treatment may be initiated at the time of opioid initiation.

Risk Factors for GI Bleeding, Ulceration, and Perforation:
Ibuprofen is contraindicated in patients with associated conditions that increase the risk of gastrointestinal injury, including history of peptic ulcer disease, gastritis, history of bleeding or perforation from a previous ulcer, or risk factors for GI bleeding such as age >60, use of corticosteroids, concomitant use of aspirin, NSAID, or other drugs that impair platelet function, history of ulcer disease or other risk factors for GI bleeding, and concurrent use of other factors that increase the risk of ulcer disease and/or gastrointestinal toxicity (e.g., anticoagulants, corticosteroids, NSAIDs, aspirin, H2 blockers, cimetidine, and so forth).

Post-MI Patients
Post-MI patients should be monitored for signs and symptoms of respiratory depression and sedation, especially those who have a history of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported in such patients. Patients with post-MI should be regarded as having an increased risk of experiencing CV events.

Status Post Coronary Artery Bypass Graft (CABG) Surgery
In patients with a history of CABG surgery, hydrocodone bitartrate and ibuprofen tablets may increase the risk of serious CV events. These events may occur at any time, with or without warning symptoms.

Geriatrics:
Use the lowest effective dosage for the shortest duration when treating patients aged 65 years or older or patients with renal or hepatic impairment (see CLINICAL PHARMACOLOGY: Pharmacokinetics) in order to minimize the risk of serious adverse events, including fatal events. Use the lowest effective dosage for the shortest duration and monitor patients closely at frequent intervals when using opioids in patients with a history of drug or alcohol addiction, abuse, or misuse. The risk of overdose is increased in patients with a history of substance abuse (including drug or alcohol abuse or addiction).

Neurological Impairments:
CNS depression may occur with the use of opioids. CNS depression with concomitant use of benzodiazepines, hypnotics, or other CNS depressants. CNS depression may occur with the use of opioids and may be fatal. CNS depression may occur with the use of opioids and may be fatal. CNS depression may occur with the use of opioids and may be fatal. CNS depression may occur with the use of opioids and may be fatal.

Pregnancy:
Hydrocodone bitartrate and ibuprofen tablets are not recommended for use during pregnancy due to the potential for serious adverse events such as neonatal respiratory depression, prematurity, and birth defects. Use in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Pediatric Use:
The safety and effectiveness of hydrocodone bitartrate and ibuprofen tablets have not been established in pediatric patients.

Drug Interactions:
Hydrocodone, as well as other opioid analgesics, may enhance the neuromuscular blocking action of skeletal muscle relaxants (e.g., succinylcholine, nondepolarizing agents), which may result in respiratory depression. In addition, opioids may produce life-threatening respiratory depression when given with other sedatives, including alcohol, tranquilizers, or general anesthetics. The concurrent use of opioid analgesics with sedative hypnotics, including benzodiazepines and other sedative hypnotics, increases the risk of respiratory depression and death.

Hydrocodone bitartrate and ibuprofen tablets may increase the risk of serious CV events in patients with post-MI or CABG surgery. The use of opioids in patients with post-MI or CABG surgery may increase the risk of serious CV events during concomitant use of opioids or other medications that increase the risk of serious CV events or increase the risk of death, including concomitant use of other opioid analgesics, sedative hypnotics, benzodiazepines, antidepressants, or other CNS depressants.

Use of hydrocodone bitartrate and ibuprofen tablets with CYP3A4 inducers or discontinuing CYP3A4 inhibitors, monitor patients closely at frequent intervals for the development of signs and symptoms of respiratory depression and sedation. Use the lowest effective dosage for the shortest duration when treating patients aged 65 years or older or patients with renal or hepatic impairment (see CLINICAL PHARMACOLOGY: Pharmacokinetics) in order to minimize the risk of serious adverse events, including fatal events. Use in pregnancy only if the potential benefit justifies the potential risk to the fetus. Use in patients with a history of substance abuse (including drug or alcohol abuse or addiction).
Anaphylaxis has been reported with ingredients contained in hydrocodone bitartrate and ibuprofen tablets.

When use of shorter-acting analgesics or other analgesic techniques are more appropriate. Opioid analgesics, including hydrocodone bitartrate and ibuprofen tablets, may offer advantages in the management of pain in some settings. The use of opioids in patients with renal impairment requires caution. The concomitant use of hydrocodone bitartrate and ibuprofen tablets and pemetrexed, in patients with renal impairment, is not recommended.

During concomitant use of hydrocodone bitartrate and ibuprofen tablets and cyclosporine, monitor patients for signs of toxicity. Methadone is a strong CYP3A4 inhibitor, and the concomitant use of methadone with hydrocodone bitartrate and ibuprofen tablets is not recommended.

Opioids cross the placenta and may produce respiratory depression and psycho-physiologic effects in neonates. An opioid antagonist should be available for reversal of opioid toxicity in neonates. The respiratory depressive effects of opioids can last for several days after the last dose of the drug is administered. Neonatal opioid withdrawal syndrome presents as irritability, hyperactivity and abnormal sleep pattern, high-pitched cry, tremor, vomiting, diarrhea, and failure to gain weight. The onset, duration, and severity of neonatal opioid withdrawal syndrome vary. The treatment involves symptomatic management.

Prolonged use of opioid analgesics during pregnancy for medical or nonmedical purposes can result in physical dependence and withdrawal syndrome in the neonate. Neonatal opioid withdrawal syndrome is an intermediate syndrome usually occurring within 5 to 7 days of birth, followed by a withdrawal syndrome, which may last for several weeks. Neonatal opioid withdrawal syndrome presents with signs and symptoms similar to those in adults suffering from opioid withdrawal syndrome. The symptoms include irritability, hyperactivity, and unusual sleep pattern. The treatment involves symptomatic management.

Opioid antagonists, naloxone or nalmefene, are specific antidotes to respiratory depression resulting from opioid overdose. They are primarily used to counteract acute opioid overdose but may also be used for the reversal of the respiratory depression associated with perioperative endotracheal intubation in opioid-dependent patients. Naloxone is rapidly metabolized by the liver, with a short half-life and a short duration of action. Nalmefene, on the other hand, has a longer half-life and a longer duration of action, making it suitable for long-term use.

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