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Media Enquiries:
Natalie Buhl
Mobile: +353 (0)85-744-6696
Email: nbuhl@its.jnj.com

Investor Relations:
Lesley Fishman
Phone: +1 732-524-3922

Joseph J. Wolk
Phone: +1 732-524-1142

EPREX® (epoetin alfa) Marketing Authorisation Extended to Include Treatment of Symptomatic Anaemia in Patients with Low or Intermediate-1-Risk Myelodysplastic Syndromes

French Health Authority ANSM grants approval in the Mutual Recognition Procedure; the relevant health authorities are required to implement the new indication within 30 days

BEERSE, BELGIUM, 24 March, 2017 – Janssen-Cilag International NV today announced the French health authority Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM), has approved EPREX® (epoetin alfa) for the treatment of symptomatic anaemia (haemoglobin concentration of ≤10 g/dL) in adults with low- or intermediate-1-risk primary myelodysplastic syndromes (MDS) who have low serum erythropoietin (<200 mU/mL).

The ANSM acted as the reference Member State within the Mutual Recognition Procedure (MRP), which has now concluded and resulted in an extension to the marketing authorisation for EPREX. Upon the conclusion of the extension procedure within the MRP the other European health authorities are required to implement the new indication into their national Summary of Product Characteristics (SmPC) and package leaflet within 30 days.

This approval was based on results from the international Phase 3, randomised, double-blind, placebo-controlled, multicentre study, EPOANE 3021 along with three registry studies from across Europe. EPOANE 3021 demonstrated the efficacy and safety of EPREX® as a treatment for anaemia, in adult patients with low or intermediate-1-risk MDS, as classified by an International Prognostic Scoring System (IPSS).[1] EPOANE 3021 data were

presented at the 21st Annual Congress of the European Hematology Association (EHA) in 2016. Janssen have data exclusivity for one year.

”This announcement is extremely welcome, as there have been no erythropoiesis stimulating agents approved to treat anaemia in patients with MDS until now, despite the fact that it contributes significantly to their symptoms,” said Pierre Fenaux, M.D., PhD., principal investigator of EPOANE 3021, and Professor of Hematology, Hôpital St Louis/Université, Paris, France.

“We are pleased with the outcome of the MRP which brings us one step closer to offering a new treatment option to patients with MDS-related anaemia throughout Europe. This approval is a testament to our long-standing commitment to patients living with cancer,” said Dr Catherine Taylor, Haematology Therapeutic Area Lead, Janssen Europe, the Middle East and Africa (EMEA).

#ENDS#

About the EPOANE 3021 Study[1]
EPOANE 3021 was a randomised, double-blind, placebo-controlled, multicentre clinical trial investigating the efficacy and safety of EPREX® (epoetin alfa) as a treatment for anaemia, in adult patients with low or intermediate-1-risk myelodysplastic syndromes (MDS), as classified by an International Prognostic Scoring System (IPSS). Results demonstrated that 31.8 percent of patients treated with epoetin alfa achieved the primary endpoint of erythroid response versus 4.4 percent of placebo patients ($p<0.001$). An ad hoc analysis, accounting for the dose adjustments as per the protocol, confirmed a statistically significant erythroid response for the epoetin alfa arm, with 45.9 percent of epoetin alfa patients, versus 4.4 percent of placebo patients achieving an erythroid response ($p<0.001$). Median erythroid response duration for epoetin alfa patients was 197 days. The number of patients needing transfusion in the epoetin alfa arm steadily decreased from 51.8 percent in the eight weeks prior to baseline, to 24.7 percent by week-24. Transfusion need remained unchanged in the placebo patients (48.9 percent - 54.1 percent) over the same interval. Time to first transfusion was longer in the epoetin alfa group ($p=0.046$). Epoetin alfa demonstrated a statistically significant improvement of quality of life in responding patients.

There were no new safety signals for epoetin alfa from the study and safety findings are consistent with the known safety profile of epoetin alfa. The proportion of patients with at least one treatment emergent adverse event was numerically higher in the placebo group compared with the epoetin alfa group (88.9 percent vs. 77.6 percent). Drug discontinuation due to adverse events was 10.6 percent in the epoetin alfa group versus 13.3 percent in placebo. Four patients in the epoetin alfa arm (4.7 percent) and none in placebo reported a thrombovascular event. There were four fatal outcomes in the epoetin alfa arm versus one in the placebo arm; none were reported to be related to the study drug. During the study, progression to acute myeloid leukaemia (AML) was similar between groups (3.5 percent in epoetin alfa; 4.4 percent in placebo).

