COVID-19

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Panel's Recommendations
COVID-19 Vaccination and Pre-Exposure Prophylaxis to Prevent COVID-19, Including Severe Disease • Children with HIV aged ≥6 months should receive COVID-19 vaccination, regardless of CD4 T lymphocyte cell count or viral load (AI). • Household members and close contacts of children with HIV aged ≥6 months should receive COVID-19 vaccination (AIII). • Although vaccine responses are likely to improve after initiation of antiretroviral therapy, vaccination against COVID-19 should not be delayed while awaiting immune reconstitution (AIII). • Pemivibart (Pemgarda) should be considered for the prevention of COVID-19 in children aged ≥12 years and who weigh ≥40 kg with HIV with severe immunosuppression (stage 3 – see HIV Infection Stage table in the Introduction) regardless of COVID-19 vaccination status (BIII) and may be considered for the prevention of COVID-19 in children aged ≥12 years and who weigh ≥40 kg with HIV with moderate to no immunosuppression (stage 1 or 2 – see HIV Infection Stage table in the Introduction) in whom COVID-19 vaccines are contraindicated or unavailable (CIII). Monoclonal antibodies, including pemivibart, are not a substitute for vaccination in people who are eligible for COVID-19 vaccines. Treatment of COVID-19 in the Outpatient Setting • Ritonavir-boosted nirmatrelvir (Paxlovid) should be considered in the outpatient setting for treatment of laboratory-confirmed or clinically suspected mild to moderate COVID-19 in children with HIV who are aged ≥12 years, weigh ≥40 kg, and are at high risk of progressing to severe COVID-19 due to advanced or untreated HIV or another high-risk condition as defined by the Centers for Disease Control and Prevention (CDC) (BI*). • Ritonavir-boosted nirmatrelvir should be started within 5 days of symptom onset (BI*). • Ritonavir-boosted nirmatrelvir may be administered with antiretrovirals, including those that contain ritonavir or cobicistat, without any interruption of or modification to the antiretroviral therapy (AIII). • Remdesivir (Veklury) may be considered in the outpatient setting for treatment of laboratory-confirmed or clinically suspected mild to moderate COVID-19 in children with HIV who are aged ≥28 days, weigh ≥3 kg, and are at high risk of progressing to severe COVID-19 due to advanced or untreated HIV or another high-risk condition as defined by CDC (CIII). • Remdesivir should be started within 7 days of symptom onset, but its use could be considered in children with HIV with severe immunosuppression who have had >7 days of symptoms (CIII). • For non-hospitalized children with HIV aged ≥12 years at high risk of progressing to severe COVID-19, ritonavir-boosted nirmatrelvir is the preferred treatment, but remdesivir may be considered if ritonavir-boosted nirmatrelvir is unavailable or contraindicated (BI*). Treatment of COVID-19 in the Inpatient Setting • Remdesivir should be considered for treatment of laboratory-confirmed or clinically suspected acute COVID-19 in children with HIV who are aged ≥28 days, weigh ≥3 kg, require hospitalization, and are receiving supplemental oxygen (BI*). • Remdesivir should be administered for treatment of laboratory-confirmed or clinically suspected acute COVID-19 in children with HIV who are aged ≥28 days, weigh ≥3 kg, are severely or critically ill, have a rapidly increasing oxygen requirement, and/or are at high risk of progressing to severe COVID-19 due to advanced or untreated HIV or another high-risk condition as defined by CDC (AI*).

- Remdesivir should be started within 7 days of symptom onset, but its use could be considered in children with HIV with severe immunosuppression who have had >7 days of symptoms (CIII).
- Corticosteroids (such as dexamethasone) should be considered for the treatment of laboratory-confirmed or clinically suspected acute COVID-19 in children with HIV who require hospitalization and are receiving supplemental oxygen (BIII).
- Corticosteroids should be administered for the treatment of laboratory-confirmed or clinically suspected acute COVID-19 in children with HIV who are severely or critically ill, have a rapidly increasing oxygen requirement, and/or who are at high risk of progressing to severe COVID-19 due to advanced or untreated HIV or another high-risk condition as defined by CDC (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

*Rating of Evidence: I = One or more randomized trials **in children**† with clinical outcomes and/or validated endpoints; I* = One or more randomized trials **in adults** with clinical outcomes and/or validated laboratory endpoints with accompanying data **in children**† from one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; II = One or more well-designed, nonrandomized trials or observational cohort studies **in children**† with long-term outcomes; II* = One or more well-designed, nonrandomized trials or observational studies **in adults** with long-term clinical outcomes with accompanying data **in children**† from one or more similar nonrandomized trials or cohort studies with clinical outcome data; III = Expert opinion*

†Studies that include children or children/adolescents, but not studies limited to postpubertal adolescents

