July 12, 2021

PROVIDER ALERT

To: Health Plan of San Joaquin (HPSJ) All Contracted and Non-Contracted Providers

From: Health Plan of San Joaquin

Subject: **For Outpatient Patient Care –**
Current Medications for Outpatient Treatment of COVID-19

Business: **Medi-Cal Managed Care**

Management of COVID-19 is rapidly evolving. There are only a few medications that have obtained Emergency Use Authorization (EUA) from the FDA to treat this disease in the ambulatory population. Many trials are still ongoing, and therapies will continue to change as data is collected. It is crucial for providers to stay in the forefront of information, to appropriately advocate for and treat patients. To assist providers, HPSJ's Pharmacy Department has brought together in this single piece all the FDA-authorized treatment options for outpatient management for COVID-19.

Key Points

- Among ambulatory patients with mild-to-moderate COVID-19 at high risk for progression to severe disease, EUAs have been approved for bamlanivimab + etesevimab, casirivimab + imdevimab, and sotrivimaab
- Patients who require carisivimab + imdevimab infusion:
  - Must be referred to San Joaquin General Hospital Infusion Center
  - Review the eligibility criteria and complete the attached referral form, also posted here: www.hpsj.com/pharmacy-announcements/.
- There is limited or no evidence supporting hydroxychloroquine, dexamethasone or other corticosteroids, ivermectin, or convalescent plasma in outpatient COVID-19 treatment.
- Consider casirivimab + imdevimab or sotrovimab in patients with mild-to-moderate COVID-19:
  - Who are ≥12 years of age, weigh at least 40 kg (88.1849 pounds), and are at high risk of progressing to severe COVID-19 and/or hospitalization
  - With treatment to be started as soon as possible after a positive result is received and within 10 days of symptom onset

Background[1]

Early in the pathogenesis of COVID-19, the disease is mostly driven by replication of SARS-CoV-2. Later in the course of infection, the disease causes an exaggerated immune and inflammatory response to the virus which leads to tissue damage.

With this understanding, it is reasonable that: **antiretrovirals exhibit the greatest effect during the early stages** of disease progression, and **immunosuppressive and anti-inflammatory therapies are more useful in the later stages**.

Attachments:

1. **Summary of Current Medications for Outpatient Treatment of COVID-19, Recommended and Non-Recommended – following pages 2 - 3**
2. **Eligibility/Referral Form – San Joaquin General Hospital Infusion Center (carisivimab + imdevimab) – 3 additional pages**

Current Medications for Outpatient Treatment of COVID-19

Recommended[2,3,4,7]			
Treatment	**EUA approval**	**Authorized use**	**Rationale**
Bamlanivimab * 700 mg + etesevimab 1400 mg	Initial: 2/9/21 Reissued: 2/25/21	For the treatment of mild-to-moderate COVID-19 patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older, weighing at least 40 kg, and are at high risk*** of progressing to severe COVID-19 and/or hospitalization. Treatment should be started as soon as possible after a positive result is received and within 10 days of symptom onset.	In ambulatory patients at high risk for severe COVID-19, bamlanivimab + etesevimab has demonstrated absolute mortality reduction and casirivimab + imdevimab has demonstrated lower relative risk of mortality. However, the overall certainty of evidence on current available data is low due to concerns with indirectness and imprecision. There is also limited data on the efficacy of these agents in high risk patients between 12 and 18 years of age. Therefore, guidelines have made a conditional recommendation for these agents.
REGEN-COV** (casirivimab 1200 mg + imdevimab 1200 mg)	Initial: 11/21/20 Reissued: 2/3/21, 2/25/21		
Sotrovimab	Initial: 5/26/2021		

** Distribution of bamlanivimab/etesevimab is paused on a national basis until further notice. Results from in vitro assays that are used to assess the susceptibility of viral variants to particular monoclonal antibodies suggest that bamlanivimab and etesevimab administered together are not active against either the P.1 or B.1.351 variants.*
*** Patients who require carisivimab/imdevimab infusion must be referred to the San Joaquin General Hospital Infusion Center via their form at www.hpsj.com/pharmacy-announcements/.*
****For a list of high-risk populations, please visit the healthcare providers fact sheet for each EUA: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs.*

Not recommended[1,5,6]	
Treatment	**Rationale**
Hydroxychloroquine ± azithromycin	Several randomized trials have not shown a clinical benefit for hydroxychloroquine in non-hospitalized patients with COVID-19. Do not use except in a clinical trial.
Dexamethasone or other corticosteroids	In a sub-group analysis of patients without hypoxia and not receiving supplemental oxygen, there was no evidence for benefit but a trend toward harm with dexamethasone use in this population.
Ivermectin	Ivermectin does have some in vitro activity against SARS-CoV-2; however, the plasma concentrations necessary for antiviral efficacy would require administration of doses up to 100-fold higher than those approved for use in humans. Therefore, its use outside of clinical trials is not recommended.
Convalescent plasma	Receipt of COVID-19 convalescent plasma may reduce progression to severe respiratory disease and reduce mortality and clinical deterioration. However, the evidence is uncertain outpatient, so its use outside of clinical trials is not recommended.
Bamlanivimab monotherapy	The EUA for bamlanivimab has been revoked as of April 16, 2021 due to the sustained increase of SARS-CoV-2 viral variants that are resistant to bamlanivimab monotherapy, which increases the risk of treatment failure.

