Leqvio® (inclisiran) – New drug approval

- On December 22, 2021, Novartis announced the FDA approval of Leqvio (inclisiran), as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of low-density lipoprotein cholesterol (LDL-C).
    - The effect of Leqvio on cardiovascular morbidity and mortality has not been determined.
- Leqvio is a small interfering ribonucleic acid (siRNA) therapeutic directed to proprotein convertase subtilisin kexin type 9 (PCSK9) mRNA. This increases LDL-C receptor recycling and expression on the hepatocyte cell surface, which increases LDL-C uptake and lowers LDL-C levels in the circulation.
- The efficacy of Leqvio was established in three randomized, double-blind, placebo-controlled studies in adults with HeFH or clinical ASCVD, who were taking maximally tolerated statin therapy and who required additional LDL-C lowering. Studies 1 (N = 1,561) and 2 (N = 1,414) were in patients with ASCVD who were randomized to receive subcutaneous (SC) injections of either Leqvio or placebo on day 1, day 90, day 270, and at day 450. The primary endpoint was the percent change from baseline to day 510 in LDL-C.
    - In study 1, the difference between the Leqvio and placebo groups in mean percentage change in LDL-C from baseline to day 510 was -52% (95% CI: -56, -49; $p < 0.0001$).
    - In study 2, the difference between the Leqvio and placebo groups in mean percentage change in LDL-C from baseline to day 510 was -51% (95% CI: -54, -47; $p < 0.0001$).
- Study 3 was in 482 patients with HeFH who were randomized to receive SC injections of either Leqvio or placebo on day 1, day 90, day 270, and at day 450. The primary endpoint was the percent change from baseline to day 510 in LDL-C.
    - The difference between the Leqvio and placebo groups in mean percentage change in LDL-C from baseline to day 510 was -48% (95% CI: -54, -42; $p < 0.0001$).
- The most common adverse reactions (≥ 3%) with Leqvio use were injection site reaction, arthralgia, urinary tract infection, diarrhea, bronchitis, pain in extremity, and dyspnea.
- The recommended dosage of Leqvio, in combination with maximally tolerated statin therapy, is 284 mg administered as a single SC injection initially, again at 3 months, and then every 6 months.
    - LDL-C should be assessed when clinically indicated. The LDL-lowering effect of Leqvio may be measured as early as 30 days after initiation and anytime thereafter without regard to timing of the dose.
    - Leqvio should be administered by a healthcare professional.
- Novartis plans to launch Leqvio in early January 2022. Leqvio will be available as a 284 mg/1.5 mL (189 mg/mL) single-dose prefilled syringe.