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## 508.BONE MARROW FAILURE: ACQUIRED

### A Real-World Evidence Review of Post-Marketing Safety and Compliance with Pegcetacoplan in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) in the US

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Introduction: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired hematologic condition characterized by complement-mediated, life-threatening hemolysis and thrombosis which are associated with significant impacts on health-related quality of life (HRQoL). Pegcetacoplan is the first targeted complement component 3 (C3) therapy approved for adults with PNH (US) and adults with PNH plus anemia despite receiving a complement component 5 inhibitor (C5i) for ≥3 months (EU). In clinical trials including patients with PNH who were C5i-experienced or -naive, pegcetacoplan significantly improved levels of hemoglobin (Hb) and lactate dehydrogenase (LDH) and reduced transfusion burden. Pegcetacoplan had a favorable safety profile in parent studies and an ongoing long-term, rollover, open-label extension study (NCT03531255). Compliance with pegcetacoplan treatment was high across all clinical studies. In the US real-world OPERA and Adelphi PNH Disease Specific Programme™ (DSP) patient-reported outcomes (PRO) studies, improvements in levels of Hb and LDH, along with self-reported fatigue and cognitive outcomes, were observed. Pegcetacoplan treatment also led to reductions in the frequency and severity of PNH symptoms (including shortness of breath and fatigue) and improvements in social, physical, and emotional HRQoL domains in the US real-world Voice of the Patient PRO study. Further, both patient and physician satisfaction with pegcetacoplan treatment was high in the Adelphi PNH DSP study. However, to date, compliance and safety with pegcetacoplan treatment in the real-world setting have not been described. The objective of this real-world evidence review study was to evaluate compliance and safety with pegcetacoplan treatment in patients with PNH in the US post-marketing setting.
Methods: Post-marketing data from the US, including the number of patients who received pegcetacoplan and reported safety events, were collected and analyzed from the pegcetacoplan Risk Evaluation and Mitigation Strategies (REMS) program which controls the distribution of pegcetacoplan and the pharmacovigilance safety database through May 13, 2023. Treatment compliance was calculated as the proportion of days a patient had the drug in possession, divided by the total number of days of follow-up, using central pharmacy prescription refill data. Thrombosis (a leading cause of death in patients with PNH prior to the availability of complement inhibitors) and meningococcal infections (a potential risk with complement inhibitors) were safety events of interest. To reduce the risk of serious meningococcal infections, clinical trial protocols and pegcetacoplan labeling required vaccination against *Streptococcus pneumoniae*; *N meningitidis* types A, C, W, Y, and B; and *Haemophilus influenzae* type B before starting treatment with pegcetacoplan. If pegcetacoplan treatment must be initiated before vaccination, the US label mandates prophylactic antibiotic use. In this study, the rates of thrombosis and meningococcal infection per 100 patient-years were estimated based on the total number of thrombosis and meningococcal infection events reported in the REMS program.
Results: As of May 13, 2023, the cumulative pegcetacoplan exposure was 273.10 patient-years in the US post-marketing setting. Based on prescription refill data, compliance with pegcetacoplan treatment was ~98%. There were 2 confirmed thrombotic events reported and the incidence of thrombotic events was 0.73 events/100 patient-years in 273.10 patient-years. Similar to clinical trials, no meningococcal infections were reported in the US post-marketing setting.
Conclusions: The high compliance rate and favorable safety profile of pegcetacoplan in the US post-marketing setting were consistent with clinical trial observations. These data, coupled with the effectiveness on hematologic parameters and improve-

ments in symptoms and HRQoL reported in pegcetacoplan real-world PRO studies, support a positive benefit:risk profile for pegcetacoplan in the real-world setting.

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