Epidemiology

COVID-19 is caused by the Severe Acute Respiratory Syndrome Coronavirus (type) 2 (SARS-CoV-2) virus, which was initially identified in December 2019 and quickly spread around the globe, causing a pandemic. The virus is spread through respiratory droplets and small particles that are inhaled during close person-to-person contact or transmitted through touching mucous membranes with hands that have been contaminated by the virus.[1] The mean incubation period for SARS-CoV-2 is 3 to 5 days, with more recent variants associated with shorter incubation periods and nearly all infections occurring within 14 days of exposure.[2] Viral shedding begins prior to the onset of symptoms, peaks around the time of symptom onset, and gradually declines over the next 7 to 10 days. Transmission of infectious virus is unlikely after 10 days of illness; however, prolonged shedding for 20 days or longer has been described in persons with immunosuppression, including those with advanced or untreated HIV infection.[3-6]

SARS-CoV-2 has evolved over time through mutations in its viral genome. Variants of interest or variants of concern are assigned letters of the Greek alphabet by the World Health Organization (WHO).[7] Some new variants and some sublineages may have increased transmissibility or virulence, ability to evade the humoral immunity induced by vaccination or previous infection, or features that impact the effectiveness of diagnostics and therapeutics. Within the United States, the proportions of variants circulating in different parts of the country are reported on the Centers for Disease Control and Prevention (CDC) Data Tracker website.[8]

As of September 9, 2023, nearly 200,000 children under 18 years have required hospital admission for COVID-19, and more than 1,600 children have died.[8,9] COVID-19 has affected people in different racial and ethnic groups unequally. People within racial and ethnic minority groups are at increased risk of SARS-CoV-2 acquisition, COVID-19–related hospitalization, and death.[10-15] Importantly, these communities have also been disproportionately affected by the HIV epidemic.

Clinical Manifestations

SARS-CoV-2 infection can cause a range of clinical presentations, from asymptomatic infection to mild respiratory symptoms to severe organ dysfunction and death. Cough, congestion, fever, myalgias, and headache are the most common presenting symptoms of COVID-19 in adults and children. Pediatric patients with COVID-19 may present with symptoms of croup or bronchiolitis. Gastrointestinal manifestations of COVID-19 occur infrequently but are reported more often in younger populations.[15-17] Disorders of smell and taste (i.e., anosmia and dysgeusia) were reported with early variants of SARS-CoV-2, but are less common with more recent variants.[18] A range of dermatologic findings, including various rashes (maculopapular, urticarial, petechial, and/or vesicular) and chilblains-like lesions on the digits, have also been reported with COVID-19.[19]

Children appear less likely to become severely ill with COVID-19 than adults.[8] Severe COVID-19 in children can lead to pneumonia, acute respiratory distress syndrome, shock, and multiple organ dysfunction. Well-described complications include cardiac (e.g., arrhythmia, myocardial injury, heart failure), neurologic (e.g., seizures, encephalopathy), thromboembolic, hyperinflammatory syndromes, and death. Underlying conditions that are associated with higher rates of severe COVID-19 in children include asthma, obstructive sleep apnea, chronic lung disease, cardiac disease, neurologic disorders, obesity, diabetes, prematurity (in young infants), immunocompromising conditions (other than HIV), and medical complexity/dependence on medical technology (such as tube feeding or chronic respiratory support).[15,16,20-23] Severe COVID-19 (i.e., resulting in hospitalization, intensive care unit [ICU] admission, or mechanical ventilation) has been reported less commonly in children with later variants of SARS-CoV-2 compared to earlier variants.[17,21,24,25]

It is unclear whether people with HIV are at increased risk of severe COVID-19. Observational cohort studies have shown conflicting results, with some reporting higher rates of hospitalization, ICU admission, mechanical ventilation support, and/or mortality among adults with HIV and others showing no increased risk associated with HIV infection.[26-42] Several studies identified an increased risk of severe COVID-19 among adults with advanced or untreated HIV infection compared to those on antiretroviral treatment (ART) with no evidence of immunosuppression.[34-38,41-43] Few publications have described the outcomes of children or adolescents with HIV who acquire SARS-CoV-2, but those available report mild COVID-19 symptoms and/or no increased risk of severe COVID-19 among children or adolescents with HIV.[44-48]

Following infection with SARS-CoV-2, which may be asymptomatic, some children may experience a post-acute manifestation of the infection, such as multisystem inflammatory syndrome in children (MIS-C) or post-acute sequelae of SARS-CoV-2 (PASC; also known as “long COVID” or “long-hauler syndrome”). An increased rate of some autoimmune complications, such as new-onset type 1 diabetes, has also been identified in the post–COVID-19 period.[49,50]

PASC is a heterogenous disorder that has been described in 4% to 66% of children after acute COVID-19.[51] The presentation of PASC may include any of a wide-ranging constellation of symptoms that involve multiple body systems, such as:

- Neurologic (fatigue, sleep disorders, attention disorders, “brain fog,” headaches)
- Psychiatric (anxiety, depression, post-traumatic stress disorder)
- Pulmonary (cough, dyspnea)

