Indiana Department of Health

COVID-19 NEW THERAPEUTICS

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12-2-21

OUR MISSION:

To promote, protect, and improve the health and safety of all Hoosiers.

OUR VISION:

Every Hoosier reaches optimal health regardless of where they live, learn, work, or play.

New and upcoming

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Molnupiravir (Merck)

- MOVe-OUT clinical trial: This Phase III part of the trial was conducted in more than 170 planned clinical trial sites worldwide including Sweden, Chile, Guatemala, Poland, Taiwan, Argentina, Brazil, Canada, Columbia, Egypt, France, Germany, Israel, Italy, Japan, Mexico, Philippines, Russia, South Africa, Spain, Ukraine, the United Kingdom and the United States.
- Reduced the risk of hospitalization or death from 9.7% in the placebo group (68/699) to 6.8% (48/709) in the molnupiravir group, for an absolute risk reduction of 3.0% (95% confidence interval [CI]: 0.1, 5.9; nominal p-value=0.0218) and a relative risk reduction of 30%
- Nine deaths were reported in the placebo group, and one in the molnupiravir group
- Orally-administered potent ribonucleoside analogue that can prevent the SARS-CoV-2 virus replication

Merck and Ridgeback Biotherapeutics Provide Update on Results from MOVe-OUT Study of Molnupiravir, an Investigational Oral Antiviral Medicine, in At Risk Adults With Mild-to-Moderate COVID-19 - Merck.com

Molnupiravir (Merck)

- Submitted for EUA Oct 12. FDA advisers voted in a narrow margin to authorize on Nov 30. FDA has not yet issued EUA.
- To treat mild-to-moderate coronavirus disease 2019 (COVID-19) in adults who have tested positive for COVID-19, and who are at high risk for progression to severe COVID-19, including hospitalization or death.
- Outpatient treatment for adult patients with mild to moderate COVID-19 at high risk for disease progression; treatment within five days of symptom onset: 200 mg capsules in a 40-count bottle; 800 mg twice daily for 5 days
- Direct testing for SARS-CoV-2 for disease confirmation; recommend pregnancy test beforehand since pregnant women excluded from study — unknown if teratogenic effects from the drug

EvuSheld (AZD7442)- AstraZenica

- Combination of two long-acting antibodies (LAAB) targeting viral spike protein: tixagevimab (AZD8895) and cilgavimab (AZD1061) - derived from B-cells donated by convalescent patients after SARS-CoV-2 virus
- The PROVENT pre-exposure prophylaxis trial : Phase 3 randomized (2:1) placebo-controlled trial evaluating AZD7442 for prevention of COVID-19 (primary endpoint: first case of any SARS-CoV-2 PCR positive symptomatic illness post-dose prior to day 183)
  - 5,197 patients with neg SARS-CoV-2 at baseline; 75% with co-morbidities
  - AZD7442 group with a relative risk reduction of symptomatic COVID-19 by 77% (95% CI: 46, 90)
- Other trials underway
- Patients likely to benefit most from AZD7442 are immunocompromised and not expected to mount an immune response to COVID-19 vaccines (last resort drug)
  - E.g., patients with hematologic and solid tumors on active therapy, hematopoietic stem cell or solid organ transplant on immunosuppressants, primary immunodeficiency

https://www.precisionvaccinations.com/vaccines/evusheld-azd7442-long-acting-antibody-cocktail

AZD7442 request for Emergency Use Authorization for COVID-19 prophylaxis filed in US (astrazeneca.com)

AZD7442- AstraZenica

- Pre-exposure prophylaxis
- Intramuscular injection x 2 (300 mg)
- Anticipated dosing: ~ every six months (TBD)
- Asked for EUA on Oct. 5

