Corlanor® (ivabradine) – New orphan indication, new formulation approval

- On April 22, 2019, the FDA approved Amgen's Corlanor (ivabradine) oral solution, for the treatment of stable symptomatic heart failure due to dilated cardiomyopathy (DCM) in pediatric patients aged 6 months and older, who are in sinus rhythm with an elevated heart rate.
    - Corlanor is also approved to reduce the risk of hospitalization for worsening heart failure in adult patients with stable, symptomatic chronic heart failure with left ventricular ejection fraction ≤ 35%, who are in sinus rhythm with resting heart rate ≥ 70 beats per minute and either are on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use.
- Corlanor was previously only available in an oral tablet formulation.
- The approval of Corlanor's new indication was based on a double-blind study in 116 patients aged 6 months to less than 18 years with DCM in sinus rhythm, NYHA/Ross class II to IV heart failure, and left ventricular ejection fraction ≤ 45%. Patients were randomized to receive Corlanor or placebo. Doses of study medication were titrated over a 2- to 8-week period to achieve a 20% heart rate reduction without inducing bradycardia.
    - The target heart rate reduction was obtained at the end of the titration period in a significantly higher proportion of patients with Corlanor vs. placebo (72% vs. 16% respectively; Odds Ratio 15; 95% CI: 5, 47).
    - A statistically significant reduction in heart rate was observed with Corlanor vs. placebo at the end of the titration period (-23 ± 11 bpm vs. -2 ± 12 bpm, respectively).
- Corlanor is contraindicated in patients with:
    - Acute decompensated heart failure
    - Clinically significant hypotension
    - Sick sinus syndrome, sinoatrial block or 3rd degree atrioventricular block, unless a functioning demand pacemaker is present
    - Clinically significant bradycardia
    - Severe hepatic impairment
    - Pacemaker dependence (heart rate maintained exclusively by the pacemaker)
    - Concomitant use of strong cytochrome P450 3A4 inhibitors
- Warnings and precautions of Corlanor include fetal toxicity, atrial fibrillation, and bradycardia and conduction disturbances.
- The most common adverse reactions (≥ 1%) with Corlanor use were bradycardia, hypertension, atrial fibrillation and luminous phenomena (phosphenes).
- The recommended starting dose of Corlanor oral solution in pediatric patients 6 months of age and older and weighing less than 40 kg is 0.05 mg/kg twice daily with food.
    - Patients should be assessed at two-week intervals and adjust dose by 0.05 mg/kg to target a heart rate reduction of at least 20%, based on tolerability.
    - The maximum dose is 0.2 mg/kg twice daily for patients 6 months to less than 1 year old, and 0.3 mg/kg twice daily for patients 1 years old and older, up to a total of 7.5 mg twice daily.

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- The recommended starting dose of Corlanor tablets in pediatric patients weighing more than 40 kg is 2.5 mg twice daily with food.
    - Patients should be assessed at two-week intervals and adjust dose by 2.5 mg to target a heart rate reduction of at least 20%, based on tolerability.
    - The maximum dose is 7.5 mg twice daily. In patients unable to swallow tablets, Corlanor oral solution can be used.
- Refer to the Corlanor drug label for dosing recommendations in adult patients.
- Amgen's launch plans for Corlanor oral solution are pending. Corlanor oral solution will be available in a 5 mg/5 mL strength.