- Cardiac (chest pain, palpitations, dizziness, exercise intolerance, autonomic dysfunction, syncope)
- Otolaryngologic (anosmia, dysgeusia)
- Musculoskeletal (arthralgias, myalgias)
- Gastrointestinal (nausea, vomiting, diarrhea, abdominal pain)

A multidisciplinary group defined PASC in children as involving one or more persistent physical symptoms, which may fluctuate and relapse, that lasts for at least 12 weeks after confirmed initial SARS-CoV-2 infection, impairs daily function, and cannot be explained by an alternative diagnosis after initial testing.[52] Limited data suggest that adults with HIV may be at higher risk of PASC than adults without HIV, but more research is needed on the incidence of PASC in children with HIV.[53-55]

MIS-C is a relatively rare postinfectious hyperinflammatory condition occurring in <1% of children 2 to 6 weeks after acute COVID-19, including following mild or asymptomatic infection.[56,57] MIS-C has been reported less commonly in children with later variants of SARS-CoV-2 compared to earlier variants. Symptoms may overlap with those of Kawasaki syndrome or toxic shock syndrome; however, MIS-C typically occurs in older children and adolescents (median age 8-9 years), whereas Kawasaki syndrome classically occurs in younger children <5 years of age.[58-61] CDC developed new case definitions for confirmed and probable MIS-C in January 2023, which include age <21 years, fever, clinical severity requiring hospitalization or resulting in death, C-reactive protein ≥3 mg/dL, new-onset manifestations in at least two categories (cardiac, mucocutaneous, shock, gastrointestinal, hematologic), absence of a more likely alternative diagnosis, and laboratory-confirmed SARS-CoV-2 infection (confirmed case) or exposure (probable case) in the last 60 days.[62] More research is needed to understand MIS-C outcomes among children with HIV.

Diagnosis

The approach to diagnosing acute SARS-CoV-2 infection is identical in children with and without HIV, involving antigen tests using upper respiratory tract samples or nucleic acid amplification tests (NAAT), which are considered the most accurate. Many rapid antigen tests are available for home use. Some of the NAAT and antigen diagnostic tests for SARS-CoV-2 are approved for use by the U.S. Food and Drug Administration (FDA), while others are available under an Emergency Use Authorization (EUA).[63]

SARS-CoV-2 serologic (i.e., antibody) tests can be used to determine whether prior exposure to SARS-CoV-2 has occurred through either vaccination or infection; however, serologic tests should not be used to make a diagnosis of acute COVID-19 because it can take 21 days or longer after symptom onset for seroconversion to occur.[64,65] SARS-CoV-2 serologic tests may have variable sensitivity and specificity, may detect different isotypes of immunoglobulins (i.e., immunoglobulin G, immunoglobulin A, and/or immunoglobulin M), and may be subject to cross-reactivity to antibodies from other coronaviruses. For these reasons, SARS-CoV-2 serologic tests **should not** be used to guide decisions about the use of vaccines, monoclonal antibodies, or other therapeutics to prevent or treat acute COVID-19 **(AIII).**

Prevention Recommendations

Preventing Exposure

Several personal preventative measures can be implemented to decrease the likelihood of SARS-CoV-2 spreading in community settings. Personal hygiene measures include frequent handwashing or use of an alcohol-based hand sanitizer and covering the nose and mouth while coughing and sneezing. During periods of high community transmission, the risk of SARS-CoV-2 acquisition can be decreased by avoiding crowds and close contact with people outside of the household and ensuring adequate ventilation of indoor spaces. Proper use of a well-fitted mask or face covering can also help decrease community spread of SARS-CoV-2, primarily by containing the secretions of infected persons, but also by reducing exposure of the mask wearer to the virus, with the degree of protection offered to the mask wearer dependent upon the filtration efficacy of the mask (with N95 masks having the highest filtration efficacy, followed by disposable medical masks, and finally by cloth masks).[66-68] Mask wearing is most beneficial during periods of high community transmission in settings where social distancing is difficult or impossible, as well as indoor settings with poor ventilation. People who acquire SARS-CoV-2 should isolate at home until at least 24 hours after their symptoms begin improving and fever has resolved to prevent spreading the infection to others.[69,70]

In the health care setting, infection prevention interventions to reduce the spread of SARS-CoV-2 include identification and isolation of people with infection, use of personal protective equipment, proper hand hygiene, and environmental disinfection. When caring for patients with COVID-19, health care providers should use a particulate respirator (i.e., N95 mask) during all aerosol-generating procedures and potentially during all interactions with the patient.[71] During periods of high SARS-CoV-2 community transmission, institutions may decide to implement the universal use of face masks for everyone in a health care setting (e.g., employees, visitors).