About Myelodysplastic Syndromes
Myelodysplastic syndromes (MDS) are a group of diverse bone marrow disorders in which the bone marrow does not produce enough healthy blood cells.[2] The low numbers of normal blood cells (cytopenias) eventually cause symptoms, including infection, anaemia, spontaneous bleeding, or easy bruising.[2,3] The natural course of MDS is highly variable, with overall survival ranging from a few weeks to several years.[4] MDS is primarily a disease of the elderly with a median age at diagnosis of 70 years, but it can affect younger patients as well.[4] The incidence in Europe is about four cases per 100,000 per year, reaching 40-50 per 100,000 in patients aged 70 years and over.[4]

Approximately 60-80 percent of patients with MDS experience symptomatic anaemia, which can significantly reduce quality of life and often requires repeated blood transfusions.[5] Controlling anaemia and improving quality of life are the principal aims of treatment in lower risk MDS patients.[4] At present, blood transfusions are currently the only approved treatment option; however these lead to iron overload, which is associated with significant morbidity and mortality.[4,5]

About EPREX®
EPREX® (epoetin alfa) is an erythreopoiesis-stimulating agent (ESA) that works by stimulating the production of red blood cells (RBCs).[6] ESAs are an important treatment option for patients with certain types of anaemia, including chemotherapy-induced anaemia and anaemia due to chronic kidney disease. Without ESAs, patients with certain types of anaemia may require regular blood transfusions to maintain RBCs at concentrations necessary to sustain normal oxygen levels throughout the body.[4]

EPREX is currently indicated for the treatment of:[6]
- Symptomatic anaemia associated with chronic renal failure (CRF):
  - In adult and paediatric patients aged 1 to 18 years on haemodialysis and adult patients on peritoneal dialysis.
  - In adults with renal insufficiency not yet undergoing dialysis for the treatment of severe anaemia of renal origin accompanied by clinical symptoms in patients.
- Adults receiving chemotherapy for solid tumours, malignant lymphoma or multiple myeloma, and at risk of transfusion as assessed by the patient's general status (e.g. cardiovascular status, pre-existing anaemia at the start of chemotherapy) for the treatment of anaemia and reduction of transfusion requirements.
- Adults in a predonation programme to increase the yield of autologous blood. Treatment should only be given to patients with moderate anaemia (haemoglobin concentration range between 10 to 13 g/dl [6.2 to 8.1 mmol/l], no iron deficiency) if blood saving procedures are not available or insufficient when the scheduled major elective surgery requires a large volume of blood (4 or more units of blood for females or 5 or more units for males).
- Non-iron deficient adults prior to major elective orthopaedic surgery having a high perceived risk for transfusion complications to reduce exposure to allogeneic blood transfusions. Use should be restricted to patients with moderate anaemia (e.g. haemoglobin concentration range between 10 to 13 g/dl) who do not have an autologous predonation programme available and with expected moderate blood loss (900 to 1,800 ml).

About the Mutual Recognition Procedure after the Granting of a Marketing Authorisation

The Mutual Recognition Procedure (MRP) is based on the principle of the mutual recognition by EU Member States of their respective national marketing authorisations. An

application for a marketing authorisation within the MRP may be addressed to one or more Member States. The submitted dossier must be identical to the one in the Member State that already granted a marketing authorisation. This Member State is called Reference Member State (RMS). Any subsequent changes to the marketing authorisation that occur post authorisation must be submitted to all Member States that are part of the MRP and will be evaluated by the RMS.[7]

This application was submitted under the Variations Regulation which governs the procedures for the amendment of the decision granting the marketing authorisation and of the technical dossier.[8] The evaluation procedure of post authorisation changes, including a new variation, undertaken by the RMS may take up to 120 days, and ends with the positive outcome of the procedure. Following the closure all involved Member States then have 30 days to implement the decision into the SmPC and package leaflet.[7]

About the Janssen Pharmaceutical Companies
At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science. We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at http://www.janssen.com/emea. Follow us at www.twitter.com/janssenEMEA.

Cautions Concerning Forward-Looking Statements
This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding an extended marketing authorisation for EPREX® (epoetin alfa). 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/or Johnson & Johnson. 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 behavior and spending patterns or financial distress 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 January 1, 2017, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," 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 or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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