FDA Accepts For Review Supplemental New Drug Application (sNDA) for RECARBRIO™ (imipenem, cilastatin, and relebactam) for the Treatment of Adults with Hospital-Acquired and Ventilator-Associated Bacterial Pneumonia (HABP/VABP)

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Filing Receives Priority Review

KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has accepted for review a supplemental New Drug Application (sNDA) for RECARBRIO™ (imipenem, cilastatin, and relebactam) to treat adult patients with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) caused by certain susceptible Gram-negative microorganisms. The application has received Priority Review by the FDA, and the Prescription Drug User Fee Act (PDUFA) date for the sNDA is June 4, 2020.

“This submission reinforces Merck’s continued dedication to researching and developing potential antibiotic treatment options which address unmet medical needs,” said Dr. Nicholas Kartsonis, senior vice president, clinical research, infectious diseases and vaccines, Merck Research Laboratories. “We are unwavering in our commitment to evaluate treatments for infections caused by certain Gram-negative pathogens.”

The submission is based on the results of the pivotal Phase 3 RESTORE-IMI 2 trial in adult patients with HABP/VABP. The full data has been accepted for presentation at the 30th European Congress of Clinical Microbiology & Infectious Diseases (ECCMID 2020), which will take place in Paris, France, April 18 – 21, 2020.

RECARBRIO was initially approved by the FDA in July 2019 for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis, and complicated intra-abdominal infections (cIAI) caused by susceptible Gram-negative bacteria, in adults who have limited or no alternative treatment options. See full indication below.

About RECARBRIO™ (imipenem 500 mg, cilastatin 500 mg, and relebactam 250 mg)

RECARBRIO is indicated in patients 18 years of age and older who have limited or no alternative treatment options, for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis, caused by the following susceptible Gram-negative microorganisms: Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella pneumoniae, and Pseudomonas aeruginosa.

RECARBRIO is also indicated in patients 18 years of age or older who have limited or no alternative treatment options, for the treatment of complicated intra-abdominal infections (cIAI) caused by the following susceptible Gram-negative microorganisms: Bacteroides caccae, Bacteroides fragilis, Bacteroides ovatus, Bacteroides stercoris, Bacteroides thetaiaotomi, Bacteroides uniformis, Bacteroides vulgatus, Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Fusobacterium nucleatum, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Parabacteroides distasonis and Pseudomonas aeruginosa.

Approval of these indications is based on limited clinical safety and efficacy data for RECARBRIO.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of RECARBRIO and other antibacterial drugs, RECARBRIO should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information is available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Selected Safety Information for RECARBRIO

Hypersensitivity Reactions: RECARBRIO is contraindicated in patients with a history of known severe hypersensitivity (severe systemic allergic reaction such as anaphylaxis) to any component of RECARBRIO. Serious and occasionally fatal
hypersensitivity (anaphylactic) reactions have been reported in patients receiving therapy with beta lactams. Before initiating therapy with RECARBRIO, careful inquiry should be made concerning previous hypersensitivity reactions to carbapenems, penicillins, cephalosporins, other beta lactams, and other allergens. If a hypersensitivity reaction to RECARBRIO (imipenem, cilastatin, and relebactam) occurs, discontinue the therapy immediately.

**Seizures and Other Central Nervous System (CNS) Adverse Reactions:** CNS adverse reactions, such as seizures, confusional states, and myoclonic activity, have been reported during treatment with imipenem/cilastatin, a component of RECARBRIO, especially when recommended dosages of imipenem were exceeded. These have been reported most commonly in patients with CNS disorders (e.g., brain lesions or history of seizures) and/or compromised renal function. Anticonvulsant therapy should be continued in patients with known seizure disorders. If CNS adverse reactions including seizures occur, patients should undergo a neurological evaluation to determine whether RECARBRIO should be discontinued.

**Increased Seizure Potential Due to Interaction with Valproic Acid:** Concomitant use of RECARBRIO, with valproic acid or divalproex sodium may increase the risk of breakthrough seizures. Avoid concomitant use of RECARBRIO with valproic acid or divalproex sodium or consider alternative antibacterial drugs other than carbapenems.

**Clostridium difficile-Associated Diarrhea (CDAD):** *Clostridium difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including imipenem/cilastatin plus relebactam, and may range in severity from mild diarrhea to fatal colitis. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against *C. difficile* may need to be discontinued.

**Development of Drug-Resistant Bacteria:** Prescribing RECARBRIO in the absence of a proven or strongly suspected bacterial infection or prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

**Adverse Reactions:** The most frequently reported adverse reactions occurring in ≥2% of patients treated with RECARBRIO were diarrhea (6%), nausea (6%), headache (4%), vomiting (3%), alanine aminotransferase increased (3%), aspartate aminotransferase increased (3%), phlebitis/infusion site reactions (2%), pyrexia (2%), and hypertension (2%).

**Merck's Commitment to Infectious Diseases**

For more than 100 years, Merck has contributed to the discovery and development of novel medicines and vaccines to combat infectious diseases. In addition to a combined portfolio of vaccines and antibacterial, antiviral and antifungal medicines, Merck has multiple programs that span discovery through late-stage development. To learn more about Merck’s infectious diseases pipeline, visit [www.merck.com](http://www.merck.com).

**About Merck**

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world’s most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer’s disease and infectious diseases including HIV and Ebola. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on [Twitter](https://twitter.com/Merck), [Facebook](https://www.facebook.com/Merck), [Instagram](https://www.instagram.com/merck), [YouTube](https://www.youtube.com/user/Merck) and [LinkedIn](https://www.linkedin.com/company/merck).