FDA broadens existing emergency use of Lilly and Incyte's baricitinib in patients hospitalized with COVID-19 requiring oxygen

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Baricitinib now authorized for emergency use as monotherapy

INDIANAPOLIS, July 29, 2021 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Incyte (NASDAQ:INCY) announced today the U.S. Food and Drug Administration (FDA) has broadened the Emergency Use Authorization (EUA) for baricitinib to allow for treatment with or without remdesivir, whereas the EUA was previously restricted to use only in combination with remdesivir. The EUA now provides for the use of baricitinib for treatment of COVID-19 in hospitalized adults and pediatric patients two years of age or older requiring supplemental oxygen, non-invasive or invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO).

"Baricitinib in combination with remdesivir has already provided many people with a treatment option that could help prevent progression to ventilation or death and increase recovery speed for certain hospitalized patients with COVID-19 under its currently authorized use," said Ilya Yuffa, senior vice president and president of Lilly Bio-Medicines. "Today's FDA action provides physicians additional treatment regimen options for baricitinib to continue to meet the urgent medical needs posed by this pandemic. Based on the increasing body of evidence, we are confident in the potential of baricitinib as an important treatment for the hospitalized COVID-19 patient population requiring supplemental oxygen."

The FDA based today's decision on data from the Phase 3 COV-BARRIER study, announced April 8, 2021. COV-BARRIER was a randomized, double-blind, placebo-controlled study of hospitalized patients comparing baricitinib 4 mg once daily plus standard of care versus placebo plus standard of care. Patients could remain on background standard of care, as defined per local guidelines, including antimalarials, antivirals, corticosteroids, and/or azithromycin. The most frequently used therapies were corticosteroids (79% of patients, mostly dexamethasone) and remdesivir (19% of patients). While the composite primary endpoint of COV-BARRIER, which was defined as a difference in the estimated proportion of participants progressing to non-invasive ventilation including high flow oxygen or invasive mechanical ventilation (including ECMO) or death by Day 28, did not meet statistical significance, baricitinib-treated patients (27.8%) were less likely than those receiving standard of care (30.5%) to progress to ventilation or death (odds ratio [OR]: 0.85; 95% CI: 0.67, 1.08; p=0.180). A pre-specified key secondary endpoint showed baricitinib, in addition to standard of care, meaningfully reduced the risk of death by 39 percent by Day 28 when compared to standard of care alone (n/N: 62/764 [8.1%] baricitinib, 101/761 [13.3%] placebo; [estimated difference in Day 28 probability of mortality = -4.9% (95% CI: -8.0%, -1.9%); hazard ratio [HR] = 0.56 (95% CI: 0.41, 0.77)]. No new safety signals potentially related to the use of baricitinib were identified. The study findings have been submitted to a peer-reviewed journal for future print publication.

The initial EUA was based on data from the Adaptive COVID-19 Treatment Trial (ACTT-2), a randomized double-blind, placebo-controlled study to evaluate the efficacy and safety of baricitinib in combination with remdesivir versus placebo with remdesivir in hospitalized patients with or without oxygen requirements conducted by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH). Data supporting the initial EUA included the primary endpoint of median time to recovery, which was seven days for baricitinib plus remdesivir compared to eight days for placebo plus remdesivir (HR: 1.15; 95% CI: 1.00, 1.31; p=0.047). Secondary endpoints included the proportion of patients who died or progressed to non-invasive ventilation/high-flow oxygen or invasive mechanical ventilation by Day 29, which was lower in baricitinib plus remdesivir (23%) compared to placebo plus remdesivir (28%) (OR: 0.74; 95% CI: 0.56, 0.99; p=0.039), and the proportion of patients who died by Day 29 was 4.7 percent (24/515) for baricitinib plus remdesivir versus 7.1 percent (37/518) for placebo plus remdesivir (Kaplan Meier estimated difference in Day 29 probability of mortality: -2.6% [95% CI: -5.8%, 0.5%]).