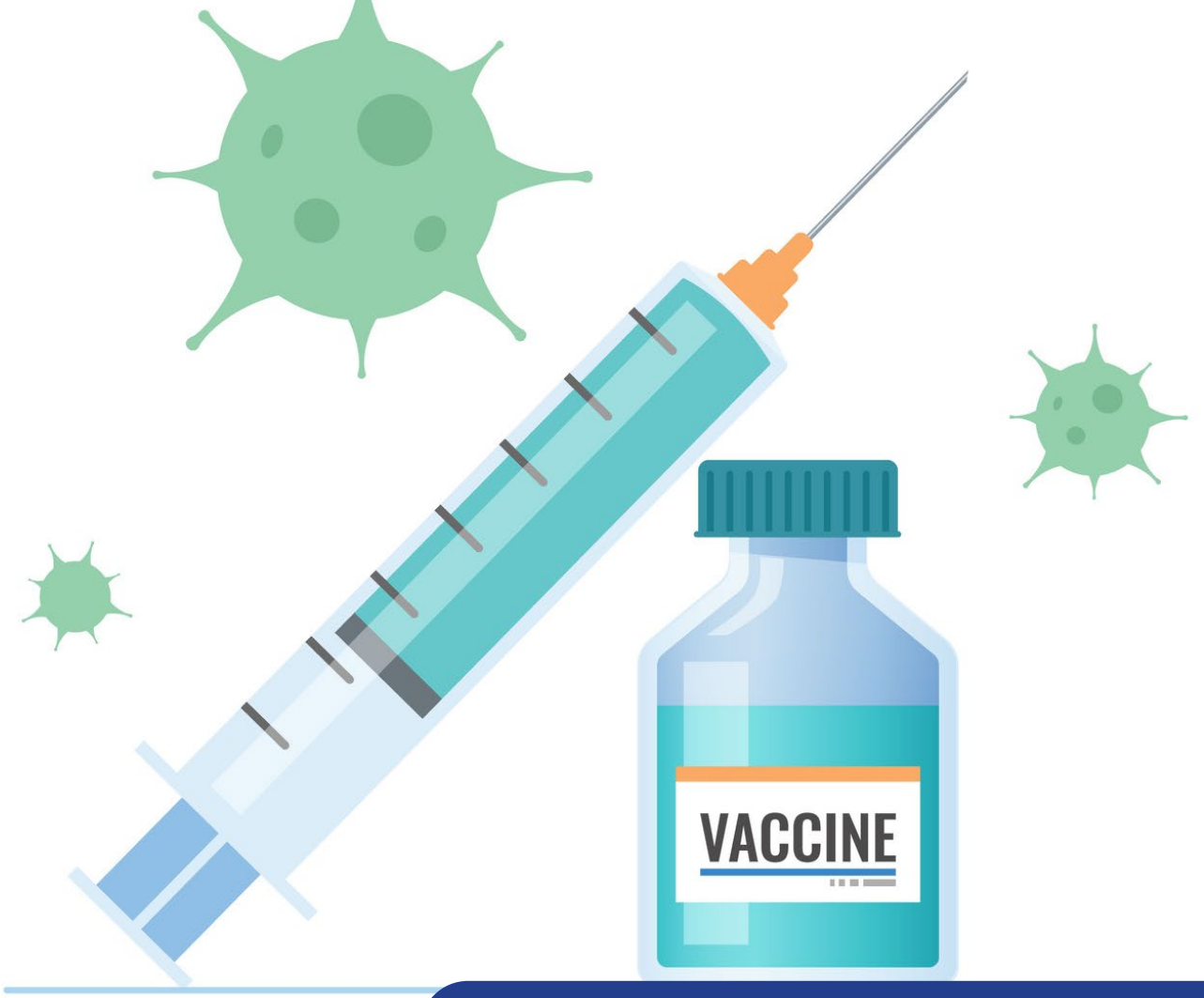
PAXLOVID™ (PF-07321332; ritonavir)- Pfizer

- Phase 2/3 EPIC-HR study, (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19 in **H**igh-**R**isk Patients),a randomized, double-blind study. Enrolled non-hospitalized adults aged 18 and older with confirmed COVID-19 who are at increased risk of progressing to severe illness.
- The primary analysis of the interim data set evaluated data from 1219 adults who were enrolled by September 29, 2021: 0.8% of patients who received PAXLOVID™ were hospitalized through Day 28 following randomization (3/389 hospitalized with no deaths), compared to 7.0% of patients who received placebo and were hospitalized or died (27/385 hospitalized with 7 subsequent deaths). 89% reduction in risk of COVID-19-related hospitalization or death from any cause in patients treated with PAXLOVID compared to placebo within three days of symptom onset, with no deaths in the treatment group. Similar results were seen with treatment started within five days of symptom onset.
- Treatment-emergent adverse events were comparable between PAXLOVID (19%) and placebo (21%), most of which were mild in intensity.
- At the recommendation of an independent Data Monitoring Committee, and in consultation with the U.S. FDA, Pfizer ceased further enrollment into the study due to the overwhelming efficacy demonstrated. Rolling submissions have commenced in several countries including in the United Kingdom, Australia, New Zealand and South Korea, with planned submissions to other regulatory agencies around the world to follow.

