

REGEN-COV (Casirivimab/Imdevimab) in Pregnancy and Lactation

What is REGEN-COV?

- Casirivimab and imdevimab, monoclonal antibodies for post-exposure prevention or treatment of early COVID infection
- Monoclonal antibodies are immune system proteins created in the lab to help the immune system recognize certain diseases and mark them for destruction.
- To prevent infection among people exposed to someone with COVID, or:
- To prevent progression of disease after testing positive

What are the benefits of REGEN-COV?ⁱ

- Reduce the incidence of hospitalization or death from any cause by approximately 70%
- Rapidly reduce the viral load
- Shorten the duration of symptoms

What are some risks of receiving REGEN-COV? What side effects can be expected?

- Anaphylaxis is rare but has been seen
- Clinical worsening has been seen – unclear if due to REGEN-COV vs. natural progression of COVID
- Has not shown benefit in individuals with severe symptoms
- As with any injection, there is the risk of temporary pain, bleeding, or bruising at the injection site
- Limited data thus far on REGEN-COV, so it is possible that there are side effects that are not yet known

Who is eligible to receive REGEN-COV?

- Adults and adolescents age 12 and older
- Not fully vaccinated (individuals are considered fully vaccinated two weeks after second shot of Moderna or Pfizer vaccine, or two weeks after a single shot of Johnson & Johnson) **OR** not expected to mount a full immune response (e.g. secondary to immune compromise)
- Either:
 - Within 10 days of symptom onset with positive COVID test and mild to moderate symptoms at high risk of disease progression (pregnancy is included in this category)
 - Within 10 days of exposure to someone with known COVID
 - Someone expected to be at considerable risk of exposure to individuals with COVID (e.g. through occupational exposure)

Who should I consider recommending REGEN-COV to?

- Any patients meeting above criteria
- Particular emphasis on patients with other risk factors, including BMI >25, chronic kidney disease, diabetes, and cardiovascular disease

How is REGEN-COV administered? What are some considerations regarding delivery?

- In general, IV is recommended, however subQ is also an option if IV is not feasible to be administered within the recommended timeframe to have the most benefit.
- Similar benefits have been seen with both IV and subQ administration, though the studies and approval were initially done on IV administration. SubQ administration has more recently been rolled out.ⁱⁱ

Is REGEN-COV FDA approved?

- Approved by the FDA under an Emergency Use Authorization, or EUA but not gone through the more extensive approval process for full FDA approval
- EUA approval based on evidence that it may be effective in preventing serious disease. It is thought that these benefits outweigh the potential risks.
- This approval also acknowledges that there are no reasonable alternatives to REGEN-COV that have full FDA approval.

What do we know about REGEN-COV and pregnancy?

- There is no safety data specifically on REGEN-COV and pregnancy.
- However, other monoclonal antibodies have been studied and we have >20 years of safety data suggesting that monoclonal antibodies (notably Humira and Remicade) are not associated with adverse pregnancy outcomes.ⁱⁱⁱ
- Covid-19 during pregnancy is associated with severe morbidity, and though we do not have safety data for REGEN-COV specifically in pregnancy, it is biologically similar to other well studied monoclonal antibodies that are considered “low to moderate risk” per ACOG classification.
- On the topic of immune modulating therapy in pregnancy, ACOG writes, “Decision making regarding patient plans should be individualized and shared and should include consideration of pregnancy and maternal risks associated with untreated disease.”^{iv}

What do we know about REGEN-COV and breastfeeding?

- There is no safety data specifically on REGEN-COV and breastfeeding.
- Adalimumab (Humira) has been well studied and found to be in breast milk in small quantities. Due to the size of this protein, it is suspected to be mostly broken down by the infant GI tract with little absorption. Most experts and professional guidelines feel that the drug is acceptable to use during breastfeeding.^v
- Casirivimab^{vi} and imdevimab^{vii} (REGEN-COV) are nearly identical in size and, according to expert opinion, are expected to act the similarly. Therefore REGEN-COV is likely acceptable to use during breastfeeding.

Can you get vaccinated after receiving REGEN-COV?

- REGEN-COV will likely reduce the body’s immune response to a COVID vaccine
- Recommended to delay vaccination for 90 days after administering REGEN-COV

How should I talk to my patients about REGEN-COV?

- Discuss risks and benefits of use, including risk of disease progression without treatment
- Discuss risk factors unique to your patient that may increase their likelihood of developing severe disease or associated morbidity (e.g. current pregnancy)
- Provide optimistic but frank assessment about current data on REGEN-COV use, including limited information on use in pregnancy
- Acknowledge limited options for treatment but overall reassuring safety profile and effectiveness of REGEN-COV
- Include discussion of other important preventative measures, most importantly vaccination, as well as mask wearing, social distancing, and hand hygiene.

How can I find a location to get REGEN-COV?

- The Department of Health and Human Services maintains a database of all sites that have REGEN-COV: <https://protect-public.hhs.gov/pages/therapeutics-distribution>

Where should I go if I want to know more?

- FDA EUA: <https://www.fda.gov/media/145801/download>
- FDA REGEN-COV Fact Sheet: <https://www.fda.gov/media/145612/download>
- ACOG FAQs: <https://www.acog.org/clinical-information/physician-faqs/covid-19-faqs-for-ob-gyns-obstetrics>

References:

Unless otherwise cited below, all information has been taken from FDA EUA, FDA REGEN-COV Fact Sheet, and ACOG fact sheet (above).

ⁱ Weinreich DM, Sivapalasingam S, Norton T, et al. REGN-COV2, a neutralizing antibody cocktail, in outpatients with Covid-19. *N Engl J Med* 2021;384:238-51.

ⁱⁱ O'Brien MP, Forleo-Neto E, Musser BJ, Isa F, Chan KC, Sarkar N, Bar KJ, Barnabas RV, Barouch DH, Cohen MS, Hurt CB, Burwen DR, Marovich MA, Hou P, Heirman I, Davis JD, Turner KC, Ramesh D, Mahmood A, Hooper AT, Hamilton JD, Kim Y, Purcell LA, Baum A, Kyratsous CA, Krainson J, Perez-Perez R, Mohseni R, Kowal B, DiCioccio AT, Stahl N, Lipsich L, Braunstein N, Herman G, Yancopoulos GD, Weinreich DM; Covid-19 Phase 3 Prevention Trial Team. Subcutaneous REGEN-COV Antibody Combination to Prevent Covid-19. *N Engl J Med*. 2021 Aug 4;NEJMoa2109682. doi: 10.1056/NEJMoa2109682. Epub ahead of print. PMID: 34347950; PMCID: PMC8362593.

ⁱⁱⁱ Geldhof A, Slater J, Clark M, Chandran U, Coppola D. Exposure to Infliximab During Pregnancy: Post-Marketing Experience. *Drug Saf*. 2020 Feb;43(2):147-161. doi: 10.1007/s40264-019-00881-8. PMID: 31677004; PMCID: PMC7007430.

^{iv} ACOG Committee Opinion No. 776 Summary: Immune Modulating Therapies in Pregnancy and Lactation. *Obstet Gynecol*. 2019 Apr;133(4):846-849. doi: 10.1097/AOG.0000000000003177. PMID: 30913195.

^v Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006-. Adalimumab. 2021 Apr 19. PMID: 30000451.

^{vi} Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006-. Casirivimab. 2021 Jun 21. PMID: 33226742.

^{vii} Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006-. Imdevimab. 2021 Jun 21. PMID: 33226741.