Arymo™ ER (morphine sulfate) – New Drug Approval

- On January 9, 2017, Egalet Corporation announced the FDA approval of Arymo ER (morphine sulfate) extended release (ER) tablets, for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

    - Arymo ER is a Schedule II controlled substance.
    - Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with ER opioid formulations, reserve Arymo ER for use in patients for whom alternative treatment options (eg, non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
    - Arymo ER is not indicated as an as-needed (prn) analgesic.

- Arymo ER uses Egalet's Guardian™ Technology, a physical and chemical barrier approach to abuse deterrence.

- The abuse potential of Arymo ER was evaluated in an *in vitro* study and an oral clinical abuse potential study.

    - The in vitro study demonstrated that in comparison to non-abuse-deterrent morphine sulfate ER tablets, Arymo ER demonstrated increased resistance to cutting, crushing, grinding or breaking using a variety of tools.
    - When subjected to a liquid environment, the manipulated Arymo ER tablets formed a viscous hydrogel that resisted passage through a hypodermic needle.
    - In the oral clinical abuse study, there was no clinically meaningful difference in drug liking scores between manipulated Arymo ER and crushed morphine ER tablets.

- Based on the results of abuse deterrent studies, Arymo ER does not have physical and chemical properties that are expected to reduce abuse via the oral route. Abuse of Arymo ER by injection, as well as by the oral and nasal routes, is still possible.

- Additional data, when available, may provide further information on the impact of the current formulation of Arymo ER on the abuse liability of the drug.

- Arymo ER carries a boxed warning for addiction, abuse, and misuse, life-threatening respiratory depression, accidental ingestion, neonatal opioid withdrawal syndrome, and risks from concomitant use with benzodiazepines or other central nervous system depressants.

- Arymo ER is contraindicated in patients with significant respiratory depression, acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment, concurrent use of monoamine oxidase inhibitors or use within the last 14 days, known or suspected gastrointestinal obstruction, including paralytic ileus, and hypersensitivity to morphine.

- Other warnings and precautions of Arymo ER include risk of life-threatening respiratory depression in patients with chronic pulmonary disease or in elderly, cachectic, or debilitated patients, adrenal insufficiency, severe hypotension, risks of use in patients with increased intracranial pressure, brain tumors, head injury or impaired consciousness, difficulty in swallowing and risk for obstruction in patients at risk for a small gastrointestinal lumen, risks of use in patients with gastrointestinal conditions, increased risk of seizures in patients with seizure disorders, withdrawal, and risks of driving and operating machinery.

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- The most common adverse events with Arymo ER use were constipation, nausea, and sedation.

- The recommended dose of Arymo ER in opioid-naïve and opioid non-tolerant patients is 15 mg orally every 8 or 12 hours.

    — The lowest effective dosage should be used for the shortest duration consistent with individual patient treatment goals.
    — The dosing regimen for each patient should be individualized, 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. The Arymo ER dose should be adjusted accordingly.
    — Consult product information for dosing recommendations for patients converting from other opioids to Arymo ER.

- Egalet Corporation plans to launch Arymo ER in the first quarter of 2017 as 15 mg, 30 mg, and 60 mg ER tablets.