Pfizer's Novel COVID-19 Oral Antiviral Treatment Candidate Reduced Risk of Hospitalization or Death by 89% in Interim Analysis of Phase 2/3 EPIC-HR Study | Pfizer

PAXLOVID™ (PF-07321332; ritonavir)- Pfizer

- PF-07321332 a 3CL protease inhibitor: It inhibits viral replication at proteolysis stage, which occurs before viral RNA replication. Co-administration with a low dose of ritonavir helps slow the metabolism, or breakdown, of PF-07321332 for it to remain active in the body for longer periods of time at higher concentrations to help combat the virus.
- In preclinical studies, PF-07321332 did not demonstrate evidence of mutagenic DNA interactions.
- Submitted for EUA on Nov. 16 for the treatment of mild to moderate COVID-19 in patients at increased risk of hospitalizations or death.
- If authorized, it could be prescribed at the first sign of infection or at first awareness of an exposure potentially helping patients avoid severe illness (which can lead to hospitalization and death), experience a decreased symptomatic period, or avoid disease development following contact.
- If authorized or approved, PAXLOVID will be administered at a dose of 300mg (two 150mg tablets) of PF-07321332 with one 100mg tablet of ritonavir, given twice-daily for five days.



Boosters

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LTC residents' boosters

- Once completed offering the boosters, each facility must fill out the attestation survey:
  LTC COVID19 Vaccine Booster Dose Attestation Form
- If you need assistance from IDOH, please email ASAP:
  outreach@probarisystems.com
  - Please include the phone number and email of the contact person.
  - Feel free to specify your needs: Need doses, need vaccinators, need data support or need assistance with the whole process.

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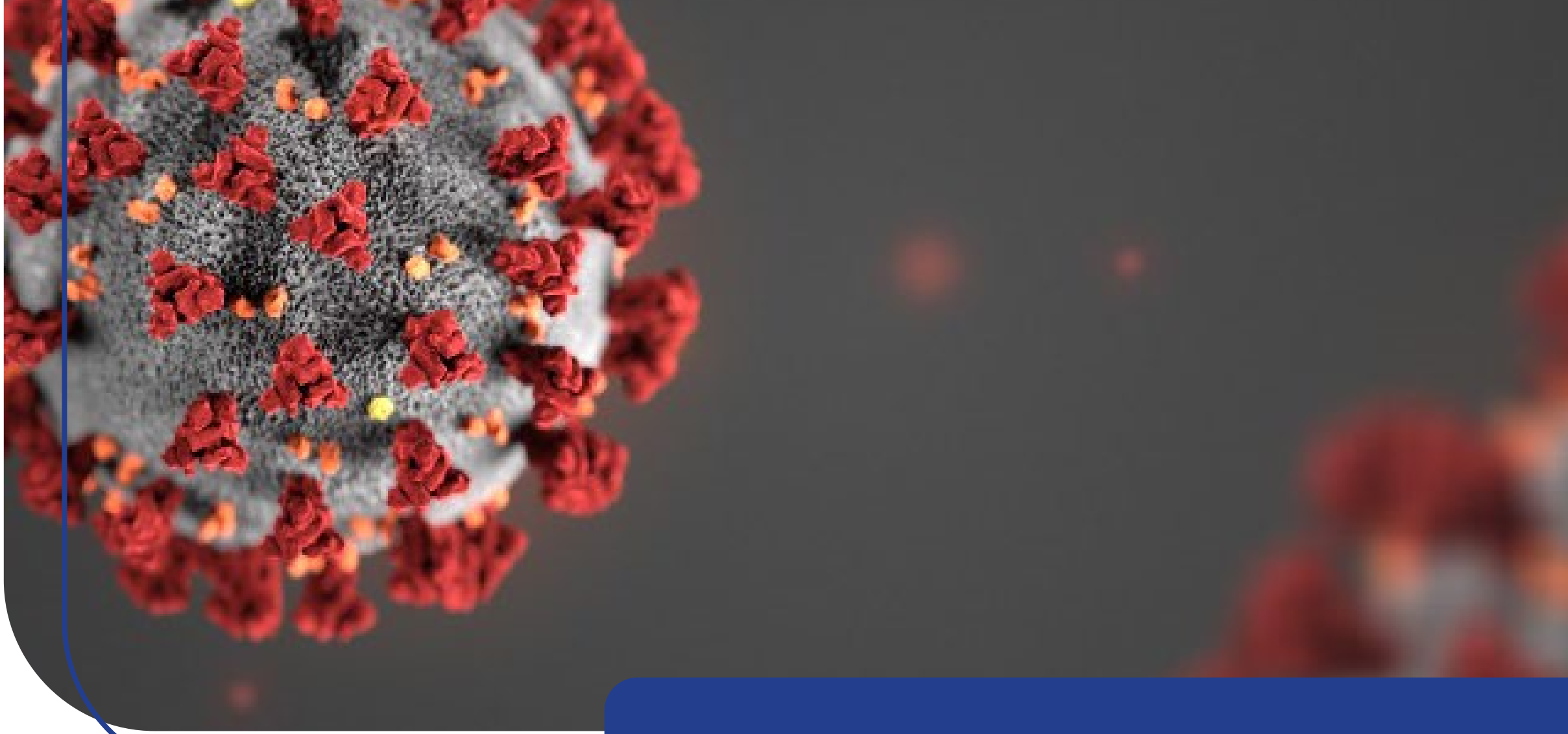
CDC Statement on B.1.1.529 (Omicron variant) | CDC Online Newsroom | CDC



