Combogesic® IV (acetaminophen/ibuprofen) – New drug approval

- On October 18, 2023, Hyloris Pharmaceuticals announced the FDA approval of Combogesic IV (acetaminophen/ibuprofen), in adults where an intravenous (IV) route of administration is considered clinically necessary for the relief of mild to moderate pain or the management of moderate to severe pain as an adjunct to opioid analgesics.
    - Combogesic is indicated for short-term use of five days or less.
- The efficacy of Combogesic IV was established in a randomized, placebo-controlled, double-blind study in 276 patients after bunionectomy surgery. Patients were randomized to Combogesic IV, acetaminophen alone, ibuprofen alone, or placebo. The primary endpoint was the time-adjusted Sum of Pain Intensity Differences over 48 hours ($SPID_{48}$) and analyzed with each pre-rescue Visual Analogue Scale (VAS) carried forward up to 2 hours.
    - The analysis of time-adjusted $SPID_{48}$ demonstrated that Combogesic IV (least square mean [LSM] = 36.7, standard error [SE] = 2.2) provided more effective pain relief than placebo (LSM = 17.5, SE = 2.7), acetaminophen (LSM = 19.3, SE = 2.2) or ibuprofen (LSM = 24.6, SE = 2.2).
- Combogesic IV carries a boxed warning for hepatotoxicity, cardiovascular risk, and gastrointestinal risk.
- Combogesic IV is contraindicated in:
    - Patients with a known hypersensitivity to acetaminophen, ibuprofen, other nonsteroidal anti-inflammatory drugs (NSAIDs) or to any other components of this product.
    - Patients with a history of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs.
    - The setting of coronary artery bypass graft surgery.
    - Patients with severe hepatic impairment or severe active liver disease.
- Refer to the Combogesic IV drug label for a complete listing of its warnings and precautions.
- The most common adverse reactions (≥ 3%) with Combogesic IV use were infusion site pain, nausea, constipation, dizziness, infusion site extravasation, vomiting, headache, somnolence.
- For adult patients weighing greater than or equal to 50 kg (actual body weight), the recommended dosage of Combogesic IV is one vial (100 mL; acetaminophen 1,000 mg/ibuprofen 300 mg) administered as a 15-minute IV infusion every 6 hours, as necessary.
- For adult patients weighing less than 50 kg (actual body weight), the recommended dosage is 15 mg/kg acetaminophen and 4.5 mg/kg ibuprofen, administered as a 15-minute IV infusion every 6 hours, as necessary. This equates to a maximum single dose of 750 mg acetaminophen and 225 mg ibuprofen (discard remaining medicine in vial), and a total daily dose of 3,000 mg (3 g) acetaminophen and 900 mg ibuprofen.

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- Hyloris Pharmaceuticals plans to make Combogesic IV available to U.S. hospitals in early 2024. Combogesic IV will be available in a single-dose vial containing 1,000 mg/100 mL (10 mg/mL) of acetaminophen and 300 mg/100 mL (3 mg/mL).