NEW DRUG APPROVAL

Brand Name	Veklury®
Generic Name	remdesivir
Drug Manufacturer	Gilead Sciences, Inc.

New Drug Approval

FDA Approval Date: October 22, 2020

Review Designation: Priority

Type of Review: Type 1 - New Molecular Entity; (New Drug Application (NDA): 214787)

Dispensing Restriction: Open Distribution

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus (SARS-CoV-2). Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness. The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so it's important that you also practice respiratory etiquette (for example, by coughing into a flexed elbow).

In December 2019, pneumonia of unknown cause occurred in Wuhan (China). On January 7, 2020, a novel corona virus, named as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), was identified in the throat swab sample of 1 patient. Globally, over 55 million confirmed cases of COVID-19 have been reported in all continents except Antarctica.

Efficacy

The safety of Veklury® is based on data from three Phase 3 studies in 1,313 hospitalized adult subjects with COVID-19, from four Phase 1 studies in 131 healthy adults, and from patients with COVID-19 who received Veklury® under the Emergency Use Authorization or in a compassionate use program.

NIAID ACTT-1 Study in Subjects with Mild/Moderate and Severe COVID-19

A randomized, double-blind, placebo-controlled clinical trial (ACTT-1, NCT04280705) of hospitalized adult subjects with confirmed SARS-CoV-2 infection and mild, moderate, or severe COVID-19 compared treatment with VEKLURY for 10 days (n=541) with placebo (n=521).

The primary clinical endpoint was time to recovery within 29 days after randomization. A key secondary endpoint was clinical status on Day 15 assessed on an 8-point ordinal scale.

Overall, the odds of improvement in the ordinal scale were higher in the VEKLURY group at Day 15 when compared to the placebo group (odds ratio 1.54 [95% CI 1.25 to 1.91]). Overall, 29-day mortality was 11% for the VEKLURY group vs 15% for the placebo group (hazard ratio 0.73 [95% CI 0.52 to 1.03]).

Study GS-US-540-5773 in Subjects with Severe COVID-19

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A randomized, open-label multi-center clinical trial (Study 5773, NCT04292899) in adult subjects with confirmed SARS-CoV-2 infection, an SpO2 of ≤94% on room air, and radiological evidence of pneumonia compared 200 subjects who received VEKLURY for 5 days with 197 subjects who received VEKLURY for 10 days. The primary endpoint was clinical status on Day 14 assessed on a 7-point ordinal scale.

Overall, after adjusting for between-group differences at baseline, subjects receiving a 5-day course of VEKLURY had similar clinical status at Day 14 as those receiving a 10-day course (odds ratio for improvement 0.75 [95% CI 0.51 to 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.

Study GS-US-540-5774 in Subjects with Moderate COVID-19

A randomized, open-label multi-center clinical trial (Study 5774, NCT04292730) of hospitalized adult subjects with confirmed SARS-CoV-2 infection, SpO2 >94% and radiological evidence of pneumonia compared treatment with VEKLURY for 5 days (n=191) and treatment with VEKLURY for 10 days (n=193) with standard of care (n=200).

The primary endpoint was clinical status on Day 11 assessed on a 7-point ordinal scale.

Overall, the odds of improvement in the ordinal scale were higher in the 5-day VEKLURY group at Day 11 when compared to those receiving only standard of care (odds ratio 1.65 [95% CI 1.09 to 2.48], p=0.017). The odds of improvement in clinical status with the 10-day treatment group when compared to those receiving only standard of care were not statistically significant (odds ratio 1.31 [95% CI 0.88 to 1.95]). All-cause mortality at Day 28 was ≤2% in all treatment groups.

Safety

ADVERSE EVENTS

The most common adverse reactions (incidence greater than or equal to 5%, all grades) observed with treatment with Veklury® are nausea, ALT increased, and AST increased.

WARNINGS & PRECAUTIONS

- Hypersensitivity
- Increased risk of transaminase elevations
- Risk of reduced antiviral activity when co-administered with chloroquine phosphate or hydroxychloroquine sulfate

CONTRAINDICATIONS

Patients with a history of clinically significant hypersensitivity reactions to the drug or any components of the product.

Clinical Pharmacology

MECHANISMS OF ACTION

Remdesivir is an adenosine nucleotide prodrug that distributes into cells where it is metabolized to form the pharmacologically active nucleoside triphosphate metabolite. Metabolism of remdesivir-to-remdesivir triphosphate has been demonstrated in multiple cell types. Remdesivir triphosphate acts as an analog of adenosine triphosphate (ATP) and competes with the natural ATP substrate for incorporation into nascent RNA chains by the SARS-CoV-2 RNA-dependent RNA polymerase, which results in delayed chain termination during

replication of the viral RNA. Remdesivir triphosphate is a weak inhibitor of mammalian DNA and RNA polymerases with low potential for mitochondrial toxicity.

Dose & Administration

ADULTS

12 years of age and older and weighing at least 40 kg: Single loading dose of Veklury® 200 mg on Day 1 via intravenous infusion followed by once-daily maintenance dose of 100 mg from Day 2 infused over 30 to 120 minutes.

PEDIATRICS

Refer to adult dosing if age ≥ 12 years and weight ≥ 40 kg.

GERIATRICS

Refer to adult dosing

RENAL IMPAIRMENT

Veklury® is not recommended in patients with eGFR less than 30 mL per minute.

HEPATIC IMPAIRMENT

The pharmacokinetics have not been evaluated in patients with hepatic impairment. Perform hepatic laboratory testing in all patients before starting and while receiving as clinically appropriate.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

For injection: 100 mg of remdesivir as a lyophilized powder, in a single-dose vial.

Injection: 100 mg/20 mL (5 mg/mL) remdesivir, in a single-dose vial.