Preventing Disease

COVID-19 vaccination effectively prevents severe outcomes such as hospitalization and post-acute COVID-19 syndromes (e.g., MIS-C and PASC) in children.[72-86] While there is evidence that vaccine effectiveness wanes over time, protection against severe disease (ICU admission, mechanical ventilation, or death) is more durable.[87,88] Several successive formulations of COVID-19 vaccines have been developed and approved or authorized for use by the FDA in an effort to best target circulating variants. For more information on currently recommended vaccine products and schedules, see CDC's Use of COVID-19 Vaccines in the United States. In the United States, COVID-19 vaccines have been authorized for children aged ≥6 months since June 2022.[89] Clinical trials evaluating COVID-19 vaccines in infants <6 months of age are ongoing (e.g., NCT05584202). Although no COVID-19 vaccines are yet approved for children <6 months of age, maternal immunization during pregnancy has been shown to increase antibody transfer and provide protection to infants for the first 6 months of life.[90,91]

All children with HIV aged ≥6 months should receive age-appropriate COVID-19 vaccines, including updated vaccines as part of routine prevention, regardless of CD4 T lymphocyte (CD4) cell count or viral load **(AI).** Household members and close contacts of children with HIV aged ≥6 months should also receive COVID-19 vaccines to prevent exposure to the child **(AIII).** Refer to CDC's Use of COVID-19 Vaccines in the United States for the most up-to-date information about

the COVID-19 vaccines available to children by age, immunocompromised status, and the recommended dosing intervals.[89] Thus far, studies of adults and children with HIV show that COVID-19 vaccines are safe and immunogenic, but humoral responses are lower in people with advanced or untreated HIV.[48,92-102] Although vaccine responses are likely to improve after initiation of ART, vaccination against COVID-19 should not be delayed while awaiting immune reconstitution **(AIII).** Children with HIV may receive additional doses of COVID-19 vaccines, as indicated by CDC's COVID-19 vaccination guidance for people who are moderately or severely immunocompromised, if they have stage 3 HIV infection (see HIV Infection Stage table in the Introduction), history of an AIDS-defining illness without immune reconstitution, clinical manifestations of symptomatic HIV, or untreated HIV infection.

There are very few contraindications or precautions associated with the COVID-19 vaccines, and these precautions are identical for children with and without HIV.[89] Common side effects that may occur after receipt of vaccines include local reactions (pain, swelling, or redness at the injection site), ipsilateral axillary lymphadenopathy, and such systemic reactions as fever, fatigue, headache, or myalgias. Anaphylaxis or syncope may occur rarely in the immediate post-vaccination period. Myocarditis and/or pericarditis has been described (see CDC's Clinical Considerations: Myocarditis and Pericarditis after Receipt of COVID-19 Vaccines) most frequently among adolescent or young adult males, typically in the week after receiving a second dose or subsequent dose of a messenger RNA (mRNA) COVID-19 vaccine. Myocarditis or pericarditis is estimated to be a rare outcome (up to two cases per 10,000 mRNA vaccine doses), and nearly all cases are mild and result in full recovery.[103] In addition, cardiac complications are estimated to occur at a rate two- to sixfold higher among adolescent males ages 12 to 17 years after SARS-CoV-2 infection than after mRNA vaccination.[104]

Pemivibart (Pemgarda™) is a recombinant human monoclonal antibody that was authorized by the FDA in March 2024 for use as pre-exposure prophylaxis against COVID-19 in adults and adolescents aged ≥12 years and who weigh ≥40 kg with moderate-to-severe immunocompromise (including those with advanced or untreated HIV infection) who are unlikely to have an adequate response to COVID-19 vaccination.[105,106] Pemivibart is administered intravenously in a health care setting with a post-infusion observation period of 2 hours due to the possibility of anaphylaxis. Doses can be repeated every 3 months if the risk of exposure to SARS-CoV-2 and moderate-to-severe immunocompromise persist. While pemivibart is the only available option for pre-exposure prophylaxis, it may be logistically challenging to administer and may not be available in all locations. For children aged ≥12 years and who weigh ≥40 kg with HIV, the Panel on Opportunistic Infections in Children with and Exposed to HIV (the Panel) recommends that pemivibart be considered for the prevention of COVID-19 in those with severe immunosuppression (stage 3 – see HIV Infection Stage table in the Introduction) regardless of COVID-19 vaccination status **(BIII)** and that it may be considered for those with moderate to no immunosuppression (stage 1 or 2 – see HIV Infection Stage table in the Introduction) in whom COVID-19 vaccines are contraindicated or unavailable **(CIII).** Monoclonal antibodies, including pemivibart, are not a substitute for vaccination in people who are eligible for COVID-19 vaccines. In individuals recently vaccinated against COVID-19, pemivibart should be administered at least 2 weeks after the most recent vaccination. Pemivibart is not authorized for post-exposure prophylaxis against COVID-19.

Treatment Recommendations

Treating Disease

The majority of pediatric SARS-CoV-2 infections are asymptomatic or mildly symptomatic, including in children and youth with HIV.[48] Isolation and supportive care with antipyretics, analgesics, hydration, and rest are the mainstays of treatment. Children who present with syndromes consistent with croup, bronchiolitis, or an asthma exacerbation and test positive for SARS-CoV-2 should receive supportive care and adjunctive treatments (including corticosteroids, if indicated) as per standard of care.

