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# JANSSEN RECEIVES CHMP POSITIVE OPINION FOR STELARA® (USTEKINUMAB) RECOMMENDING APPROVAL FOR THE TREATMENT OF MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS IN THE EU

*If approved, ustekinumab will be the first interleukin (IL)-12/23 inhibitor licensed for ulcerative colitis*

**BEERSE, BELGIUM, 26 July, 2019** – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending marketing authorisation in the European Union (EU) for the use of ustekinumab for the treatment of adult patients with moderately to severely active ulcerative colitis (UC), who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic or have medical contraindications to such therapies.[1]

UC is a serious and chronic immune-mediated inflammatory disease of the large intestine, affecting 2.6 million people in Europe, for which there is currently no cure.[2] Symptoms vary but may include abdominal cramps, bloody diarrhoea and

fatigue, which can be painful, embarrassing and debilitating, placing a significant burden on people with the condition.[3,4] For up to two thirds of people with UC, current treatments are not completely successful or complications may arise.[5,6,7,8]

"Ulcerative colitis is a particularly disruptive, life-long condition with unpredictable flares that can negatively impact every aspect of patients' lives. More treatments that offer long-term relief are urgently needed as, despite currently available treatment options, many people with the condition continue to suffer symptoms," said Jaime Oliver, MD, Janssen Therapeutic Area Lead, Immunology, Europe, Middle East & Africa, Cilag GmbH International. "We welcome the CHMP's positive opinion on ustekinumab, which brings us one step closer to making this important medicine available for people with ulcerative colitis in Europe, potentially offering them a chance of durable remission and symptomatic relief."

Ustekinumab is the first treatment to selectively target the IL-12/IL-23 pathway, an important therapeutic target in UC.[9] The CHMP adopted the opinion based on data from the pivotal Phase 3 UNIFI trial programme which demonstrated ustekinumab's efficacy as a treatment option for patients with moderately to severely active UC who demonstrated an inadequate response to or were unable to tolerate conventional (e.g. corticosteroids or immunomodulators) or biologic (tumour necrosis factor [TNF]-alpha antagonists or vedolizumab) therapies:[10]

- As early as week 2 of an eight-week Induction study (UNIFI-I), a higher proportion of patients who received a single intravenous (IV) infusion dose of ustekinumab had no bleeding or achieved normal stool frequency as compared with those randomised to placebo. The primary endpoint (clinical remission[a] as defined by Mayo score[b]) and all key secondary endpoints were significant for ustekinumab vs. placebo (multiplicity controlled).[11]

[a] Clinical remission is Mayo score ≤2 with no individual subscore >1.

[b] Mayo score is designed to measure the severity of UC, with a higher score indicating more severe disease activity and gives a score from 0–12 points.

- For the recommended dose of ustekinumab 62 percent of patients achieved clinical response[c] compared with 31 percent of patients receiving placebo ($p<0.001$) at week 8.
    - Full results of the UNIFI-I study were previously shared during a plenary session at the American College of Gastroenterology Annual Scientific Meeting and in a press release on 9 October, 2018.[12]
- All patients who were randomised into the 44-week Maintenance study (UNIFI-M) were induction responders to IV ustekinumab. Among patients subsequently randomised to receive subcutaneous ustekinumab (q8w or q12w) a significantly greater percentage achieved clinical remission vs. initial responders randomised to placebo.[10]
    - The sustained effect of ustekinumab was observed in those in the ustekinumab q8w and q12w groups compared to placebo (57.4 percent and 48.3 percent respectively, vs. 35.4 percent, $p<0.001$ and $p=0.010$, respectively), as measured by durable partial Mayo remission[d] (partial Mayo remission at ≥80 percent of all visits and at the last visit).
    - Full results of the UNIFI-M study were previously presented during plenary session at 14th Congress of the European Crohn's and Colitis Organisation and shared in a press release on 11 March, 2019.[13]