"Recent clinical data have helped improve our understanding of the potential role of baricitinib in the treatment of certain hospitalized patients with COVID-19 and the broadened EUA represents a critical step in fighting the pandemic," said E. Wesley Ely, M.D., M.P.H., professor of medicine and co-director of the Critical Illness, Brain Dysfunction, and Survivorship (CIBS) Center at Vanderbilt University Medical Center and co-principal investigator of COV-BARRIER.

The FDA grants emergency use authorization to provide availability of a medicine that may help diagnose, treat or prevent a life-threatening disease when no adequate and approved alternatives are available. This use of baricitinib is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use, unless the declaration is terminated or authorization revoked sooner. The authorization is temporary and does not replace the formal review and approval process. In the U.S., baricitinib has not been approved by the FDA to treat COVID-19, and the efficacy, safety and optimal duration of treatment of baricitinib for COVID-19 has not been established. Evaluation of baricitinib's efficacy and safety as a treatment for COVID-19 is ongoing in clinical trials. Essential safety information on the authorized emergency use of baricitinib includes warnings related to serious infections, thrombosis, abnormal laboratory values, vaccinations and hypersensitivity. Serious side effects observed in COVID-19 patients include serious venous thrombosis and serious infections. Additional safety information can be viewed below.

In December 2020, Lilly initiated an addendum to the COV-BARRIER study to evaluate baricitinib in mechanically ventilated patients (ordinal scale 7) at baseline. The study is currently ongoing with data expected in the coming months. In addition, baricitinib is being tested in the NIH-led ACTT-4 study, UK's RECOVERY Trial, EU-SolidAct Trial and other investigator-initiated research to further our understanding of how baricitinib may help certain hospitalized COVID-19 patients.

Under the EUA, inpatient pharmacies in the U.S. may order 1-mg and 2-mg tablets of baricitinib through Lilly's authorized distributors. More details about the baricitinib EUA are available here or by contacting Lilly's 24-hour support line at 1-855-LillyC19 (1-855-545-5921).

Lilly is committed to collaborating with governments, hospitals and payers to provide access to baricitinib for certain hospitalized patients with COVID-19. To date, more than 325,000 patients globally are estimated to have been treated with baricitinib for COVID-19.

Baricitinib is an oral JAK inhibitor discovered by Incyte and licensed to Lilly. For media resources, including product images and fact sheets, please click here.

Authorized Use Under the EUA and Important Safety Information for baricitinib (in the United States) for COVID-19

Baricitinib is authorized for use under an Emergency Use Authorization (EUA) for treatment of COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

Baricitinib has not been approved for the treatment of COVID-19, but has been authorized for emergency use by the FDA. Baricitinib is authorized under an EUA only for the duration of the declaration that circumstances exist justifying the authorization of the EUA of baricitinib under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization revoked sooner.

For more information about the authorized use of baricitinib in COVID-19 and mandatory requirements of the EUA, please see the FDA Letter of Authorization, Fact Sheet for Healthcare Providers and Fact Sheet for Patients, Parents and Caregivers (English) (Spanish).

Important Safety Information about baricitinib for COVID-19
The following provides essential safety information on the unapproved use of baricitinib under the Emergency Use Authorization.

Warnings

Serious Infections: There is limited information regarding use of baricitinib in patients with COVID-19 and concomitant active serious infections.

Serious infections have occurred in patients receiving baricitinib. Avoid the use of baricitinib with known active tuberculosis. Consider if the potential benefits outweigh the potential risks of baricitinib treatment in patients with active serious infections other than COVID-19 or chronic/recurrent infections.

Thrombosis: In hospitalized patients with COVID-19, prophylaxis for venous thromboembolism is recommended unless contraindicated. If clinical features of deep vein thrombosis or pulmonary embolism occur, patients should be evaluated promptly and treated appropriately.

Abnormal Laboratory Values: There is limited information regarding use of baricitinib in patients with COVID-19 and any of the following clinical findings: absolute neutrophil count (ANC) <1000 cells/mm^3, absolute lymphocyte count (ALC) <200 cells/mm^3, and hemoglobin <8 g/dL.

Evaluate estimated glomerular filtration rate (eGFR), liver enzymes, and complete blood count at baseline and thereafter according to local patient management practice. Monitor closely when treating patients with abnormal baseline and post-baseline laboratory values. Follow dose adjustments as recommended in the Fact Sheet for Healthcare Providers for patients with abnormal renal, hematological and hepatic laboratory values. Manage patients according to routine clinical guidelines.