Omicron variant

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Omicron Variant B 1.1.529

- First reported out of South Africa to World Health Organization on Nov. 25, now in 5 continents
  - Had been circulating for few weeks, recent sharp increases
  - WHO and US both declared it as a variant of concern
- Now detected in travelers to several other countries; countries have issued travel bans
- One case identified in the United States to date
- Studies are underway to determine the effect of this variant on:
  - Transmission
  - Treatment drugs
  - Disease severity
  - Vaccine efficacy
  - Reinfection

First Confirmed Case of Omicron Variant Detected in the United States | CDC Online Newsroom | CDC

Omicron Variant

- Mutation profile clearly very different from other circulating VOIs/VOCs, not derived from Delta or any other variant
- Anecdotal description of symptoms includes extreme fatigue, no loss of taste or smell
- CDC will post new travel guidance in the next few days that will include new testing guidance
- Should know more in 3-6 weeks on the effectiveness of vaccines, monoclonal antibodies, and antivirals
- CDC statement: CDC Statement on B.1.1.529 (Omicron variant) | CDC Online Newsroom | CDC

Omicron Variant: Preliminary Observations

- Seems to be more contagious than Delta, but not causing more severe illness
- Some cases in vaccinated also, but not serious. Unknown if those cases were in individuals who have received the booster.

Core IP principles and vaccination are key

CDC Statement on B.1.1.529 (Omicron variant) | CDC Online Newsroom | CDC

Vaccine questions

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Vaccination Questions

- Consider delaying vaccination until recovery from illness *and* for 90 days after the date of diagnosis of MIS-C or MIS-A.
- No data are available on the safety or efficacy of COVID-19 vaccination in people who received monoclonal antibodies* or convalescent plasma as part of COVID-19 treatment or post-exposure prophylaxis.
  - To avoid interference with vaccine-induced immune responses, vaccination should be deferred at least 90 days for persons who receive passive antibody therapy before any COVID-19 vaccine dose.
  - Receipt of passive antibody therapy in the past 90 days is not a contraindication to receipt of COVID-19 vaccine.

Vaccination Questions: After Exposure

- Residents with known exposure or undergoing screening in congregate healthcare settings or non-healthcare settings may be vaccinated if they do not have any symptoms consistent with COVID-19, as exposure to and transmission of SARS-CoV-2 can occur repeatedly for long periods of time.
- Unvaccinated people in the community or in outpatient settings with a known COVID-19 exposure should defer vaccination until their quarantine period has ended.

Interim Clinical Considerations for Use of COVID-19 Vaccines | CDC
And click on HCP presentation link

Vaccination Questions: Myopericarditis

For people who develop myocarditis or pericarditis **after** receipt of the first dose of an mRNA COVID-19 vaccine but **before** administration of a subsequent dose:

- Unclear if there is increased risk of further adverse cardiac effects following a second dose
- Until additional safety data are available, defer receiving a subsequent dose
- Can consider administration of a second dose in certain circumstances
  - Personal risk of severe acute COVID-19 (e.g., age, underlying conditions)
  - Level of COVID-19 community transmission and personal risk of infection
  - Availability of additional data on
    - Risk of myocarditis or pericarditis following an occurrence of either condition after a dose
    - Long-term outcomes of myocarditis or pericarditis after receipt of an mRNA COVID-19 vaccine
- Timing of any immunomodulatory therapies