Ustekinumab has demonstrated a favourable safety profile in UC where trials show the treatment is well tolerated. In the primary randomised population of the Induction and Maintenance studies, a similar proportion of patients in the ustekinumab and placebo groups experienced adverse events (AE), serious AEs, infections and serious infections through to week 44. During the UNIFI Induction phase one death from an oesophageal varices hemorrhage was reported, and no malignancies, opportunistic infections or tuberculosis were reported. During the UNIFI Maintenance phase, no deaths and two malignancies other than

[c] Clinical response was defined as a decrease from baseline in the Mayo score by ≥30 percent and ≥3 points, with either a decrease from baseline in the rectal bleeding subscore ≥1 or a rectal bleeding subscore of 0 or 1.
[d] Partial Mayo remission = Mayo score ≤2. The partial Mayo score includes stool frequency, rectal bleeding, and physician's global assessment subscores and ranges from 0 to 9.

non-melanoma skin cancer (NMSC) were reported (90 mg ustekinumab q8w: colon cancer [n=1]; 90 mg ustekinumab q12w: papillary renal cell carcinoma [n=1]). There was one patient-reported NMSC in the 90 mg ustekinumab q12w group (2 squamous cell carcinoma events).[10,11]

Following this positive opinion, a final decision from the European Commission (EC) regarding its marketing authorisation is expected later this year.

#ENDS#

**About the UNIFI Programme**

UNIFI is a Phase 3 programme, designed to evaluate the safety and efficacy of ustekinumab induction and maintenance dosing for the treatment of moderately to severely active UC in adults who demonstrated an inadequate response to, or were unable to tolerate, conventional (i.e. corticosteroids, immunomodulators) or biologic (i.e. one or more tumour necrosis factor [TNF]-alpha antagonists and/or vedolizumab) therapies. Both the Induction and Maintenance studies were randomised, double-blind, placebo-controlled, parallel group, multicentre studies. The Induction study was of at least 8 weeks duration for participants, who were each administered a single intravenous (IV) ustekinumab infusion.

Participants achieving clinical response in the induction study were eligible to enter into the Maintenance study. The Maintenance study was 44 weeks in duration, representing a total treatment duration of 1 year. The primary endpoint of the Induction study was clinical remission at week 8, and the primary endpoint for the Maintenance study was clinical remission at week 44. After completion of the Maintenance study, eligible participants are continuing in a long-term extension study for an additional three years.[10,11]

## About ulcerative colitis (UC)

UC affects up to 2.6 million people in Europe.[2] It is a chronic disease of the large intestine, also known as the colon, in which the lining becomes inflamed and develops tiny open sores, or ulcers, that produce pus and mucous. UC is the result of an abnormal response by the body's immune system. Symptoms vary, but may include loose and more urgent bowel movements, persistent diarrhoea, abdominal pain, bloody stools, loss of appetite, weight loss and fatigue.[4]

## About STELARA® (ustekinumab)[14]

In the EU, ustekinumab is approved for the treatment of moderate to severe plaque psoriasis in adults who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies including ciclosporin, methotrexate (MTX) or psoralen plus ultraviolet A, and is also indicated for the treatment of moderate to severe plaque psoriasis in adolescent patients aged 12 years and older who are inadequately controlled by or are intolerant to other systemic therapies or phototherapies. In addition, ustekinumab is approved alone or in combination with MTX for the treatment of active psoriatic arthritis in adult patients when the response to previous non-biological disease-modifying antirheumatic drug therapy has been inadequate. In November 2016, the European Commission approved ustekinumab for the treatment of adult patients with moderate to severe Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNF-alpha antagonist or have medical contraindications to such therapies.

The Janssen Pharmaceutical Companies of Johnson & Johnson maintain exclusive worldwide marketing rights to STELARA®. In December 2018, a Group Type II Variation Application to the EMA was submitted, which seeks approval of ustekinumab for the treatment of adults with moderate to severe UC.

