MAT Workgroup Name: Clinical Care **Date: December 16, 2020**

Question or request:

1. How should baricitinib (Olumiant) be administered in New Mexico healthcare facilities?
2. Which patients should be prioritized for treatment with baricitinib?

Recommendation/s:

1. Baricitinib should be consider for use by healthcare providers, in combination with remdesivir (Veklury), to treat suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO. It is not authorized for use in patients who are not hospitalized or who are hospitalized but not on oxygen.

2. Baracitinib should be given as soon as possible after positive test results of direct SARS-CoV-2 viral testing in the hospitalized patient for best benefit.

3. Providers should follow all of the dosing and administration guidance provided by the manufacture and the FDA[1], which include:

    a. Dosage for adults and pediatric patients 9 years of age and older is 4 mg orally once daily, and pediatric patients 2-8 years old is 2 mg orally once daily, all with normal renal function. It can be given via NGT/PEG tube dispersed in water.

    b. Duration of therapy is 14 days or until hospital discharge, whichever is first.

    c. Dose adjustments should be made for renal impairment: do not give in patients with ESRD on HD or those with eGFR <15 ml/min/1.73m^2. For adults or pediatrics, give half the dose for eGFR 30 to <60 ml/min/1.73m^2. For adults and pediatric patients 9 years and older, give 1 mg once daily if eGFR is 15 to <30 ml/min/1.73m^2. Hold for children less than 9 if eGFR is <30 ml/min/1.73m^2.

    d. Dose adjustments should be made for leukopenia. Consider holding dose until absolute lymphocyte count $\geq$ 200 cells/ul and absolute neutrophil count $\geq$ 500 cells/ul.

    e. Dose should be held if increases in ALT or AST enzymes are detected and drug induced liver injury is suspected. It has not been studied in patients with severe hepatic impairment.

    f. Dose should be reduced per the EUA fact sheet if patients are taking OAT3 inhibitors such as probenecid.

4. Baricitinib should be stored at 20° to 25°C (68° to 77°F) with excursions permitted to 15° to 30°C (59° to 86°F).

5. Baricitinib could be used in pregnancy only if potential benefit justifies potential risk for mother and fetus.

6. Providers should be aware that baricitinib is not recommended for patients with known active tuberculosis (TB).

7. Providers should ensure that the required documentation of patient consent (including Fact sheet) is used, and report adverse events to FDA MedWatch, following the requirements under Emergency Use Authorization.

Assessment:

1. Baricitinib is a Janus kinase inhibitor that is commonly used for treatment of rheumatoid arthritis. As an immune modulator, it blocks JAK pathways and thus inflammatory cytokine production. Blocking of these cytokines and cytokine storm in COVID-19 patients is felt to be important in improving outcomes.
2. Baricitinib in combination with remdesivir should be considered in patients on high flow nasal cannula or non-invasive ventilation as it shortens duration of illness by several days and can limit progression of disease.
3. Baricitinib was well tolerated and showed improvement in many parameters in the clinical trial ACTT-2 though does increase risk of thrombosis.
4. It is not known what the combination of steroids in addition to baricitinib might offer but one of the two immune modulators should be used in patients hospitalized with severe COVID-19 infection.
5. The use of baricitinib covered by the EUA must be in accordance with the dosing regimens as detailed in the authorized Fact Sheets.

Red flags and concerns:

1. Serious infections have occurred in patient receiving baricitinib so assuring no active TB or bacterial sepsis as the etiology of illness is important.
2. There is a risk of venous thromboembolism (VTE) while on baricitinib, so all patients should be on VTE prophylaxis.
3. Laboratory tests including CBC with differential, liver function tests and renal function tests should be assessed prior to and during the course of therapy as appropriate to allow for dosage alterations.
4. Dexamethasone is less expensive and may be as effective as baricitinib but this is now the subject of NIH clinical trial and remains to be determined.
5. If tablets need to be dispersed for those unable to swallow pills, proper precautions need to be taken such as preparation in a ventilated hood or the preparer needs to wear an N-95. IT is not known if the powder from crushed tablets constitute a reproductive hazard.
6. Hypersensitivity reactions are possible and so it should be stopped if these occur.

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Resources/Reference:

1. Baricitinib EUA FDA Authorization Letter: https://www.fda.gov/media/143822/download

2. Fact sheet for Health care providers Emergency use authorization (EUA) of baricitinib: https://www.fda.gov/media/143823/download

Kalil et al. Baricitinib plus remdesivir for hospitalized adults with COVID-19. NEJM 2020 https://www.nejm.org/doi/full/10.1056/NEJMoa2031994