References:

1. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed June 27, 2021.
2. Fact Sheet for Healthcare Providers Emergency Use Authorization (EUA) of Bamlanivimab and Etesevimab. U.S. Food and Drug Administration. https://www.fda.gov/media/145802/download. Accessed April 15, 2021.
3. Fact Sheet for Healthcare Providers Emergency Use Authorization (EUA) of REGEN-COV™ (casirivimab with imdevimab). U.S. Food and Drug Administration. https://www.fda.gov/media/145611/download. Accessed April 15, 2021.
4. Fact Sheet for Healthcare Providers Emergency Use Authorization (EUA) of Sotrovimab. U.S. Food and Drug Administration. https://www.fda.gov/media/149534/download. Accessed June 27, 2021.
5. Fact Sheet for Healthcare Providers Emergency Use Authorization (EUA) of Bamlanivimab. U.S. Food and Drug Administration. https://www.fda.gov/media/143823/download. Accessed April 15, 2021.
6. Bhimraj A, Morgan RL, Shumaker AH, Lavergne V, Baden L, Cheng VC, Edwards KM, Gandhi R, Gallagher J, Muller WJ, O'Horo JC, Shoham S, Murad MH, Mustafa RA, Sultan S, Falck-Ytter Y. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. Infectious Diseases Society of America **2021**; Version 4.4.0. Available at https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/. Accessed June 27, 2021.
7. Pause in the Distribution of bamlanivimab/etesevimab. Public Health Emergency. https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Bamlanivimab-etesevimab/Pages/bamlanivimab-etesevimab-distribution-pause.aspx. Accessed June 27, 2021.

Eligibility/Referral Form – San Joaquin General Hospital Infusion Center (carisivimab + imdevimab)

3 additional pages

San Joaquin General Hospital
And
San Joaquin County Clinics

REGEN-COV (casirivimab/imdevimab)

Dear Provider,

Thank you for referring your patient for REGEN-COV infusion as an outpatient treatment for Covid 19. Based on the Emergency Use Authorization of REGEN-COV:

1. Inclusion Criteria for patients who have laboratory confirmed SARS-CoV-2 infection either by antigen or molecular PCR Test at higher risk for progressing to severe Covid-19 includes but is not limited to the following conditions:
    - Adult or Pediatric Patient (12 years of age and older weighing at least 40 kg).
    - Have at least one symptom of mild or moderate Covid-19
    - Onset of symptoms ≤ 10 days
    - Age ≥ 65 years
    - BMI ≥ 25 kg/m2
    - Pregnancy
    - Chronic kidney disease
    - Diabetes
    - Immunosuppressive disease or treatment
    - Cardiovascular disease including hypertension
    - Chronic lung disease
    - Sickle cell disease
    - Neurodevelopmental disorders
    - Having a medical-related technological dependence
    - Other medical conditions or factors such as race or ethnicity that may place the individual patient at high risk for progressing to severe Covid-19

2. Patients with any of the following exclusion criteria **will not** be eligible for treatment:

    - Onset of symptoms > 10 days prior to start of treatment
    - Need for hospital admission
    - Requiring supplemental oxygen OR requiring increase in baseline oxygen flow rate if on chronic oxygen supplementation
    - Presence of any condition likely to predict poor clinical outcome with SARs-Covid-19

San Joaquin General Hospital
And
San Joaquin County Clinics

REGEN-COV (casirivimab/imdevimab)

Basic demographic information

Patient Name: _____

Date of Birth: _____ Age: _____ Telephone: _____

Preferred Language: _____

Referring Provider's name: _____

Referring Provider's phone number: _____

Referring Provider's address: _____

Provider has reviewed FDA EUA with patient for REGEN-COV (Casirivmab/imdevimab) and patient consents to proceed. ☐ Yes

COVID19 related information

Date of symptom onset: _____

Date of positive test for SARS-CoV-2 (COVID-19): _____

Is the patient on home oxygen at baseline? ☐ Yes ☐ No

If yes, what is the patient's baseline oxygen requirement? _____ L/min

What is the patient's current oxygen requirement? ☐ None (room air) ☐ _____ L/min

Relevant Medical History

Patient's weight (kg): _____ Patient's height (inches): _____ BMI: _____

Current medications: _____

Allergies _____

Is the patient pregnant? ☐ Yes ☐ No

San Joaquin General Hospital
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REGEN-COV (casirivimab/imdevimab)

Please check if patient has history of any of the following

- ☐ Age ≥ 65
- ☐ Body Mass Index (BMI) ≥ 35
- ☐ Cardiovascular disease
- ☐ Hypertension
- ☐ Chronic obstructive pulmonary disease or other chronic lung disease
- ☐ Chronic kidney disease
- ☐ Diabetes
- ☐ Immunosuppressive disease (not including diabetes)
- ☐ Use of immunosuppressive agents

Referring Provider will obtain patient consent for treatment:

- Provide patient with fact sheet for REGEN-COV (Casirivimab/imdevimab)
- Inform of alternatives to REGEN-COV (Casirivmab/imdevimab)
- Must inform that REGEN-COV (Casirivmab/imdevimab) is authorized for Emergency Use only and is not approved by FDA to treat Covid 19.

If patient meets inclusion criteria and consents to treatment Provider or representative will call:
(209) 468- 6820 to schedule next available appointment.

Patient is to bring a copy of signed consent and referral documents to infusion appointment.