Yale NewHaven Health

TO: **YNHHS MEDICAL STAFF**

FROM: **YNHHS COVID 19 TREATMENT TEAM**
YNHHS ANTIMICROBIAL STEWARDSHIP COMMITTEE

SUBJECT: **Review of Emergency Use Authorization (EUA) for Baricitinib**

DATE: **NOVEMBER 25, 2020**

Situation:
On November 19, 2020, The US Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for baricitinib in combination with remdesivir for hospitalized patients with COVID-19 disease.

Background:
The baricitinib EUA was granted based on data from a recent double-blind, placebo-randomized controlled trial (ACTT-2) from which the FDA concluded the known and potential benefits of baricitinib in combination with remdesivir outweighed the known and potential risks for the treatment of COVID-19.

The primary endpoint of the ACTT-2 trial revealed that baricitinib, in combination with remdesivir, reduced the time to recovery by 1 day within 29 days after initiating treatment compared to patients who received a placebo with remdesivir (7 vs. 8 days respectively, p=0.047; 95% CI 1.00-1.1),

However, the mortality rate by day 29 was 4.7% (24/515) baricitinib + remdesivir versus 7.1% (37/518) for placebo + remdesivir (p NS; 95% CI -5.8%. 0.5%).

While ACTT-2 was already underway, data from the RECOVERY trial revealed a mortality benefit for dexamethasone therapy in moderate to severe COVID-19 that in turn has guided our current COVID-19 treatment algorithm.

The safety and efficacy of baricitinib in combination with dexamethasone, the only medication shown to have an effect on mortality for COVID-19, has not been established though an increased risk of infection could be possible. Additionally, baricitinib has a risk for thrombosis which dexamethasone does not have.

Assessment:
Based on current information, the YNHHS COVID-19 Treatment Team met to review the data behind the FDA's EUA for baricitinib.

Recommendations:
Given the data that is currently available, it is recommended to not make changes to the YNHHS COVID-19 Adult Treatment Algorithm at this time. Dexamethasone will continue to be recommended with remdesivir as the therapy for COVID-19 inpatients who have a RA O2 sat of $\leq$ 95% and require supplemental oxygen.

Baricitinib will not be added to the YNHHS COVID-19 Adult Treatment Guideline at this time.
As additional data become available, the use baricitinib may be re-evaluated as we have done with all of our COVID-19 therapies to date.

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References:

1. Anonymous. Fact sheet for healthcare providers Emergency Use Authorization (EUA) of baricitinib. http://pi.lilly.com/eua/baricitinib-eua-factsheet-hcp.pdf

2. RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, Staplin N, Brightling C, Ustianowski A, Elmahi E, Prudon B, Green C, Felton T, Chadwick D, Rege K, Fegan C, Chappell LC, Faust SN, Jaki T, Jeffery K, Montgomery A, Rowan K, Juszczak E, Baillie JK, Haynes R, Landray MJ. Dexamethasone in Hospitalized Patients with Covid-19 - Preliminary Report. NEJM 2020; :NEJMoa2021436. doi: 10.1056/NEJMoa2021436.