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FDA program spurs development of therapeutics for COVID-19 in children, adults

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The COVID-19 pandemic has resulted in over 31 million cases and over 564,000 deaths in the U.S. (http://bit.ly/3lHyneq). In response, the Food and Drug Administration (FDA) created the Coronavirus Treatment Acceleration Program (CTAP) program to speed the development of new treatments for COVID-19.

More than 600 drug development programs are in planning stages, and the FDA has reviewed over 400 clinical trials through CTAP (http://bit.ly/37pY8t6). Multiple effective therapies against COVID-19 have been identified, many of which have received FDA approval or an emergency use authorization (EUA) (see table).

Select therapeutics used to treat COVID-19 in children

Product/drug	Company	Status	Patient population
Remdesivir	Gilead Sciences Inc.	FDA-approved	• Hospitalized children ages 12 years and weighing 40 kilograms (kg) requiring supplemental oxygen, invasive mechanical ventilation or

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			extracorporeal membrane oxygenation (ECMO)
		EUA	• Hospitalized children <12 years weighing 3.5-40 kg requiring respiratory support as above
Dexamethasone	N/A	Off-label use	• Hospitalized children (no age requirement) requiring supplemental oxygen, invasive mechanical ventilation or ECMO
Baracitinib	Eli Lilly and Company	EUA	• Hospitalized children 2 years requiring supplemental oxygen, invasive mechanical ventilation or ECMO • Given with remdesivir
Convalescent plasma	N/A	EUA	• Not the

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			standard of care. Should be used only in clinical trials.
Bamlanivimab/etesevimab	Eli Lilly and Company	EUA	• Outpatients 12 years and weighing 40 kg with positive SARS-CoV-2 test results who are at high risk of progressing to severe COVID-19 and/or hospitalization *
Casirivimab/imdevimab	Regeneron Pharmaceuticals Inc.	EUA	
*Including body mass index 85th percentile for age and gender, sickle cell disease, congenital or acquired heart disease, neurodevelopmental disorders, medical-related technological dependence or chronic respiratory disease that requires daily medication for control			

Notably, data for all of these therapies are limited to adults, and recommendations for children are extrapolated from adult data. Clinical trials are needed to demonstrate benefit in children.

Remdesivir

Remdesivir is an intravenous antiviral medication that inhibits viral replication. In a randomized clinical trial performed by the National Institutes of Health (NIH), remdesivir shortened the duration of symptoms in adults with COVID-19. Results also suggested that progression to more severe disease was prevented, particularly in patients requiring supplemental oxygen (Beigel JH, et al. *N Engl J Med*. 2020;383:1813-1826, https://bit.ly/2OXpqSk). Subsequent studies have not confirmed these findings, and no study has shown that remdesivir decreases COVID-19-associated mortality.

The drug is recommended for hospitalized patients requiring respiratory support such as supplemental oxygen. It should be administered in a hospital or other setting providing a similar level of care.

Dexamethasone

Dexamethasone, a corticosteroid used to treat common pediatric conditions associated with inflammation, has

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been tested extensively in patients with COVID-19. Early in the pandemic, it was hypothesized that corticosteroids could lessen the inflammation associated with COVID-19.

A randomized trial in adults with COVID-19 demonstrated that dexamethasone decreased mortality in patients who needed supplemental oxygen or mechanical ventilation (RECOVERY Collaborative Group. *N Engl J Med*. 2021;384:693-704, https://bit.ly/2NKonVt).

Similar studies in children are being performed and results are pending. It has become common clinical practice to administer dexamethasone to hospitalized children with COVID-19 requiring respiratory support.

Baracitinib

Baracitinib is a Janus kinase inhibitor used to treat rheumatoid arthritis. Baracitinib may benefit patients with COVID-19 through its anti-inflammatory properties and potentially by blocking entry of the virus into cells during infection.

A randomized trial performed by the NIH compared remdesivir therapy to remdesivir combined with baracitinib in adults with COVID-19 (Kalil AC, et al. *N Engl J Med*. 2021;384:795-807, https://bit.ly/3reNo91). Patients who received baracitinib were less likely to require mechanical ventilation, and those with severe COVID-19 were more likely to recover from their disease.

The data were sufficiently compelling to result in the FDA providing an EUA for baracitinib in hospitalized patients ages 2 years and older requiring respiratory support, particularly patients who cannot tolerate corticosteroids.

Convalescent plasma

Convalescent plasma obtained from patients who have recovered from COVID-19 contains antibodies against SARS-CoV-2. Convalescent plasma was given an EUA based on large, descriptive studies in adults who were given convalescent plasma under an expanded access program. Infusions of this therapy were well-tolerated, with few safety events. However, the efficacy of convalescent plasma is unclear, and small clinical trials have not shown significant effect on mortality.

Convalescent plasma is still under investigation, and its use in children varies across institutions. If used, convalescent plasma should have high levels of antibodies.

Monoclonal antibodies

Bamlanivimab/etesevimab and casirivimab/imdevimab are the monoclonal antibody products that have received an EUA for use in outpatients with positive SARS-CoV-2 tests and mild to moderate clinical symptoms who are at high risk for progressing to severe disease and/or hospitalization. These antibodies bind virus and decrease the amount of free virus present in the airway. Bamlanivimab had previously received an EUA from the FDA, but this EUA was revoked due to the increase of SARS-CoV-2 variants and risk of treatment failure with balminivimab when administered alone.

Preliminary data from small trials indicate that monoclonal antibodies lower hospitalization rates and decrease numbers of subsequent medical visits.

The utility of the monoclonal antibody products is balanced against challenges associated with administration, including a prolonged duration needed for intravenous infusion. To date, use of these products in children has been limited.

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