Qdolo® (tramadol) – New drug approval

- On September 1, 2020, the FDA approved Athena Biosciences' Qdolo (tramadol) oral solution, in adults for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

    - Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Qdolo for use in patients for whom alternative treatment options [eg, non-opioid analgesics]: have not been tolerated or are not expected to be tolerated or have not provided adequate analgesia or are not expected to provide adequate analgesia.
    - Qdolo is a schedule IV controlled substance.

- Qdolo is an opioid agonist and inhibitor of norepinephrine and serotonin re-uptake. Although the mode of action is not completely understood, the analgesic effect of tramadol is believed to be due to both binding to μ-opioid receptors and weak inhibition of re-uptake of norepinephrine and serotonin.

- Tramadol is also available generically as a tablet, extended-release tablet, and a tablet in combination with acetaminophen.

    - The tablet carries the same indication as Qdolol.
    - The extended-release tablet is approved the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.
    - The tablet in combination with acetaminophen is approved for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate for the short-term use of five days or less.

- The efficacy of Qdolo was established by performing pharmacokinetic studies compared to immediate release tablets and utilizing clinical studies performed with tramadol as oral tablets.

- Qdolo carries a boxed warning for risk of medication errors; addiction, abuse, and misuse; risk evaluation and mitigation strategy (REMS); life-threatening respiratory depression; accidental ingestion; ultra-rapid metabolism of tramadol and other risk factors for life-threatening respiratory depression in children; neonatal opioid withdrawal syndrome; interactions with drugs affecting cytochrome P450 isoenzymes; and risks from concomitant use with benzodiazepines or other central nervous system depressants.

- Qdolo is contraindicated in patients with:

    - Significant respiratory depression
    - Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment
    - Known or suspected gastrointestinal obstruction, including paralytic ileus
    - Hypersensitivity to tramadol, any other component of this product or opioids
    - Concurrent use of monoamine oxidase inhibitors or use within the last 14 days.

- Qdolo is contraindicated for all children younger than 12 years of age, and postoperative management in children younger than 18 years of age following tonsillectomy and/or adenoidectomy.

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- Additional warnings and precautions for Qdolo include serotonin syndrome risk; increased risk of seizure; suicide risk; adrenal insufficiency, life-threatening respiratory depression in patients with chronic pulmonary disease or in elderly, cachectic, or debilitated patients; severe hypotension; risks of use in patients with increased intracranial pressure, brain tumors, head injury, or impaired consciousness; risks of use in patients with gastrointestinal conditions; anaphylaxis and other hypersensitivity reactions; withdrawal; and driving and operating machinery.

- The most common adverse reactions (≥ 15.0%) with Qdolo use were dizziness/vertigo, nausea, constipation, headache, somnolence, vomiting and pruritus.

- The recommended initial dose of Qdolo for patients not requiring rapid onset of analgesic effect is 25 mg orally per day and titrate in 25 mg increments as separate doses every 3 days to reach 100 mg/day (25 mg four times a day). Thereafter, the total daily dose may be increased by 50 mg as tolerated every 3 days to reach 200 mg/day (50 mg four times a day). After titration, Qdolo 50 mg to 100 mg can be administered as needed for pain relief every 4 to 6 hours not to exceed 400 mg/day.

    - For the subset of patients for whom rapid onset of analgesic effect is required and for whom the benefits outweigh the risk of discontinuation due to adverse events associated with higher initial doses, Qdolo 50 mg to 100 mg can be administered as needed for pain relief every four to six hours, not to exceed 400 mg/day.
    - Qdolo should not be administered at a dose exceeding 400 mg (80 mL) per day.
    - Patients should be instructed on how to measure and take the correct dose of Qdolo and to use extreme caution when measuring the dose.
    - Patients should be strongly advised to always use a calibrated oral syringe or other oral dosing device, with metric units of measurements (ie, mL), to correctly measure the prescribed amount of medication.
    - The lowest effective dosage should be used for the shortest duration consistent with individual patient treatment goals.
    - The dosing regimen should be initiated for each patient individually, taking into account the patient's severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse.
    - Patients should be monitored closely for respiratory depression, especially within the first 24–72 hours of initiating therapy and following dosage increases with Qdolo and adjust the dosage accordingly.

- Athena Biosciences launch plans for Qdolo are pending. Qdolo will be available as a 5 mg/mL oral solution.