**INDICATIONS AND USAGE**

REPREXAIN™ tablets are indicated for the short-term (generally less than 10 days) management of acute pain. REPREXAIN™ should be used at the lowest effective dose for the shortest duration consistent with individual patient treatment goals. Use of the combination product, and should be avoided.

**CLINICAL PHARMACOLOGY**

Hydrocodone is a semi-synthetic agonist analgesic and an antitussive with a profile similar to those of codeine. Most of these involve the central nervous system and smooth muscle. The precise mechanism of action of hydrocodone and other opioids is unknown, although it is believed to relate to the existence of opiate receptors in the central nervous system. In addition to analgesia, opioids may produce drowsiness, changes in mood, and mental clouding. The clinical significance of these effects is unknown. In most patients, the analgesic effects of hydrocodone occur without mental clouding.

Hydrocodone Component

Hydrocodone is metabolized primarily by the liver and a 10-fold increased risk for developing a GI bleed compared to patients with neither of these risk factors. Other factors that increase the risk of GI toxicity are given in the section on ‘‘Precautions’’ (See the end of this Medication Guide for the end of this Medication Guide). Patients who have a history of hypothyroidism, Addison’s disease, prostatic hypertrophy or urethral stricture should be evaluated for evidence of the development of more severe hepatic reactions while on REPREXAIN™ therapy. If clinical signs and symptoms suggest liver dysfunction, the drug should be discontinued immediately. If symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be tapered slowly if a decision is made to discontinue corticosteroids. Discontinuation of corticosteroids may lead to disease exacerbation. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids. This should include discontinuation of the NSAID until a serious GI adverse event is ruled out. For high-risk patients, treatment with NSAIDs including ibuprofen, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia. Anemia is sometimes seen in patients receiving NSAIDs including ibuprofen, as found in REPREXAIN™. This may be due to hemodilution, hemolysis, decreased RBC survival, decreased erythropoiesis, or decreased erythrocyte production (bone marrow suppression).

Selective Pain Relief

Acute Abdominal Conditions

Rifaximin is absorbed from the gastrointestinal tract and is not associated with analgesic and antipruritic properties. In clinical trials, the maximum serum concentration was attained 2 hours post oral administration. The elimination half-life of rifaximin in the human was 5.8 ± 1.8 hours. The single-dose area under the curve (AUC) of rifaximin was 10.2 ± 3.6 mg·h/L and the maximum predicted concentration (Cmax) was 2.6 ± 0.8 mg/L. The single-dose pharmacokinetics of rifaximin remain unchanged following multiple doses of 850 mg given once daily for 7 days. The AUC and Cmax following dosage of rifaximin at 850 mg once daily for 7 days were 73.7 ± 23.6 mg·h/L and 21.3 ± 7.3 mg/L, respectively. These values were statistically significantly lower than those following 850 mg daily for 1 day.

**ACUTE HYPERGLUCAGON-LIKE PEPTIDE-1 AGONISTS**

This should be considered when selecting a patient for treatment with REPREXAIN™. Use the lowest effective dose for the shortest duration possible. Physicians and patients should remain alert for the possibility of opioid addiction or physical dependence even in patients who have received prolonged opioid therapy. There may be a risk of addiction in patients with a history of drug dependence or in patients with a family history of drug dependence. Patients should be questioned periodically regarding use of prescription drugs, over-the-counter medications, and other substances.

**Rifampin**

Rifampin is extensively metabolized by the liver and is not associated with analgesic and antipruritic properties. In clinical trials, the maximum serum concentration was attained 2 hours post oral administration. The elimination half-life of rifampin in the human was 5.8 ± 1.8 hours. The single-dose area under the curve (AUC) of rifampin was 10.2 ± 3.6 mg·h/L and the maximum predicted concentration (Cmax) was 2.6 ± 0.8 mg/L. The single-dose pharmacokinetics of rifampin remain unchanged following multiple doses of 850 mg given once daily for 7 days. The AUC and Cmax following dosage of rifampin at 850 mg once daily for 7 days were 73.7 ± 23.6 mg·h/L and 21.3 ± 7.3 mg/L, respectively. These values were statistically significantly lower than those following 850 mg daily for 1 day. Following oral administration by enteral route, rifampin undergoes extensive (~80%) first pass metabolism, and is therefore not available in intact form for absorption at the portal vein. Oral administration of rifampin to rats produces a 10-fold increase in the levels of rifaximin in the portal vein compared to levels of rifampin in the blood. Oral administration of rifampin to humans produces a 10-fold increase in the levels of rifaximin in the portal vein compared to levels of rifampin in the blood. Oral administration of rifampin to humans produces a 10-fold increase in the levels of rifaximin in the portal vein compared to levels of rifampin in the blood.
Get emergency help right away if you have any of the following symptoms:

- shortness of breath or trouble breathing
- chest pain
- weakness in one part or side of your body
- slurred speech

Swelling of the face or throat

Stop your NSAID medicine and call your healthcare provider right away if you have any of the following symptoms:

- there is blood in your bowel movement or it is black and sticky like tar
- more tired or weaker than usual
- unusual bleeding, bruising, or nosebleeds
- itching
- skin rash or blisters with fever
- your skin or eyes look yellow
- swelling of the arms and legs, hands, and feet
- stomach pain
- flu-like symptoms

These are not all the side effects with NSAID medicines. Talk to your healthcare provider or pharmacist for more information about NSAID medicines. Call 1-800-FDA-1088 to report side effects.

NSAID medicines requiring a prescription

- aspirin
- ibuprofen
- ketoprofen
- meloxicam
- naproxen
- celecoxib
- diclofenac
- ketorolac
- indomethacin
- naproxen sodium
- ketorolac tromethamine
- indomethacin
- dicloxacillin
- carbenicillin
- amoxicillin
- ampicillin
- nafcillin
- clindamycin
- penicillin
- sulfa antibiotics
- macrolides
- tetracyclines
- cephalosporins
- vancomycin
- doxycycline
- erythromycin
- streptomycin
- kanamycin
- neomycin
- gentamicin
- tobramycin
- amikacin

This is not a complete list of all possible side effects. Side effects may be serious in some cases, and some side effects may be dangerous. Report any side effect to your healthcare provider or pharmacist as soon as possible. For more information about side effects, call 1-800-FDA-1088.

For the full prescribing information, please see the prescribing information for REPREXAIN™.

NSAID medicines are available over-the-counter (OTC) and also require a prescription.

The full prescribing information is available at www.represxain.com or by calling 1-800-FDA-1088.

Reprints of this Medication Guide can be obtained by calling 1-800-FDA-1088.

The information in this Medication Guide is updated regularly. It is not intended to take the place of your healthcare provider’s medical advice or recommendations for treatment.

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When prescribing NSAID medicines, it is important to understand the potential risks and benefits of these medications. It is also important to consider the patient’s medical history, allergies, and any other medications they may be taking.

This Medication Guide is designed for the patient and is not intended to replace the advice of a healthcare provider.

It is important to follow the instructions on the label when using any over-the-counter NSAID.

This Medication Guide is approved by the U.S. Food and Drug Administration.