COVID-19 Treatment in the Community Pharmacy Setting

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Disclosure Statement

- Dr. Coby and Dr. Abraham have no relevant financial relationship(s) with ineligible companies to disclose.

AND

- None of the planners for this activity have relevant financial relationships with ineligible companies to disclose.

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Learning Objectives

At the completion of this presentation, the participant will be able to:

1. Recognize the opportunity for pharmacists to provide Covid-19 therapeutics to non-hospitalized patients through the emergency use authorization (EUA) provided by the U.S. Food and Drug Administration (FDA).
2. Identify Covid-19 therapeutics that are appropriate to be provided in the community pharmacy setting.
3. Discuss best practices for implementing Covid-19 therapeutic services in the community pharmacy setting.
4. Outline how to develop a collaborative practice agreement draft for expansion of Covid-19 services in the community pharmacy.

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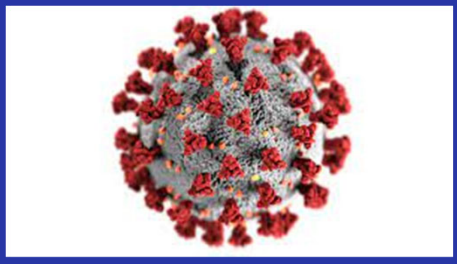

The COVID-19 pandemic has impacted the scope of practice for pharmacists in a tangible way through emergency use authorizations (EUA) for the provision of point-of-care testing, vaccines, and certain COVID-19 therapies. This session is meant to provide information on past, present, and potential future opportunities to provide COVID-19 therapeutics in the community pharmacy setting.

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Background

PREP Act

- Enacted in December 2005
- Amended the PHS Act
- Extended liability protections to those that manufacture, distribute, or administer medical countermeasures against public health threats and emergencies.
- Who are qualified persons?

US Department of Health and Human services. Expanding Access to COVID 19 Therapeutics. https://www.phe.gov/Preparedness/legal/prepact/Pages/PREPact-NinethAmendment.aspx. Accessed 01/30/2022

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Background

Qualified Persons (Who?)

- Pharmacists
- Pharmacy Technicians
- Pharmacy Interns

US Department of Health and Human services. Expanding Access to COVID 19 Therapeutics. https://www.phe.gov/Preparedness/legal/prepact/Pages/PREPact-NinethAmendment.aspx. Accessed 01/30/2022

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Background

How?

- Must be administered subcutaneously, intramuscularly, or orally in accordance with the FDA approval, authorization, clearance, or licensing.
- Must comply with recordkeeping and reporting requirements of the jurisdiction in which he or she administers COVID-19 therapeutics (i.e. reporting adverse events).

US Department of Health and Human services. Expanding Access to COVID 19 Therapeutics. https://www.phe.gov/Preparedness/legal/prepact/Pages/PREPact-NinethAmendment.aspx. Accessed 01/30/2022

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Background

Ohio Implementation

On September 10, 2021, the State of Ohio Board of Pharmacy made a document available highlighting the decision of the Department of Health and Human Services (HHS) to amend the PREP Act, allowing pharmacists to administer covered COVID 19 therapeutics.

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COVID-19 Treatment

Past and Present COVID-19 Therapeutics

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Hydroxychloroquine

FDA-approved indications: Prevention or treatment of malaria, treatment of chronic discoid lupus erythematosus, systemic lupus erythematosus in adults, and rheumatoid arthritis.

EUA for hydroxychloroquine

- Granted on March 28, 2020
  - Early data suggested that both hydroxychloroquine and chloroquine decreased SARS-CoV-2 viral shedding.
- Revoked on June 15, 2020
  - These early results were not able to be replicated and later data from a large randomized controlled trial showed no benefit.

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Hydroxychloroquine

- Although some observational and unpublished anecdotal reports have suggested a clinical benefit of hydroxychloroquine, those are subject to a number of potential confounders, and randomized trials offer higher-quality evidence that hydroxychloroquine has no proven role for COVID-19.
- In an open-label trial including 293 patients with mild COVID-19 who did not warrant hospitalization, hydroxychloroquine administered within five days of symptom onset did not reduce viral levels at day 3 or 7 compared with no treatment, and there was no statistically significant reduction in hospitalization rates or time to symptom resolution.

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Ivermectin

FDA Approved Indications:

Oral: Treatment of intestinal strongyloidiasis and onchocerciasis, two conditions caused by parasitic worms.

Topical: treat external parasites (i.e. head lice) and skin conditions (i.e. rosacea).

- No clear benefit, lack of high quality data to identify safety and efficacy for treatment of COVID-19
- No FDA authorization of use in COVID-19

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Ivermectin

In a July 2021 meta-analysis that identified four trials comparing ivermectin with placebo or standard care in outpatients with mild COVID-19, there was:

- No clear reduction in all-cause mortality at 28 days (RR 0.33 in two trials, 95% CI 0.01-8.05)
- No reduction in need for invasive mechanical ventilation at 14 days (RR 2.97 in one trial; 95% CI 0.12-72.47)
- No clear impact on symptom resolution at 14 days (RR 1.04 in one trial, 95% CI 0.89-1.21).

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REGEN-COV

Viruses and monoclonal antibodies (mAbs)

Mechanisms in viral etiology:

- Similar to natural humoral immunity
- Most mAbs target proteins on the surface of a virus, thus neutralizing the virus from entering cells.
- Several mAbs have been produced that target the spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).
- MAbs are one of the first-line COVID-19-specific treatment options for symptomatic outpatients with risk factors for severe disease.

