Byfavo™ (remimazolam) – New drug approval

- On July 2, 2020, Cosmo Pharmaceuticals and Acacia Pharma announced the FDA approval of Byfavo (remimazolam), for the induction and maintenance of procedural sedation in adults undergoing procedures lasting 30 minutes or less.

- Byfavo is a very rapid onset/offset benzodiazepine sedative.

- The efficacy of Byfavo was established in three randomized, double-blind studies in adult patients receiving procedural sedation. The first study was in 461 American Society of Anesthesiologists Physical Status (ASA-PS) class I to III patients undergoing colonoscopy. Patients received Byfavo 5 mg as an initial bolus, followed by 2.5 mg top-up doses vs. placebo. Midazolam rescue was dosed per investigator discretion in both treatment groups. The primary efficacy endpoint was success of the colonoscopy procedure.

    — The colonoscopy sedation success rate was 91.3% with Byfavo vs. 1.7% with placebo.

- The second study was in 431 ASA-PS class I to III patients undergoing bronchoscopy. The treatment groups and primary endpoint were similar to study 1.

    — The bronchoscopy success rate was 80.6% with Byfavo vs. 4.8% with placebo.

- The third study was in 77 ASA-PS class III and IV patients undergoing colonoscopy. In this study, patients received Byfavo 2.5 mg to 5 mg as an initial bolus, followed by 1.25 mg to 2.5 mg top-up doses vs. placebo administered with midazolam rescue, dosed per investigator discretion. The primary objective of the study was to assess the safety of multiple doses of Byfavo vs. placebo and midazolam. Procedure success was a secondary objective.

    — There were no serious adverse reactions and no discontinuations due to adverse reactions observed in the Byfavo group. The incidence of hypotension was 61.3% in the Byfavo group and 75% in the placebo group.
    — Patients who received Byfavo for sedation during scheduled colonoscopy responded at a numerically greater rate than patients who received placebo (randomized analysis population – remimazolam: 27/32 [84.4%]; placebo: 0/16 [0%]).

- Byfavo carries a boxed warning for personnel and equipment for monitoring and resuscitation and risks from concomitant use with opioid analgesics and other sedative-hypnotics.

- Byfavo is contraindicated in patients with a history of severe hypersensitivity reaction to dextran 40 or products containing dextran 40.

- Additional warnings and precautions for Byfavo include hypersensitivity reactions, neonatal sedation, and pediatric neurotoxicity.

- The most common adverse reactions (> 10%) with Byfavo use for procedural sedation were hypotension, hypertension, diastolic hypertension, systolic hypertension, hypoxia, and diastolic hypotension.

- The recommended initial dose of Byfavo in adults is 5 mg, administered as an intravenous (IV) push injection over a 1-minute time period. If necessary, supplemental doses of 2.5 mg IV over a 15-second time period can be administered. At least 2 minutes must elapse prior to the administration of any supplemental dose.

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- The recommended initial dose of Byfavo in ASA-PS III and IV patients is 2.5 mg to 5 mg IV over 1 minute based on the general condition of the patient. If necessary, supplemental doses of 1.25 mg to 2.5 mg IV over a 15-second time period can be administered. At least 2 minutes must elapse prior to the administration of any supplemental dose.

- Only personnel trained in the administration of procedural sedation, and not involved in the conduct of the diagnostic or therapeutic procedure, should administer Byfavo.

- Acacia Pharma plans to launch Byfavo in the second half of 2020. Byfavo will be available as a 20 mg lyophilized powder for reconstitution in a single-patient-use vial.

    — Byfavo may not be marketed in the U.S. until the DEA has determined its scheduling under the Controlled Substances Act, which is expected to take place within the next few months.