Interim Clinical Considerations for Use of COVID-19 Vaccines | CDC
And click on HCP presentation link
ACIP General Best Practice Guidelines for Immunization | CDC

Vaccination Questions: Myopericarditis

People with a history of myocarditis or pericarditis prior to vaccination OR people who choose to receive a subsequent dose of an mRNA COVID-19 vaccine following an occurrence of myocarditis or pericarditis after receipt of a dose should:

- Wait at least until an episode of myocarditis or pericarditis has completely resolved:
  - Including all symptoms attributed to myocarditis or pericarditis
  - No evidence of ongoing heart inflammation or sequelae as determined by the person's clinical team, which may include a cardiologist, and special testing to completely assess cardiac recovery
- Decisions about proceeding with vaccination should include a conversation between the patient, their parent, guardian, or caregiver (as relevant), and their clinical team.
- Clinicians should consult current clinical guidance for information on the evaluation and management of myocarditis.

Vaccination Questions: TTS

- A review of available data found that Janssen COVID-19 vaccine's known, and potential benefits outweigh its known and potential risks.
- Women aged <50 years:
  - Can receive any COVID-19 vaccine authorized or approved by FDA
  - Should be made aware of the rare risk of TTS after the Janssen vaccine and the availability of other COVID-19 vaccines (i.e., mRNA vaccines)
- People with prior episode of an immune-mediated syndrome characterized by thrombosis and thrombocytopenia, such as heparin-induced thrombocytopenia (HIT):
  - Should be offered another FDA-authorized or -approved COVID-19 vaccine (i.e., mRNA vaccine) if it has been ≤90 days since their illness resolved
  - May be vaccinated with any COVID-19 vaccine authorized or approved by FDA if more than 90 days have passed since their illness resolved

Delayed location reactions

- Delayed-onset local reactions (e.g., erythema, induration, pruritus around the injection site area) beginning a few days through the second week after the first dose are **not** a contraindication or precaution to receiving a second dose.
- Whether persons who experienced a delayed-onset injection site reaction after the first dose will experience a similar reaction after the second dose is unknown. However, such reactions are believed not to represent a risk for anaphylaxis upon receipt of the second dose.
- Persons with delayed injection site reactions after the first mRNA COVID-19 vaccine dose should receive a second dose of the same vaccine product at the recommended interval, **preferably in the opposite arm**.

Timing of TB test and other vaccines

- COVID-19 vaccination should not be delayed because of testing for tuberculosis (TB) infection
- Testing for TB infection with tuberculin skin test (TST) or an interferon release assay (IGRA) can be done before, after, or during the encounter for COVID-19 vaccination
- COVID-19 vaccine can be administered at the same as other vaccines

Agents already in use

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Authorized for non-hospitalized patients

ARS-COV-2-targeting Monoclonal Antibodies

SARS-COV-2-targeting monoclonal antibodies (mAbs) are laboratory-produced antibodies that can help the immune system's attack on SARS-COV-These mAbs block entry into human cells, thus neutralizing the virus. The following SARS-COV-2-targeting mAbs are authorized for use through an EUA for the treatment of certain patients with COVID-19.

- REGEN-COV (Casirivimab and Imdevimab)
- Sotrovimab
- Bamlanivimab and Etesevimab

Approved

- Veklury (Remdesivir) is an antiviral drug approved for use in adults and pediatric patients [12 years of age and older and weighing at least 40 kilograms (about 88 pounds)] for the treatment of COVID-19 requiring hospitalization.
- While not FDA-approved, the EUA for Veklury continues to authorize Veklury for emergency use by licensed healthcare providers for the 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. For additional information on the authorized use of Veklury under the EUA, refer to the Fact Sheet for Healthcare Providers.

Authorized for hospitalized patients

- FDA issued an EUA for baricitinib (Olumiant), an immune modulator, in combination with remdesivir (Veklury) for treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older and requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygen (ECMO).
- FDA issued an EUA for Actemra (Tocilizumab), a monoclonal antibody that reduces inflammation by blocking the interleukin-6 receptor, for the treatment of COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO. Actemra does not directly target SARS-COV-2. Actemra is FDA-approved for the treatment of multiple inflammatory diseases, including rheumatoid arthritis. Actemra is not FDA-approved as a treatment for COVID-19.

Questions?

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