In general, the management of COVID-19 in people with HIV is similar to the management of people without HIV, with two exceptions: (1) people with advanced or untreated HIV who have COVID-19 and for whom there is concern for clinical worsening should be evaluated for opportunistic infections, and (2) people with HIV may be eligible for certain antiviral medications due to having a higher risk of progression to severe COVID-19. Of note, no clinical trials have been performed to specifically evaluate the efficacy of any currently available antiviral medications that target SARS-CoV-2 among people with HIV. In addition, very few published studies have evaluated these medications in children. Recommendations for the therapeutic management of children with COVID-19 are largely extrapolated from adult safety and efficacy data, established management of other viral infections in children, and expert opinion. The decision to use antiviral medications in children with COVID-19 should take into account the child's risk factors for progression to severe disease, including medical comorbidities, degree of immunosuppression, and history of vaccination against COVID-19.

As the SARS-CoV-2 virus evolves over time, the efficacy of antiviral medications used to treat COVID-19 may change. Antiviral drugs currently available for use in pediatric patients <18 years of age that have activity against currently circulating SARS-CoV-2 variants include remdesivir (available to those aged ≥28 days) and ritonavir-boosted nirmatrelvir (Paxlovid) (available to those aged ≥12 years). Molnupiravir is an antiviral with an EUA for people ≥18 years of age; therefore, it will not be discussed further in this guidance.

Remdesivir (Veklury)

Remdesivir (Veklury) is approved by the FDA for the treatment of COVID-19 in adults and children aged ≥28 days and who weigh ≥3 kg who are hospitalized with COVID-19 and for those with mild to moderate COVID-19 who are not hospitalized and are at high risk of progression to severe disease. In clinical trials of non-hospitalized adolescents and adults at high risk of progression to severe COVID-19, remdesivir was associated with significant reductions in hospitalization or death.[107,108] Clinical trials that evaluated remdesivir in hospitalized adults with severe COVID-19 consistently showed benefit among a subgroup of patients who required supplemental oxygen but not mechanical ventilation.[109-112] Publications describing the use of remdesivir in children are limited to one single-arm, open-label study of 53 hospitalized children and a small number of case series; these studies reported high rates of clinical recovery and few adverse events.[113-116]

Based on these data, the Panel recommends that remdesivir may be considered in the outpatient setting for treatment of laboratory-confirmed or clinically suspected mild to moderate COVID-19 in children with HIV who are aged ≥28 days and weigh ≥3 kg and are at high risk of progressing to

severe COVID-19 due to advanced or untreated HIV or another high-risk condition as defined by CDC **(CIII).** For non-hospitalized children with HIV aged ≥12 years and at high risk of progressing to severe COVID-19, ritonavir-boosted nirmatrelvir is the preferred treatment, but remdesivir may be considered if ritonavir-boosted nirmatrelvir is unavailable or contraindicated **(BI*).** For non-hospitalized children with HIV aged <12 years and at high risk of progressing to severe COVID-19, remdesivir is currently the only treatment option but may be logistically challenging to administer and may not be available in all locations.

Among hospitalized children with HIV who are aged ≥28 days and weigh ≥3 kg with laboratory-confirmed or clinically suspected acute COVID-19, remdesivir should be considered in children who are receiving supplemental oxygen **(BI*)** and should be administered in children who are severely or critically ill, have a rapidly increasing oxygen requirement, and/or who are at high risk of progressing to severe COVID-19 due to advanced or untreated HIV or another high-risk condition as defined by CDC **(AI*).**

Remdesivir is administered intravenously once daily for 3 days to non-hospitalized patients and for 5 days or until discharge (whichever occurs first) in hospitalized patients. The duration of remdesivir for hospitalized patients who are critically ill or have immunosuppression can be extended to 10 days. Ideally, remdesivir should be started within 7 days of symptom onset, as active viral replication has often ceased after this time in the majority of previously healthy patients. However, in children with HIV with severe immunosuppression who may have prolonged viral replication and shedding, antiviral therapy could be considered even if presenting with >7 days of symptoms **(CIII).** Common side effects attributed to remdesivir include nausea/vomiting and elevation of serum transaminases. Although remdesivir has potential for drug–drug interactions, the potential for interactions with antiretroviral (ARV) drugs is thought to be unlikely. Providers should consult a drug interactions resource, such as the University of Liverpool COVID-19 Drug–Drug Interaction website, for further guidance.[117]

Ritonavir-Boosted Nirmatrelvir (Paxlovid)

