European Medicines Agency
Pre-Authorisation Evaluation of Medicines for Human Use

London, 20 November 2008
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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
SUMMARY OF POSITIVE OPINION*
for
STELARA

International Nonproprietary Name (INN): ***ustekinumab***

On 20 November 2008 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion,** recommending to grant a marketing authorisation for the medicinal product Stelara, 45 mg or 90 mg powder for solution for injection, intended for the treatment of moderate to severe plaque psoriasis in adults who have failed to respond to, or who have a contraindication to, or who are intolerant to other systemic therapies including cyclosporine, methotrexate and psoralen plus ultra-violet A light [PUVA]). The applicant for this medicinal product is Janssen-Cilag International NV.

The active substance of Stelara is ustekinumab, an interleukin inhibitor (ATC code: L04AC) and a fully humanised monoclonal antibody, composed of an IgG1 heavy chain isotype and a kappa light chain isotype, that binds with high affinity and specificity to the p40 protein subunit of the human cytokines interleukin (IL)-12 and IL-23. Ustekinumab neutralises IL-12 and IL-23 bioactivity preventing their binding to the IL-12Rβ1 receptor protein expressed on the surface of natural killer (NK) or T cells. Ustekinumab prevents IL-12 and IL-23 contributions to immune cell activation, such as intracellular signaling and cytokine secretion and is therefore believed to interrupt signaling and cytokine cascades that are central to psoriasis pathology.

The benefits with Stelara are that its efficacy in PASI (Psoriasis Area and Severity Index), PGA (Physician's Global Assessment) and DLQI (Dermatology Life Quality Index) scores was statistically significantly superior to placebo and etanercept in plaque psoriasis after 12 weeks of treatment. The proportion of patients achieving PASI 75 response at week 12 was 72.2% and 65% on 45 mg and 90 mg respectively versus 56.8% on etanercept. Approximately 35 to 50% of subjects achieved a PASI 90 response at week 12. Similar efficacy with ustekinumab treatment was observed when efficacy was assessed using the PGA.

Re-treatment was effective and a response was maintained with continued treatment (through week 76). The availability of an injection which can be self-administered and which is required only once every 12 weeks would benefit patients with severe disease who need immunosuppressive therapy. The lack of identified cumulative toxicity with biological therapies to date (in contrast to PUVA, methotrexate etc.) offers additional benefits.

In common with other immunosuppressives, the risks associated with potentially life-long life-long immunosuppression exist. The most common side effects seen in the trials included infection (particularly upper respiratory tract infections), malignancies, antibody formation and psychiatric disorders. Risks pertaining to infections, malignancies, hypersensitivity reactions, depression, concomitant immunosuppressive medication, pregnancy, lactation, vaccinations and co-morbidities (such as marked renal or hepatic impairment) are detailed in the SPC. In addition, Stelara is contraindicated in patients with a clinically important, active infection.

* Summaries of positive opinion are published without prejudice to the Commission Decision, which will normally be issued within 67 days from adoption of the Opinion.

** Applicants may request a re-examination of any CHMP opinion, provided they notify the EMEA in writing of their intention to request a re-examination within 15 days of receipt of the opinion.

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A pharmacovigilance plan for Stelara, as for all medicinal products, will be implemented as part of the marketing authorisation.

The approved indication is: “treatment of moderate to severe plaque psoriasis in adults who have failed to respond to, or who have a contraindication to, or who are intolerant to other systemic therapies including cyclosporine, methotrexate and psoralen plus ultra-violet A light [PUVA]).”

Detailed recommendations for the use of this product will be described in the Summary of Product Characteristics (SPC) which will be published in the European Public Assessment Report (EPAR) and will be available in all official European Union languages after the marketing authorisation has been granted by the European Commission.

The CHMP, on the basis of quality, safety and efficacy data submitted, considers that there is a favourable benefit to risk balance for Stelara and therefore recommends the granting of the marketing authorisation.