PLEGRIDY™ (peginterferon beta-1a)

OVERVIEW
PLEGRIDY™ (peginterferon beta-1a) is a new first-line treatment for relapsing-remitting multiple sclerosis (RRMS), the most common form of MS.¹ PLEGRIDY, the only pegylated beta interferon approved for use in RRMS, is dosed once every two weeks and can be administered subcutaneously via PLEGRIDY Pen, a ready-to-use autoinjector, or prefilled syringe.

BACKGROUND ON MS AND BETA INTERFERONS
MS is a chronic, often disabling disease that attacks the central nervous system (CNS),² which is made up of the brain, spinal cord and optic nerves. Symptoms result when a person’s immune system attacks the myelin sheath and interferes with the transmission of nerve signals between the brain, spinal cord and other parts of the body.²

Beta interferons are a commonly used class of RRMS treatments.³ Beta interferons are thought to stimulate the natural defenses of the immune system and help regulate the body’s immune response.⁴

ABOUT PEGYLATION
Pegylation—the attachment of polyethylene glycol (PEG) molecules—is a well-established scientific process that has been used for more than 20 years.⁵,⁶ Pegylation:
- Prolongs circulation time by increasing molecular size, resulting in a longer half-life
- Stabilizes the molecule by improving chemical stability and solubility for a longer shelf life
- Shields from degradation and decreases immunogenicity⁷

The process of pegylation allows patients to receive the benefits of an interferon treatment with less frequent dosing, which may be an attractive option for appropriate patients with RRMS seeking treatment with a less frequent dosing schedule.

PHASE 3 ADVANCE STUDY
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ADVANCE was a multi-center, randomized, double-blind, parallel-group, placebo-controlled (for the first year), Phase 3 study that evaluated the efficacy, safety and tolerability of PLEGRIDY 125 mcg compared to placebo in people with RRMS. After the first year, patients on placebo received PLEGRIDY for the remainder of the study. With more than 1,500 patients in over 180 sites in 26 countries, ADVANCE was one of the largest pivotal studies with interferons conducted in people living with RRMS.

The primary endpoint of ADVANCE was to determine the efficacy of PLEGRIDY in reducing annualized relapse rate (ARR) at year one. Secondary endpoints included determining the efficacy of PLEGRIDY in reducing the risk of 12-week confirmed disability progression, the proportion of patients who relapsed and MRI assessments. The analysis for all primary and secondary efficacy endpoints occurred at the end of year one.

After completing two years in the ADVANCE study, patients had the option of enrolling in an open-label extension study called ATTAIN and may be followed for up to four years.
ADVANCE EFFICACY & SAFETY RESULTS

Results from year one of ADVANCE showed that PLEGRIDY dosed every two weeks reduced ARR by 36 percent (p=0.0007) compared to placebo. PLEGRIDY also met additional study endpoints at one year.

Additional efficacy results:
- Demonstrated significant positive effects on disability progression by reducing the risk of 12-week confirmed disability progression by 38 percent (p=0.0383) and at 24 weeks (post-hoc analysis) by 54 percent (p=0.0069) compared to placebo.
- PLEGRIDY significantly reduced the number of gadolinium-enhancing (Gd+) lesions by 86 percent (p<0.001) compared to placebo.
- PLEGRIDY reduced the number of new or newly enlarging T2-hyperintense lesions on brain MRI scans by 67 percent (p<0.001) compared to placebo.

Safety and tolerability results:
The most common adverse reactions associated with PLEGRIDY treatment are injection site reaction, flu-like illness, fever, headache, muscle pain, chills, injection site pain, weakness, injection site itching, and joint pain.

The ADVANCE two-year data were consistent with the positive safety results observed in year one.

REGULATORY STATUS

The European Commission (EC) granted marketing authorization for PLEGRIDY in the European Union in July 2014, following the positive opinion adopted by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) in May 2014.

Indication
PLEGRIDY is indicated for the treatment of patients with relapsing-remitting multiple sclerosis.

Important Safety Information
Plegridy should be administered with caution to patients with previous depressive disorders, seizures, severe hepatic impairment and severe renal impairment. Cytopenias, including rare severe neutropenia and thrombocytopenia, have been observed in patients treated with Plegridy. The following have been reported with interferon beta medicinal products including Plegridy: Elevations in hepatic enzymes, serious hypersensitivity reactions, injection site reactions with subcutaneous administration, including injection site necrosis, and worsening of cardiac disease.

In addition, the EU SmPC indicates that the use of interferon beta products is associated with cases of nephrotic syndrome, thrombotic microangiopathy manifested as thrombotic thrombocytopenic purpura (TTP) or haemolytic uraemic syndrome (HUS), hyper and hypothyroidism, hepatitis, autoimmune hepatitis, rare cases of severe hepatic failure, and decreased peripheral blood counts, including rare pancytopenia.
References

8 Calabresi PA et al. Peginterferon Beta-1a Provides Improvements in Clinical and Radiological Disease Activity in Relapsing-Remitting Multiple Sclerosis: Year 1 Findings from the Phase 3 ADVANCE. Poster presented at 29th Congress of the European Committee for Research and Treatment in Multiple Sclerosis, 2013.