Ritonavir-boosted nirmatrelvir (Paxlovid) is an oral protease inhibitor (PI) that has an EUA for the treatment of COVID-19 in children aged ≥12 years and who weigh ≥40 kg who are at high risk of progression to severe disease. In the EPIC-HR trial, ritonavir-boosted nirmatrelvir reduced the risk of hospitalization or death by 89% compared to placebo in non-hospitalized adults (≥18 years) with COVID-19 who were at high risk of progression to severe disease.[118] It is unclear whether any participants had HIV. Clinical trials, such as EPIC-Peds (NCT05261139),[119] are underway to evaluate the safety and efficacy of ritonavir-boosted nirmatrelvir in children. A case series of nine children who received ritonavir-boosted nirmatrelvir reported few adverse events and no hospitalizations after receiving treatment.[120] Ritonavir-boosted nirmatrelvir is expected to achieve similar drug exposure in adolescents aged ≥12 years and who weigh ≥40 kg as in adults, and there is extensive experience with the use of ritonavir in children.[121] Based on these data, the Panel recommends that ritonavir-boosted nirmatrelvir should be considered in the outpatient setting for the treatment of laboratory-confirmed or clinically suspected mild to moderate COVID-19 in children with HIV who are aged ≥12 years and weigh ≥40 kg who are at high risk of progressing to severe COVID-19 due to advanced or untreated HIV or another high-risk condition as defined by CDC **(BI*).**

Ritonavir-boosted nirmatrelvir may be administered with other ARVs, including those that contain ritonavir or cobicistat, without any interruption or modification to the child's usual antiretroviral therapy **(AIII).**[122] Children taking an ARV regimen that includes ritonavir or cobicistat should be monitored for increased side effects (e.g., nausea, vomiting, diarrhea, abdominal pain, jaundice, hepatic transaminase elevations) while taking ritonavir-boosted nirmatrelvir, but the doses of ritonavir-boosted nirmatrelvir and/or the other ARVs do not need to be adjusted. Patients with untreated or poorly controlled HIV could theoretically develop PI resistance while taking ritonavir-boosted nirmatrelvir. Ritonavir-boosted nirmatrelvir has potential for drug–drug interactions due to being both a cytochrome P450 (CYP) 3A inhibitor and a CYP3A substrate. Providers should consult the FDA Paxlovid Emergency Use Authorization Fact Sheet for Healthcare Providers, the Infectious Diseases Society of America Management of Drug Interactions with Nirmatrelvir/Ritonavir (Paxlovid): Resource for Clinicians, and/or the University of Liverpool COVID-19 Drug–Drug Interaction website for guidance on drug–drug interactions. Renal and hepatic function should be evaluated prior to initiating ritonavir-boosted nirmatrelvir, and doses should be adjusted if needed.[121] Ritonavir-boosted nirmatrelvir should be started within 5 days of symptom onset **(BI*)** and administered orally twice daily for 5 days. Patients should be advised that a small proportion of people experience "rebound" (i.e., return of symptoms, testing positive after a previous negative test, or both) 2 to 8 days after taking ritonavir-boosted nirmatrelvir.[123] The potential for viral rebound should not dissuade providers from offering ritonavir-boosted nirmatrelvir to patients who are at high risk of progressing to severe COVID-19 and could potentially benefit from its use **(AIII).** Other potential side effects of ritonavir-boosted nirmatrelvir include gastrointestinal upset (nausea, vomiting, diarrhea), altered taste, and increased blood pressure.

Other Treatment Considerations

Corticosteroids have demonstrated benefit in hospitalized adults with severe COVID-19. The RECOVERY trial reported a decrease in 28-day all-cause mortality among hospitalized adults ≥18 years of age who received 10 days of dexamethasone, with the greatest effect among adults receiving mechanical ventilation or extracorporeal membrane oxygenation (ECMO), a moderate effect among patients receiving supplemental oxygen or noninvasive positive pressure ventilation, and no effect among patients who did not require supplemental oxygen.[124] A small number of participants (<1%) had HIV. No clinical trials have evaluated the efficacy of corticosteroids in children with COVID-19. However, given the strong safety record of corticosteroids and abundant pediatric experience with corticosteroids in other settings, the possible benefits likely outweigh the potential risks in critically ill and severely ill children. Therefore, the Panel recommends that corticosteroids (such as dexamethasone) should be considered for treatment of laboratory-confirmed or clinically suspected acute COVID-19 in children with HIV who require hospitalization and are receiving supplemental oxygen **(BIII)** and should be administered for treatment of laboratory-confirmed or clinically suspected acute COVID-19 in children with HIV who are severely or critically ill, have a rapidly increasing oxygen requirement, and/or who are at high risk of progressing to severe COVID-19 due to advanced or untreated HIV or another high-risk condition as defined by CDC **(AIII).**

Dexamethasone can be administered to hospitalized children with COVID-19 orally or intravenously for ≤10 days. Dexamethasone has potential for drug–drug interactions; of particular importance to children with HIV is a potential interaction with non-nucleoside reverse transcriptase inhibitors (NNRTIs), which may result in decreased serum concentrations of either dexamethasone or the NNRTI, depending on which NNRTI is used. Providers should consult a drug interactions resource,

such as the University of Liverpool COVID-19 Drug–Drug Interaction website, for further guidance. Alternative corticosteroids, such as hydrocortisone or methylprednisolone, may be considered if dexamethasone is not available or if alternative corticosteroids are being administered for another indication. Except for considering potential drug–drug interactions, recommendations for the use of corticosteroids in children hospitalized with severe COVID-19 are no different for children with and without HIV. Corticosteroids should be avoided in non-hospitalized children with COVID-19 unless they are used for an indication (e.g., croup, asthma exacerbation).