**Important safety information**

Please refer to the full Summary of Product Characteristics for full prescribing information for ustekinumab:
https://www.medicines.org.uk/emc/product/7638/smpc

**About the Janssen Pharmaceutical Companies of Johnson & Johnson**

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com/EMEA. Follow us at www.twitter.com/JanssenEMEA.

Janssen-Cilag International NV, the marketing authorisation holder for STELARA® in the EU, and Cilag GmbH International are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

**Cautions Concerning Forward-Looking Statements**

*This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding regulatory approvals and benefits of a new treatment option. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialise, actual results could vary materially from the expectations and projections of Janssen-Cilag International NV and Cilag GmbH International. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and*

*delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behaviour and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended 30 December, 2018, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.*

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## References


[1] European Medicines Agency. Stelara opinion from Committee for Medicinal Products for Human Use (CHMP) 25 July 2019. Available at: https://www.ema.europa.eu/en/medicines/human/summaries-opinion/stelara (Last accessed July 2019).

[2] Ng SC, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *Lancet* 2017;390:2769-78

[3] Crohn's & Colitis Foundation. 'Living with Ulcerative Colitis' leaflet. Available at: https://www.crohnscolitisfoundation.org/sites/default/files/legacy/assets/pdfs/living-with-ulcerative.pdf (Last accessed July 2019).

[4] Crohn's & Colitis UK. What is Ulcerative Colitis? Available at: https://www.crohnsandcolitis.org.uk/about-inflammatory-bowel-disease/ulcerative-colitis (Last accessed July 2019).

[5] Lopez-Sanroman A, et al. Perceived emotional and psychological impact of ulcerative colitis on outpatients in Spain: UC-LIFE survey. Dig Dis Sci 2017;62:207-216.

[6] Rubin D, et al. The impact of ulcerative colitis on patients' lives compared to other chronic diseases: A patient survey. Dig Dis Sci 2010;55:1044–1052.

[7] Devlen J, et al. The burden of inflammatory bowel disease: A patient-reported qualitative analysis and development of a conceptual model. Inflamm Bowel Dis 2014:20:545–552.

[8] Lonnfors S, et al. IBD and health-related quality of life – Discovering the true impact. J Crohn's Colitis 2014;8:1281–1286.

[9] Toussirot E. The IL23/Th17 pathway as a therapeutic target in chronic inflammatory diseases. *Inflamm Allergy Drug Targets* 2012;11(2):159–68.

[10] Sandborn WJ, *et al.* Abstract OP37: Efficacy and safety of ustekinumab as maintenance therapy in ulcerative colitis: Week 44 results from UNIFI. ECCO 2019.

[11] Sands BE, Sandborn WJ, Panaccione R et al. Safety and efficacy of ustekinumab induction therapy in patients with moderate to severe ulcerative colitis: results from the Phase 3 UNIFI study [abstract]. Presented at the American College of Gastroenterology (ACG) Annual Scientific Meeting, 5–10 October 2018; Philadelphia, Pennsylvania.
[12] Johnson & Johnson. New Phase 3 Data Show Single Dose of Stelara® (Ustekinumab) Induces Clinical Remission and Response in Adults with Moderate to Severe Ulcerative Colitis. Available at: https://www.jnj.com/new-phase-3-data-show-single-dose-of-stelara-ustekinumab-induces-clinical-remission-and-response-in-adults-with-moderate-to-severe-ulcerative-colitis (Accessed July 2019).
[13] Johnson & Johnson. New Phase 3 Stelara® (Ustekinumab) Data Show Positive Results as Maintenance Therapy in Adults with Moderate to Severe Ulcerative Colitis. Available at: https://www.jnj.com/new-phase-3-stelara-ustekinumab-data-show-positive-results-as-maintenance-therapy-in-adults-with-moderate-to-severe-ulcerative-colitis (Last accessed July 2019).
[14] European Medicines Agency. 2018. https://www.ema.europa.eu/en/documents/product-information/stelara-epar-product-information_en.pdf (Accessed July 2019).