Veklury® (remdesivir) – New drug approval

- On October 22, 2020, the FDA announced the approval of Gilead's Veklury (remdesivir), for adults and pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of coronavirus disease 2019 (COVID-19) requiring hospitalization.

    — Veklury should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care.
    — The approval decision comes just two and half months after Gilead announced completion of their New Drug Application.

- Since Veklury must be administered intravenously by a healthcare professional, and is intended for use in the hospital setting, it is not likely to be used in the ambulatory setting.

- This approval does not include the entire population that had been authorized to use Veklury under an Emergency Use Authorization (EUA) originally issued on May 1, 2020. In order to ensure continued access to the pediatric population previously covered under the EUA, the FDA revised the EUA for Veklury to authorize the drug's use for treatment of suspected or laboratory confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg. Clinical trials assessing the safety and efficacy of Veklury in this pediatric patient population are ongoing.

- Veklury is an antiviral drug with activity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

- The efficacy of Veklury is supported by three randomized, controlled clinical trials that included patients hospitalized with mild-to-severe COVID-19. The first study (NIAID ACTT-1) evaluated how long it took for patients to recover from COVID-19 within 29 days of being treated. The trial looked at 1,062 hospitalized subjects with mild, moderate and severe COVID-19 who received Veklury or placebo, plus standard of care. Recovery was defined as either being discharged from the hospital or being hospitalized but not requiring supplemental oxygen and no longer requiring ongoing medical care.

    — The median time to recovery was 10 days in the Veklury group vs. 15 days in the placebo group (recovery rate ratio 1.29, 95% CI: 1.12, 1.49, $p < 0.001$).
    — Overall, 29-day mortality was 11% for the Veklury group vs. 15% for the placebo group and were not statistically significant (hazard ratio 0.73, 95% CI: 0.52, 1.03).

- The second study (SIMPLE-Moderate) evaluated hospitalized adult patients with moderate COVID-19 and compared treatment with Veklury for 5 days (n = 191) or 10 days (n = 193) plus standard of care vs. standard of care alone (n = 200). The primary endpoint was clinical status on day 11 assessed on a 7-point ordinal scale (refer to prescribing information for complete details).

    — Overall, the odds of improvement in the ordinal scale were higher in the 5-day Veklury group at day 11 vs. standard of care (odds ratio [OR] 1.65, 95% CI: 1.09, 2.48, $p = 0.017$).
    — The odds of improvement in clinical status with the 10-day treatment group vs. standard of care were not statistically significant (OR 1.31, 95% CI: 0.88, 1.95).
    — All-cause mortality at day 28 was ≤ 2% in all treatment groups.

- The third study (SIMPLE-Severe) evaluated hospitalized adult patients with severe COVID-19 and compared treatment with Veklury for 5 days (n = 200) or 10 days (n = 197). All patients also received

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background standard of care. The primary endpoint was clinical status on day 14 assessed on a 7-point ordinal scale (refer to prescribing information for complete details).

  - Overall, after adjusting for between-group differences at baseline, patients receiving a 5-day course of Veklury had similar clinical status at day 14 as those receiving a 10-day course (OR for improvement 0.75, 95% CI: 0.51, 1.12).
  - There were no statistically significant differences in recovery rates or mortality rates in the 5-day and 10-day groups once adjusted for between-group differences at baseline. All-cause mortality at day 28 was 12% vs. 14% in the 5- and 10-day treatment groups, respectively.

- Warnings and precautions for Veklury include hypersensitivity including infusion-related and anaphylactic reactions, increased risk of transaminase elevations, and risk of reduced antiviral activity when coadministered with chloroquine phosphate or hydroxychloroquine sulfate.

- The most common adverse reactions (≥ 5%) with Veklury use were nausea, increased alanine aminotransferase (ALT), and increased aspartate transaminase (AST).

- The recommended dose of Veklury is a single loading dose of 200 mg on day 1 via intravenous (IV) infusion followed by once-daily maintenance doses of 100 mg from day 2 via IV infusion.

  - The recommended treatment duration for patients not requiring invasive mechanical ventilation and/or extracorporeal membrane oxygenation (ECMO) is 5 days. If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days for a total treatment duration of up to 10 days.
  - The recommended total treatment duration for patients requiring invasive mechanical ventilation and/or ECMO is 10 days.
  - Veklury must be prepared and administered under the supervision of a healthcare provider.

- Per the Gilead press release, Veklury is now widely available in hospitals across the country.

- Veklury will be available as a 100 mg lyophilized powder in a single-dose vial and a 100 mg/20 mL (5 mg/mL) single-dose vial.