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AbbVie GK
Eisai Co., Ltd.
EA Pharma Co., Ltd.

Fully Human Anti-TNFα Monoclonal Antibody HUMIRA® Obtains Additional Approval for High-Dose Regimen of Ulcerative Colitis in Adult Patients and for New Regimen in Pediatric Patients

AbbVie GK (Headquarters: Tokyo, President: James Feliciano, "AbbVie"), Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai"), and EA Pharma Co., Ltd. (Headquarters: Tokyo, CEO: Yuji Matsue, "EA Pharma") announced today the additional approval for a high-dose regimen in adult patients with ulcerative colitis and for a new regimen in pediatric patients regarding fully Human Anti-TNFα Monoclonal Antibody HUMIRA® (generic name, adalimumab [recombinant]; “HUMIRA”) .

This approval allows for 40 mg weekly treatment or 80 mg biweekly treatment in addition to conventional 40 mg biweekly treatment as a remission maintenance therapy, which is expected to maintain remission in many patients. Furthermore, by having been added as a treatment option for ulcerative colitis in pediatric patients, it is expected that as the first at-home/self-injectable drug in Japan for pediatric patients with ulcerative colitis, HUMIRA will improve convenience for pediatric patients and their guardians in addition to reducing burdens due to hospital visits.

Ulcerative colitis (UC) is designated as an intractable disease in Japan. It is characterized by intestinal inflammation of unknown cause and subsequent damage to the colonic mucosa that results in erosion (a sore lesion) or ulceration. Patients with UC experience chronic diarrhea and hematochezia, abdominal pain, fever, anemia, etc. These symptoms resolve (remission) and flare up (relapse) repeatedly. It remains a long-term condition that is not adequately controlled in some patients; more treatment options are needed.[1,2] Although the etiology of UC is still unclear, it may be associated with abnormalities in the immune system that protects the body from bacteria and other foreign substances. About 220,000 people suffer from UC in Japan and the number is increasing year by year.[3] Many patients receive a diagnosis of UC in their late 10s to early 30s. The disease rarely develops in childhood, with an estimated prevalence in Japan of 15 per 100,000 between the ages of 0 to 19.[4]
In both adults and pediatric patients, the goal of treatment for UC is achieving long-term maintenance of remission with drug treatment. However, total colectomy may eventually be required in 30% of patients with severe UC. [5]

In Japan, AbbVie is the marketing and manufacturing authorization holder for HUMIRA. Abbvie and Eisai are co-promoting HUMIRA for the indications in the fields of rheumatoid arthritis, plaque psoriasis, arthropathic psoriasis, ankylosing spondylitis, juvenile idiopathic arthritis, uveitis, pustular psoriasis, hidradenitis suppurativa and pyoderma gangrenosum. For the indications in the field of gastrointestinal disease (i.e., Crohn's disease, intestinal Bechet's disease and ulcerative colitis), AbbVie is co-promoting HUMIRA with EA Pharma, commissioned by Eisai for promotion.

AbbVie, Eisai and EA Pharma are committed to make a further contribution to treatment for patients with autoimmune diseases through providing more treatment options to adult and pediatric patients with UC.

Notes to editors

About HUMIRA

HUMIRA® is a fully human anti-TNF-α monoclonal antibody. In Japan, it is approved for "the treatment of rheumatoid arthritis (including inhibition of the progression of structural damage); hidradenitis suppurativa, pyoderma gangrenosum, the treatment of plaque psoriasis, arthritic psoriasis, pustular psoriasis, ankylosing spondylitis, polyarticular juvenile idiopathic arthritis,[*1] intestinal Behçet's disease, and non-infectious intermediate, posterior and panuveitis that are refractory to the conventional therapies, induction and maintenance therapy for moderate to severely active Crohn's disease (limited to patients who have had an inadequate response to conventional therapy), and treatment of moderate to severe ulcerative colitis[*2] (limited to patients who have had an inadequate response to conventional therapy)."

[*1] HUMIRA for Subcutaneous Injection 20 mg Syringe 0.2 mL is approved. HUMIRA for Subcutaneous Injection 80 mg Syringe 0.8 mL and HUMIRA for Subcutaneous Injection 80 mg Pen 0.8 mL are yet to be approved

[*2] HUMIRA for Subcutaneous Injection 20 mg Syringe 0.2 mL is approved only for pediatric patients.