Anti-inflammatory medications—such as anakinra, baricitinib, tocilizumab, and tofacitinib—have been used in hospitalized adults with severe COVID-19. Of note, the EUAs of baricitinib and tocilizumab for hospitalized patients with COVID-19 include children as young as 2 years of age.[125,126] Several of these medications have been used in other pediatric rheumatologic or inflammatory disorders. However, there is less experience with the use of these anti-inflammatory agents than with corticosteroids in children with COVID-19. These anti-inflammatory medications can be considered on a case-by-case basis in children with HIV who are hospitalized with severe COVID-19 (i.e., requiring mechanical ventilation or ECMO, with critical illness, or with evidence of hyperinflammation) who are not improving despite treatment with antivirals and corticosteroids **(CIII).** The choice of anti-inflammatory agent may differ among institutions; consultation with a pediatric rheumatologist is suggested. Recommendations for the use of anti-inflammatory medications in children hospitalized with severe COVID-19 are no different for children with and without HIV.

Anticoagulation is often used in hospitalized adults with COVID-19 to prevent thromboembolic disease. In two large case series of children hospitalized with acute symptomatic COVID-19, between 1% to 2% experienced a thromboembolic complication.[127,128] No trials to define the optimal approach to anticoagulation have been conducted among hospitalized children with COVID-19. Prophylactic anticoagulation can be considered in hospitalized children with HIV with COVID-19 according to local institutional guidelines and consideration of the patient's underlying risk factors for thromboembolic disorders **(CIII).** Recommendations for the use of prophylactic anticoagulation in children hospitalized with COVID-19 are no different for children with and without HIV.

Managing Treatment Failure

In children hospitalized for severe COVID-19, high-quality supportive care in a pediatric critical care unit is vital to recovery. The duration of remdesivir can be extended to 10 days in critically ill patients that have not shown substantial improvement by Day 5. Corticosteroids can also be used for up to 10 days in children who are severely or critically ill. Immune modulation (e.g., treatment with anti-inflammatory medications, such as anakinra, baricitinib, tocilizumab, and tofacitinib) has been used in children who are not improving despite treatment with antivirals and corticosteroids.

Managing Multisystem Inflammatory Syndrome in Children

The approach to treating MIS-C is identical in children with and without HIV. Supportive management is tailored to the patient's presenting symptoms and degree of clinical severity and should include fluid resuscitation, inotropic support, and respiratory support as needed. MIS-C is typically treated with anti-inflammatory medications, although the choice of agents (e.g., corticosteroids, intravenous immune globulin, anakinra, infliximab), dose, and duration used

varies between institutions. The American College of Rheumatology has developed clinical guidance documents for the management of MIS-C.

Managing Post-acute Sequelae of SARS-CoV-2

The approach to treating PASC is identical in children with and without HIV. Some symptoms (e.g., anosmia) may require only watchful waiting, whereas others (e.g., heart palpitations, psychiatric symptoms) may require diagnostic testing and/or referral to a subspecialist. Symptoms of fatigue and exercise intolerance may benefit from a gradual increase in physical activity through an exercise program, possibly with oversight from a physical or occupational therapist. In some locations, multidisciplinary clinics have been formed to manage pediatric PASC, but these are not likely to be accessible for all children. Further guidance on the management of pediatric PASC can be found in published consensus statements from the Multi-Disciplinary Post-Acute Sequelae of SARS-CoV-2 Infection Collaborative and the American Academy of Pediatrics.

Management of HIV During the COVID-19 Pandemic

During periods of elevated community transmission of SARS-CoV-2, clinicians managing HIV should make every effort to maintain routine health care visits and viral load monitoring. Health care facilities should offer virtual (telehealth) visits, if possible, for patients isolating at home or patients who wish to avoid potential exposure to COVID-19. The importance of maintaining adherence to ART should be emphasized, and clinicians should ensure that people with HIV can access an adequate supply of ART. One such strategy includes providing refills every 3 or 6 months instead of every 30 days. There is no evidence that any ARVs used for the treatment of HIV (e.g., lopinavir/ritonavir, boosted darunavir, or tenofovir disoproxil fumarate/emtricitabine) have efficacy against SARS-CoV-2; therefore, children with HIV should not change their ARV regimen in an effort to prevent or treat COVID-19 **(AIII).** When children with HIV acquire SARS-CoV-2, regardless of whether they require hospitalization or treatment for COVID-19, they should continue their usual ART **(AIII).** Clinicians should note that lymphopenia is a common laboratory finding in patients with COVID-19 (and MIS-C); therefore, in patients with HIV, the CD4 counts obtained during acute COVID-19 or MIS-C may not accurately reflect the HIV disease stage.