Vaccinations: Avoid use of live vaccines with baricitinib.

Hypersensitivity: If a serious hypersensitivity occurs, discontinue baricitinib while evaluating the potential causes of the reaction.

See **Warnings and Precautions** in the FDA-approved full Prescribing Information and Medication Guide for additional information on risks associated with longer-term treatment with baricitinib.

Serious Side Effects

Serious venous thrombosis, including pulmonary embolism, and serious infections have been observed in COVID-19 patients treated with baricitinib and are known adverse drug reactions of baricitinib.

Adverse Reactions

In the COVID-19 clinical trials, adverse drug reactions in the safety population occurring in ≥ 1% of patients treated with baricitinib were alanine aminotransferase (ALT) ≥3 x upper limit of normal (ULN) (18.0%), aspartate aminotransferase (AST) ≥3 x ULN (11.5%), thrombocytosis >600,000 cells/mm^3 (8.2%), creatine phosphokinase (CPK) >5 x ULN (3.7%), neutropenia <1000 cells/mm^3 (2.2%), deep vein thrombosis (1.5%), pulmonary embolism (1.4%), and urinary tract infection (1.3%).

Use in Specific Populations

Pregnancy: Baricitinib should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus.

Renal Impairment: There are limited data for baricitinib in patients with severe renal impairment. Baricitinib is not recommended for patients who are on dialysis, have end-stage renal disease, or have acute kidney injury.

Hepatic Impairment: Baricitinib has not been studied in patients with severe hepatic impairment. Baricitinib should only be used in patients with severe hepatic impairment if the potential benefit outweighs the potential risk.

Please see Fact Sheet for Healthcare Providers and Fact Sheet for Patients, Parents and Caregivers (English) or Fact Sheet for Patients, Parents and Caregivers (Spanish).

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About OLUMIANT ® (baricitinib)

OLUMIANT, a once-daily, oral JAK inhibitor was discovered by Incyte and licensed to Lilly. It is approved in the U.S. and more than 75 countries as a treatment for adults with moderate to severe rheumatoid arthritis. It is also approved for the treatment of certain hospitalized patients with COVID-19 in Japan. The U.S. FDA-approved labeling for OLUMIANT includes a Boxed Warning for Serious Infections, Malignancy, and Thrombosis. See the full

Prescribing Information here.

In December 2009, Lilly and Incyte announced an exclusive worldwide license and collaboration agreement for the development and commercialization of baricitinib and certain follow-on compounds for patients with inflammatory and autoimmune diseases.

About Lilly's COVID-19 Efforts

Lilly is bringing the full force of its scientific and medical expertise to attack the coronavirus pandemic around the world. Existing Lilly medicines are being studied to understand their potential in treating complications of COVID-19, and the company is collaborating with partner companies to discover and develop novel antibody treatments for COVID-19. Click here for resources related to Lilly's COVID-19 efforts.

About Eli Lilly and Company

Lilly is a global health care leader that unites caring with discovery to create medicines that make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at lilly.com and lilly.com/newsroom.

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About Incyte

Incyte is a Wilmington, Delaware-based, global biopharmaceutical company focused on finding solutions for serious unmet medical needs through the discovery, development and commercialization of proprietary therapeutics. For additional information on Incyte, please visit Incyte.com and follow @Incyte.

Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about OLUMIANT (baricitinib) as a potential treatment for patients with COVID-19 and reflects Lilly's and Incyte's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of research, development and commercialization. Among other things, there can be no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with the results to date, that OLUMIANT will receive additional regulatory approvals or authorizations or be commercially successful, that OLUMIANT will be safe and effective as a treatment or successful preventative therapy for COVID-19, or that we can provide an adequate supply of OLUMIANT in all circumstances. For further discussion of these and other risks and uncertainties, see Lilly's and Incyte's most recent respective Form 10-K, Form 10-Q, and Form 8-K filings with the United States Securities and Exchange Commission. Except as required by law, Lilly and Incyte undertake no duty to update forward-looking statements to reflect events after the date of this release.

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