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# What factors allowed for timely pediatric approvals of remdesivir for treatment of COVID-19?

July 1, 2024
Food and Drug Administration
Article type: FDA Update
Topics: COVID-19, Pharmacology

Earlier this year, the Food and Drug Administration (FDA) expanded approval for remdesivir (Veklury) for the treatment of COVID-19 to include term neonates from birth to less than 28 days who weigh at least 1.5 kilograms (kg).

While it typically takes six to 10 years for a drug approved for adults to receive pediatric labeling, remdesivir was approved for use in pediatric patients, including neonates, about three years after approval for use in adults and adolescents (see table).

The FDA published details about the data used to support the remdesivir approvals for pediatric patients 28 days and older (Chan-Tack K, et al. *J Clin Pharmacol*. 2023;63:259-265) and highlighted factors that accelerated the timeline for pediatric approvals. Such factors include the following:

**Public health emergency and unmet medical need**. The COVID-19 public health emergency and high number of cases, including in children, at the time of clinical development for remdesivir contributed to timely completion of trial enrollment.

**Leveraging existing data**. Before being studied for the treatment of COVID-19,

remdesivir was studied for other conditions, including Ebola virus disease. Leveraging existing clinical and non-clinical data facilitated rapid initiation of clinical trials and inclusion of adolescents in the adult trials, reduced the time to pediatric trial initiation and facilitated inclusion of pediatric dosing recommendations in labeling.

**Pediatric Research Equity Act (PREA)**. The FDA was able to require pediatric studies under PREA to ensure pediatric safety and efficacy information and dosing recommendations were included in the product labeling.

**Pediatric extrapolation**. Under the Pediatric Labeling Rule, evidence of a drug's effectiveness from adult studies can be extrapolated to the pediatric population if the disease course and expected response to the intervention are sufficiently similar in children and the reference population. These criteria were met for use of remdesivir in children with COVID-19.

**Modeling and simulation.** Mathematical/statistical models and computer simulations can support decision- making about dose selection and optimization. Physiologically based pharmacokinetic (PK) and population PK modeling were used to support dosing recommendations for adolescents and pediatric patients 28 days and older and weighing at least 3 kg. The studied doses resulted in pediatric exposures to remdesivir and its metabolites that were comparable to adults.

For term neonates and infants (gestational age greater than 37 weeks), the February 2024 approval incorporated the subpopulation of pediatric patients weighing at least 1.5 kg and was based on PK and safety data from term neonates. In these youngest cohorts, exposures were higher for remdesivir and its metabolites compared to adults, but the increases were not considered clinically significant. Additional analyses were conducted using a simulated population. Results led to the recommended dosing regimen as they more closely align with adult exposures compared to the doses studied for the youngest patients.

**Intravenous route of administration**. Intravenous administration of remdesivir could be used in all ages without additional, age-appropriate formulation development.

The approval and availability of remdesivir for all age groups are important public health milestones. Yet, it remains important to continue developing additional safe and effective COVID-19 treatment options, particularly oral agents for adult and pediatric patients, including neonates.

**New drug application (NDA) or supplemental NDA approval dates for remdesivir**

| Approval date | Approved indication and usage |
|---|---|
| Oct. 22, 2020 (original NDA approval) | Adults and pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of COVID-19 requiring hospitalization |
| Jan. 21, 2022 | Treatment of COVID-19 in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, who are:<br>• hospitalized or<br>• not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death |
| April 25, 2022 | Treatment of COVID-19 in adults and pediatric patients (28 days of age and older and weighing at least 3 kg) with positive results of direct SARS-CoV-2 viral testing, who are:<br>• hospitalized or<br>• not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death |
| Feb. 28, 2024 | Treatment of COVID-19 in adults and pediatric patients (birth to less than 18 years of age weighing at least 1.5 kg) who are:<br>• hospitalized or<br>• not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death |

*The FDA Office of New Drug's Division of Antivirals, Office of Clinical Pharmacology's Division of Infectious Disease Pharmacology, Division of Pediatrics and Maternal Health, and the Office of Pediatric Therapeutics contributed to this article.*