Dosing Recommendations for Prevention and Treatment of COVID-19

Indication	First Choice	Alternative	Comments/Special Issues
Primary Prophylaxis	COVID-19 vaccines and updated vaccines	Pemivibart (Pemgarda) *Aged ≥12 Years and ≥40 kg* • Pemivibart injection solution: 4,500 mg administered as a single IV infusion	COVID-19 Vaccination Indicated for— • All children with HIV aged ≥6 months regardless of CD4 cell count or viral load • Household members and close contacts of children with HIV aged ≥6 months For up-to-date vaccine guidance, see CDC's Use of COVID-19 Vaccines in the United States webpage. Children with HIV may qualify for additional doses of COVID-19 vaccines if they have stage 3 HIV infection (see HIV Infection Stage table in the Introduction), history of an AIDS-defining illness without immune reconstitution, clinical manifestations of symptomatic HIV, or untreated HIV infection. Pemivibart Indicated for— • Adults and adolescents aged ≥12 years and who weigh ≥40 kg with moderate-to-severe immunocompromise (including those with advanced or untreated HIV infection) who are unlikely to have an adequate response to COVID-19 vaccination.
Secondary Prophylaxis	N/A	N/A	N/A
Treatment	Non-hospitalized Children at High Risk of Progression to Severe COVID-19 *Aged ≥28 Days to <12 Years* • Remdesivir (Veklury) o ≥3 to <40 kg: Lyophilized powder only; IV loading dose: 5 mg/kg/dose on Day 1, followed by 2.5 mg/kg/dose once daily on Days 2 and 3	Non-hospitalized Children at High Risk of Progression to Severe COVID-19 *Aged ≥28 Days to <12 Years* • N/A *Aged ≥12 Years* • Remdesivir (Veklury) o ≥3 to <40 kg: Lyophilized powder only, IV: loading dose: 5 mg/kg/dose on Day 1, followed by 2.5 mg/kg/dose	Remdesivir is administered intravenously. When given to non-hospitalized patients, duration is for 3 days. When given to hospitalized patients, duration is generally 5 days or until hospital discharge, whichever is first, but may extend to up to 10 days based on clinical response. Remdesivir should be started within 7 days of symptom onset but could be considered if presenting with >7 days of symptoms in children with severe immunosuppression. Ritonavir-boosted nirmatrelvir is an oral PI that may be administered with other ARVs, including those that contain ritonavir or cobicistat, without any interruption or modification to the usual ART. However, there is potential for significant drug–drug

Indication	First Choice	Alternative	Comments/Special Issues
	○ ≥40 kg: Injection solution or lyophilized powder; IV loading dose: 200 mg on Day 1, followed by 100 mg once daily on Days 2 and 3 *Aged ≥12 Years and ≥40 kg* • Nirmatrelvir 300 mg and ritonavir 100 mg, administered together (Paxlovid), twice daily for 5 days Hospitalized Children • Remdesivir (Veklury) ○ ≥3 to <40 kg: Lyophilized powder only; IV loading dose: 5 mg/kg/dose on Day 1, followed by 2.5 mg/kg/dose once daily on Days 2 through 5 ○ ≥40 kg: Injection solution or lyophilized powder; IV loading dose: 200 mg on Day 1, followed by 100 mg once daily on Days 2 through 5 • Dexamethasone 0.15 mg/kg (with a maximum dose of 6 mg), oral or IV, once daily for up to 10 days	once daily on Days 2 and 3 ○ ≥40 kg: Injection solution or lyophilized powder, IV: loading dose: 200 mg on Day 1, followed by 100 mg once daily on Days 2 and 3	interactions with other medications, requiring dose or frequency adjustment or avoidance. Consult a drug interactions database, such as the University of Liverpool COVID-19 Drug–Drug Interaction website, for further guidance. Ritonavir-boosted nirmatrelvir should be started within 5 days of symptom onset. Renal and hepatic function should be evaluated prior to initiating ritonavir-boosted nirmatrelvir, and doses should be adjusted if needed. Dexamethasone has potential for drug–drug interactions, including with NNRTIs. Providers should consult a drug interactions resource, such as the University of Liverpool COVID-19 Drug–Drug Interaction website, for further guidance. Alternative corticosteroids, such as hydrocortisone or methylprednisolone, may be considered if dexamethasone is not available or if alternative corticosteroids are being administered for another indication.

Key: ART = antiretroviral therapy; ARV = antiretroviral drug; CDC = Centers for Disease Control and Prevention; IV = intravenous; NNRTI = non-nucleoside reverse transcriptase inhibitors; PI = protease inhibitor

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