Nonproprietary name: Adalimumab <recombinant>

Brand name: Fully Human Anti-TNF-α Monoclonal Antibody "HUMIRA for Subcutaneous Injection 20 mg Syringe 0.2 mL; HUMIRA for Subcutaneous Injection 40 mg Syringe 0.4 mL; HUMIRA for Subcutaneous Injection 80 mg Syringe 0.8 mL; HUMIRA for Subcutaneous Injection 40 mg Pen 0.4 mL; and HUMIRA for Subcutaneous Injection 80 mg Pen 0.8 mL"

Details of the above approval (Underlined text indicates newly approved dosage and administration)

Dosage and administration (only the section of UC is excerpted.)

Adults:

The usual initial dose of adalimumab (recombinant) is 160 mg administered by subcutaneous injection, which is followed by 80 mg administered 2 weeks after the initial

dose. After 4 weeks of the initial dose, 40 mg of adalimumab is subcutaneously injected once every 2 weeks. However, after 4 weeks of the initial dose, adalimumab can be subcutaneously injected at 40 mg once weekly or at 80 mg once every 2 weeks, depending on the patient's condition.

Pediatric patients:
For pediatric patients weighing 40 kg or more, the usual initial dose of adalimumab (recombinant) is 160 mg administered by subcutaneous injection, which is followed by 80 mg administered 1 week and 2 weeks after the initial dose. After 4 weeks of the initial dose, adalimumab is subcutaneously injected at 40 mg once weekly or at 80 mg once every 2 weeks.
For pediatric patients weighing 25 kg or more and less than 40 kg, the usual initial dose of adalimumab (recombinant) is 80 mg administered by subcutaneous injection, which is followed by 40 mg administered 1 week and 2 weeks after the initial dose. After 4 weeks of the initial dose, adalimumab is subcutaneously injected at 20 mg once weekly or at 40 mg once every 2 weeks.
For pediatric patients weighing 15 kg or more and less than 25 kg, the usual initial dose of adalimumab (recombinant) is 40 mg administered by subcutaneous injection, which is followed by 20 mg administered 1 week and 2 weeks after the initial dose. After 4 weeks of the initial dose, adalimumab is subcutaneously injected at 20 mg every 2 weeks.

About AbbVie

AbbVie's mission is to discover and deliver innovative medicines that solve serious health issues today and address the medical challenges of tomorrow. We strive to have a remarkable impact on people's lives across several key therapeutic areas: immunology, oncology, neuroscience, eye care, virology, women's health and gastroenterology, in addition to products and services across its Allergan Aesthetics portfolio. For more information about AbbVie, please visit us at www.abbvie.com. Follow @abbvie on Twitter, Facebook, Instagram, YouTube and LinkedIn.

About Eisai

Eisai Co., Ltd. is a leading global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our human *health care (hhc)* philosophy. With approximately 10,000 employees working across our global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our *hhc* philosophy by delivering innovative products to address unmet medical needs, with a particular focus in our strategic areas of Neurology and Oncology. For more information about Eisai Co., Ltd., please visit www.eisai.com.

About EA Pharma

EA Pharma Co., Ltd., a subsidiary of Eisai Co., Ltd. for gastrointestinal disease area, was established in April 2016 by integration of the gastrointestinal business unit with more than 60 year's history of the Eisai Group and the gastrointestinal business unit of the Ajinomoto Group having amino acid as its business core. EA Pharma Co., Ltd., is a gastrointestinal specialty pharmaceutical company with a full value chain covering R&D, production & logistics and sales & marketing.

For further information on EA Pharma Co., Ltd., please visit https://www.eapharma.co.jp/en.

1. Australian Crohn's and Colitis Association (ACCA). The Economic Costs of Crohn's Disease and Ulcerative Colitis. 2007 Jun.
2. Romano C, Syed S, Valenti S, Kugathasan S. Management of acute severe colitis in children with ulcerative colitis in the biologics era. *Pediatrics*. 2016 May; 137(5):e20151184. doi: 10.1542/peds.2015-1184.
3. Research committee of inflammatory bowel disease, Research program on rare and intractable diseases, Health, Labour and Welfare Sciences Research Grants. For the patients of ulcerative colitis, the basic knowledge of treatments. Revised in 2020, March.
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5. Gajendran M, Loganathan P, Jimenez G, et al. A comprehensive review and update on ulcerative colitis. *Dis Mon.* 2019 Dec; 65(12):100851.

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