Report VOYDEYA® - Danicopan

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Danicopan **Brand Name:** Voydeya **Originator/licensee:** Alexion Europe SAS **Classification:** NCE **ATC code:** L04AJ09 **Orphan Status:** **Eu:** Yes **Us:** / **Mechanism of action:** Danicopan, is a complement inhibitor which reversibly binds to factor D to prevent alternative pathway-mediated haemolysis and deposition of complement C3 proteins on red blood cells, thereby helping to relieve the symptoms of PNH [1].	**Authorized Indication:** **EMA:** Danicopan is indicated as an add-on to RAV or ECU for the treatment of adults with PNH who have residual haemolytic anaemia [1]. **FDA:** / **Route of administration:** OS **Licensing status** **EU CHMP P.O. date:** 22/02/2024 **FDA M.A. date:** / **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** / --- **ABBREVIATIONS:** **AE:** adverse event **ALT:** Alanine aminotransferase **CE-EVH:** Clinically Evident Extravascular Hemolisis **CHMP:** Committee for Medicinal Products for Human Use **ECU**: Eculizumab **Hgb:** Hemoglobin **LS**: Least Square **LTE**: Long-Term Extension **M.A.:** Marketing Authorization **PNH**: Paroxysmal Nocturnal Haemoglobinuria **P.O.:** Positive Opinion **Pts:** Patients **RAV**: Ravulizumab **RBC:** Red Blood Cell **SAE**: Serious adverse event **TID**: Three times daily **ULN:** Upper limit of normal	**Summary of clinical EFFICACY:** **ALPHA (NCT04469465)** is an ongoing, international, phase 3, randomised, double-blind, placebo-controlled trial evaluating danicopan as add-on therapy to RAV or ECU. The study consists of a 12-week treatment period 1, followed by a 12-week danicopan+C5 inhibitor treatment period 2 and a LTE up to 1-year. Pts (target enrolment, N=84) were randomized to danicopan or matched placebo TID in a 2:1 ratio for the 12-week treatment period 1. Pts randomized to placebo for treatment period 1 switched to danicopan at week 12. Eligible pts (age ≥18 years) must have been receiving a stable regimen (no change in drug/dose/interval for ≥24 weeks) of ECU (dose level every two weeks ranged from 900mg to 1500mg) or RAV (dose level monthly or every 8 weeks ranged from 3000mg to 3600mg), and had CE-EVH, defined by anaemia (Hgb ≤9.5 g/dL), absolute reticulocyte count ≥120 x 109/L, and ≥1 transfusion within 6 months before study entry. The starting dose of danicopan was 150 mg TID. Pts with ALT or direct bilirubin values >1.5 ×ULN have started at 100 mg TID. Doses could be escalated in 50-mg increments, with ≥4 weeks between escalations, to a maximum of 200 mg TID based on safety and clinical effect at protocol-specified time points [2,3]. The primary endpoint was change in Hgb concentration from baseline to week 12. Baseline was defined as the lowest Hgb value observed between and including Screening and Day 1 [4]. Primary efficacy analyses have been performed on the intent-to-treat population [2]. The protocol-prespecified interim efficacy analysis set included the first 63 participants (danicopan, N=42; placebo, N=21). At week 12, danicopan plus RAV or ECU increased Hgb versus placebo plus RAV or ECU (LS change from baseline: danicopan, 2,94 g/dL [2,52 to 3,36]; placebo, 0,50 g/dL [-0,13 to 1,12]; LS difference, 2,44 g/dL [95% CI 1,69 to 3,20]; p<0·0001) [3]. **Summary of clinical SAFETY:** The safety set included all participants (n=73 at data cut off) that received at least 1 dose of study drug (danicopan [n=49] or placebo). For danicopan no deaths, meningococcal infections, or discontinuations due to haemolysis were reported. Grade 3 AEs in the danicopan group were increased ALT (two [4%] of 49 patients), leukopenia (one [2%]), neutropenia (two [4%]), cholecystitis (one [2%]), COVID-19 (one [2%]), increased aspartate aminotransferase (one [2%]), and increased blood pressure (one [2%]). In the placebo group grade 3 AEs were anaemia (one [4%] of 24 patients), thrombocytopenia (one pt [4%]), and asthenia (one pt[4%]). The SAEs reported in the danicopan group were cholecystitis (one [2%] patient) and COVID-19 (one pt [2%]), while in the placebo group were anaemia and abdominal pain, both in one (4%) patient [3]. **Ongoing studies:** ● ***For the same indication:*** *Yes* ● ***For other indications:*** Yes **Discontinued studies (for the same indication):** No --- **References:** [1] https://www.ema.europa.eu/en/documents/smop/chmp-summary-positive-opinion-voydeya_en.pdf [2] https://www.sciencedirect.com/science/article/pii/S0006497118700177 [3] https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(23)00315-0/abstract [4] https://classic.clinicaltrials.gov/ct2/show/study/NCT04469465?view=results [5] https://www.rarediseaseadvisor.com/disease-info-pages/paroxysmal-nocturnal-hemoglobinuria-epidemiology/ [6] https://www.osservatoriomalattierare.it/malattie-rare/emoglobinuria-parossistica-notturna/19952-emoglobinuria-parossistica-notturna-al-via-la-campagna-what-ai-feel [7] https://www.io.nihr.ac.uk/techbriefings/danicopan-with-eculizumab-or-ravulizumab-for-treating-paroxysmal-nocturnal-haemoglobinuria/	**Cost of therapy:** The price of Voydeya is not yet available. **Epidemiology:** PNH is an ultra-rare disease, the annual global incidence of PNH is around 5 to 6 individuals per 1 million people [5]. In Italy there are at least 350 affected people (within July 2023) [6]. --- **POSSIBLE PLACE IN THERAPY**: Current clinical management for PNH pts include treatment with complement inhibitor ECU or RAV. Allogeneic stem cell transplantation may be curative but is only considered for pts with severe bone marrow failure. Other interventions, notably RBC transfusion, folic acid, iron tablets and anti-coagulant treatments are offered to prevent or treat complications associated with PNH. Danicopan may offer an additional treatment option for pts with PNH who have clinically evident EVH despite current treatment with ECU or RAV [7]. **OTHER INDICATIONS IN DEVELOPMENT:** Geographic Atrophy (NCT05019521) **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: - **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Crovalimab (NCT04654468), Pegcetacoplan (NCT03500549), LPN023 (NCT04558918) *Service reorganization: *No* *Possible off label use: *No*

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