combogesic®

(acetaminophen and ibuprofen) Tablets 325 mg/97.5 mg

COMBOGESIC® IS INDICATED IN ADULTS FOR THE SHORT-TERM MANAGEMENT OF MILD TO MODERATE ACUTE PAIN.

Shorter Onset to Analgesia

- Time to meaningful pain relief was shorter for patients in the COMBOGESIC® group than in the groups given comparable doses of acetaminophen, ibuprofen and placebo*
- COMBOGESIC® provided a more rapid, statistically significant analgesic effect compared with comparable doses of either individual constituent alone or placebo[1*]

Superior Analgesia Efficacy. Comparable Safety in Common AEs

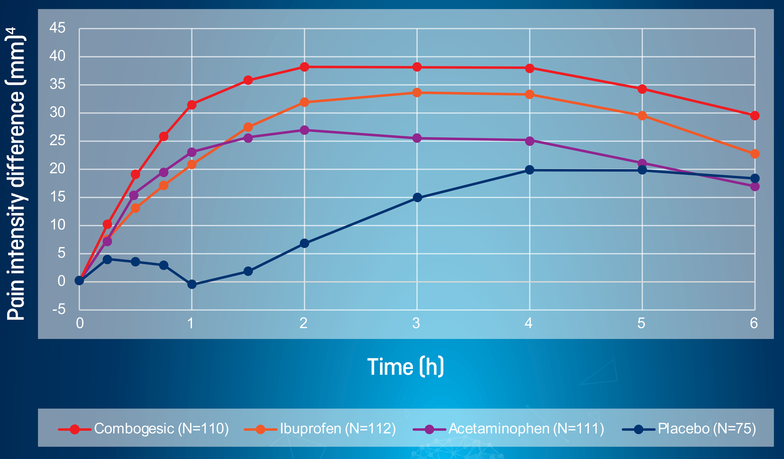
- COMBOGESIC® allows for superior analgesic efficacy and comparable safety in common AEs versus ibuprofen or acetaminophen alone*, [1, 2]
- The incidence of common AEs was largely comparable between the COMBOGESIC® group and the other active treatment groups*, [2]

Sustained Pain Management Results

- Superior analgesic effect over a single dosing interval, with average pain scores lowest in the COMBOGESIC® group at all time points.
- A superior analgesic effect throughout the full dosing period[1,3]

Average pain intensity difference was highest in the COMBOGESIC® group at all time points. The observed treatment differences over the first six hours are illustrated by the separation of pain curves as shown in the graph below.

PAIN INTENSITY DIFFERENCES FROM BASELINE OVER THE FIRST DOSE INTERVAL OF AFT-MX-6*



[1]A superior analgesic effect of COMBOGESIC® was observed during a single dosing interval (SPID6) and sustained across the study duration of 48 hours (SPID48).*

[2]The percentage of patients reporting adverse events was 37.3% in the COMBOGESIC®, with no significant differences between treatment groups. Nausea was the most common adverse event across all groups.

[3] According to the SPID48 and mean Pain Intensity Difference at each scheduled timepoint.*

[4] Derived from self-reported mean pain intensity scores using a 100-mm visual analog scale over the first dosing interval (6 hours)

AE=adverse event; SPID6=Sum of Pain Intensity Differences over 6 hours (secondary efficacy outcome); SPID48=Sum of Pain Intensity Differences over 48 hours (primary efficacy outcome).

The section numbers presented below reference the full Prescribing Information. For complete safety information, including the Boxed Warning, Contraindications, Warnings and Precautions, Adverse Reactions, Drug Interactions, and Use in Specific Populations, please refer to the full Prescribing Information

WARNING: HEPATOTOXICITY, CARDIOVASCULAR RISK AND GASTROINTESTINAL RISK

See full prescribing information for complete boxed warning.

- COMBOGESIC contains acetaminophen, which has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with doses of acetaminophen that exceed 4,000 milligrams per day, and often involve more than one acetaminophen containing product (5.1).
- Nonsteroidal anti-inflammatory drugs (NSAIDS), like the ibuprofen in COMBOGESIC, cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use (5.2).
- COMBOGESIC tablets are contraindicated in the setting of coronary artery bypass graft (CABG) surgery (5.2).
- NSAIDS, like the ibuprofen in COMBOGESIC, cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events (5.3).

CONTRAINDICATIONS

COMBOGESIC is contraindicated in:
- patients with known hypersensitivity to acetaminophen, ibuprofen, other
- NSAIDs, or to any of the excipients in this product (4).

patients with 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 (4)
- the setting of coronary artery bypass graft (CABG) surgery (4).

WARNINGS AND PRECAUTIONS

- Hypertension: Patients toking some antihypertensive medications may have impaired response to these therapies when taking NSAIDs. Monitor blood pressure (5.4).
- Heart Failure and Edema: Avoid use of COMBOGESIC in patients with severe heart failure unless benefits are expected to outweigh risk of worsening heart failure (5.5).
- Renal Toxicity: Long-term administration of NSAIDs, including the ibuprofen component of COMBOGESIC, has resulted in renal papillary necrosis and other renal injury (5.6).
- Anaphylactic Reactions: Seek emergency help if an anaphylactic reaction occurs (5.7).
- Exacerbation of Asthma Related to Aspirin Sensitivity: COMBOGESIC is contraindicated in patients with aspirin-sensitive asthma. Monitor patients with preexisting asthma (without aspirin sensitivity) (5.8).
- Serious Skin Reactions: Discontinue COMBOGESIC at first appearance of skin rash or other signs of hypersensitivity (5.9).
- Drug Rash with Eosinophilia and Systemic Symptoms (DRESS): Discontinue and evaluate clinically (5.10).
- Fetal Toxicity: Limit use of NSAID-containing products, including COMBOGESIC, between about 20 to 30 weeks in pregnancy due to the risk of oligohydramnios/fetal renal dysfunction. Avoid use of NSAID- containing products, including COMBOGESIC in women at about 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/fetal renal dysfunction and premature closure of the fetal ductus arteriosus (5.11).
- Hematologic Toxicity: Monitor hemoglobin or hematocrit in patients with any signs or symptoms of anemia (5.12).

ADVERSE REACTIONS

The most common adverse reactions (greater than or equal to 2%) are nausea, vomiting, headache, dizziness, somnolence, post-procedural hemorrhage, and swelling of the face (6).

DRUG INTERACTIONS

A number of known or potential interactions between COMBOGESIC and other drugs/drug classes exist. Please refer to the Drug Interactions section (7) in the PI for further information.

USE IN SPECIFIC POPULATIONS

- Infertility: NSAID-containing products, including COMBOGESIC, are associated with reversible infertility. Consider withdrawal of COMBOGESIC tablets in women who have difficulties conceiving. (8.3)
- Renal or hepatic impairment: Not recommended (5.1, 5.6, 8.6, 8.7).

* Daniels, S. E., Atkinson, H. C., Stanescu, I., & Frampton, C. (2018). Analgesic efficacy of an acetaminophen/ibuprofen fixed-dose combination in moderate to severe postoperative dental pain: a randomized, double-blind, parallel-group, placebo-controlled trial. Clinical Therapeutics, 40 (10), 1765-1776.

** Combogesic Prescribing Information. For current labeling information, please visit https://www.fda.gov/drugsatfda

AFT Pharmaceuticals US, Inc. United States Orange Book Patent No. 10532036, 11197830, 11534407

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Working to improve your health

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