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REGEN-COV

Casirivimab-imdevimab (600mg-600mg)

- Casirivimab (IgG1 kappa) and imdevimab (IgG1 lambda) are two recombinant human monoclonal antibodies which are unmodified in the Fc regions.
- Casirivimab and imdevimab bind to non-overlapping epitopes of the spike protein receptor binding domain (RBD) of SARS-CoV-2.
- Casirivimab and imdevimab together block RBD binding to the human ACE2 receptor and prevents viral attachment to host cells.

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REGEN-COV

Casirivimab-imdevimab (600mg-600mg)

Phase 3 RCT

- Included 4,000 non-hospitalized adults with mild-to-moderate COVID-19 with one or more risk factors for severe disease
- Received combination casirivimab-imdevimab, at two different doses (1200 and 2400 mg total doses) administered intravenously within seven days of symptom onset was compared with placebo.
- At 29 days, there was a reduction in the combined outcome of hospitalization and death among those treated with both doses of casirivimab-imdevimab compared with placebo (1200 mg total dose, 1 versus 3.2 percent [70 percent RR reduction, 95% CI 32-87]; 2400 mg dose, 1.3 versus 4.6 percent [71 percent RR reduction, 95% CI 52-83]).

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REGEN- COV Administration

For the administration of 600 mg of casirivimab and 600 mg of imdevimab 600 mg (co-formulated), gather 4 syringes and prepare for subcutaneous injection.

- Administer the subcutaneous injections consecutively, each at a different injection site, into the thigh, back of the upper arm, or abdomen, except for 2 inches around the navel. The waistline should be avoided.
- Administer into different quadrants of the abdomen or upper thighs or back of the upper arms to space apart each 2.5 mL injection. DO NOT inject into skin that is tender, damaged, bruised or scarred.
- Clinically monitor patients after injections and observe patients for at least one hour.

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Molnupiravir

MOA: Prodrug, activated through metabolism by the ribonucleoside analogue N-hydroxycytidine (NHC).

- NHC distributes into cells where it is phosphorylated to form the pharmacologically active ribonucleoside triphosphate (NHC-TP).
- NHC-TP incorporation (as NHC-monophosphate [NHC-MP]) into SARS-CoV-2 RNA by the viral RNA polymerase (nsp12) results in an accumulation of errors in the viral genome leading to inhibition of replication.

Dosing:

- 800 mg (four 200 mg capsules) taken orally every 12 hours for five days.
- It should be initiated as soon as possible following COVID-19 diagnosis and within five days of symptom onset. No dose adjustment is necessary based upon kidney or hepatic impairment.

Contraindications:

- Patients <18 years old due to bone and cartilage toxicity.
- Pregnant and lactating women

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Molnupiravir

International RCT

- 1433 non-hospitalized, unvaccinated adults with mild-to-moderate COVID-19 within 5 days with at least one risk factor for severe disease
- Found to reduce the risk of hospitalization or death by approximately 31% (HR 0.69, 95% CI 0.48-1.01); the combined outcome occurred in 6.8 versus 9.7 percent of patients compared with placebo, which trended toward, but did not achieve statistical significance [121].
- Of the 10 deaths reported among trial participants, one occurred in the molnupiravir group and nine occurred in the placebo group. The rates of drug-related adverse events were comparable between the two groups.

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Nirmatrelvir/Ritonavir

MOA:

- Nirmatrelvir is a peptidomimetic inhibitor of the SARS-CoV-2 main protease (Mpro), also referred to as 3C-like protease (3CLpro) or nsp5 protease. Inhibition of SARS-CoV-2 Mpro renders it incapable of processing polyprotein precursors, preventing viral replication.
- Ritonavir is an HIV-1 protease inhibitor but is not active against SARS-CoV-2 Mpro. Ritonavir inhibits the CYP3A-mediated metabolism of nirmatrelvir, resulting in increased plasma concentrations of nirmatrelvir.

Dosing:

- 300 mg nirmatrelvir (two 150 mg tablets) and 100 mg ritonavir (one tablet) taken together orally twice daily for 5 days.
- It should be initiated as soon as possible following COVID-19 diagnosis and within five days of symptom onset.

Precautions: Dose decrease required for patients with reduced kidney function

Contraindications: GFR < 30 mL/min, severe hepatic impairment

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Nirmatrelvir/Ritonavir

MAJOR Drug Interactions: Co-administration is **contraindicated**

- Substrates majorly metabolized by CYP3A4
- Potent CYP3A4 Inducers

RCT: EPIC-HR (Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients)

- 2246 unvaccinated adult outpatients with at least one risk factor for severe disease
- When administered within three days of symptom onset, reduced the risk of hospitalization or death at 28 days by 89 percent compared with placebo (0.7 versus 6.5 percent, risk difference -5.8, 95% CI -7.8 to -3.8)
- Results were similar when the drug was administered within five days of symptom onset.
- Mortality: 13 trial deaths were COVID-19 related and occurred in the placebo group; no reported drug-related adverse effects compared with placebo.

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Service Implementation

Test-to-Treat Model

- With the implementation of these novel therapies there becomes an opportunity to bridge the gap from test to treatment.
- Utilizing a COVID-19 testing program under a CLIA Certificate of Waiver as authorized by the U.S. Food and Drug Administration.

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Service Implementation

Collaborative Practice Agreement (CPA)

- As defined in Section 4729.39 of the Ohio Revised Code.
- Necessary in order to implement the test-to-treatment model.
- Many templates are available for CPA formation in Ohio. Such a template has been provided by the Ohio Pharmacist Association and can be found at the following link: https://www.ohiopharmacists.org/aws/OPA/pt/sp/collaborative-practice-agreements

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Any Questions?

Reach out!

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