Danicopan (VOYDEYA) in Paroxysmal Nocturnal Hemoglobinuria (PNH)
National Drug Mini-monograph
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VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION

Description / MOA	Danicopan binds to Factor D of the alternative compliment pathway
Indication Under Review[1]	Danicopan is indicated as add-on therapy to ravulizumab or eculizumab for the treatment of extravascular hemolysis in adults with Paroxysmal Nocturnal Hemoglobinuria (PNH)
Dosage Regimen	Danicopan 150mg to 200mg three times daily
Dosage Forms Under Review	Danicopan 50mg and 100mg oral tablets

EFFICACY CONSIDERATIONS

Trial	**ALPHA**[2]
Design	R, DB, PC Trial
Population	Adult patients (n=73) who had confirmed PNH with clinically significant extravascular hemolysis (e.g. Hgb<9.5) despite stable anti-C5 treatment (e.g. eculizumab or ravulizumab)
Intervention	Patients were randomized 2:1 to 12 weeks of danicopan 150mg to 200mg TID in addition to continued eculizumab or ravulizumab followed by 12 weeks of open label danicopan for all enrolled pts
Comparator	Continuation of anti-C5 therapy plus placebo
Results	Primary endpoint was change in Hgb from baseline at 12 weeks. Pts receiving danicopan + antiC5 had an increase in Hgb of 2.9 g/dl vs. 0.5 g/dL for the antiC5 + placebo arm.

SAFETY CONSIDERATIONS

Boxed Warnings	Serious infections caused by encapsulated bacteria. Complete or update vaccination for encapsulated bacteria at least 2 weeks prior to the first dose of danicopan, unless the risks of delaying therapy with danicopan outweigh the risk of developing a serios infection.
Contraindications	Hypersensitivity to danicopan Unresolved serious infection caused by encapsulated bacteria, including: Strep. Pneumoniae, Niesseria meningitidis, or H. influenzae type B.
Other Warnings	Use not recommended in severe hepatic impairment (Child-Pugh class C) Insufficient data to make recommendation regarding risk of birth defects in pregnancy. Cessation of breastfeeding recommended during treatment with danicopan and for 3 days after final dose Hepatic enzyme elevations have been reported. Baseline screening and monitoring recommended Monitor for hemolysis after cessation of therapy
Top 5 AEs	Headache (11%), vomiting (7%), pyrexia (7%), ALT increase (5%), hypertension (5%)
Drug Interactions	Danicopa is a Breast Cancer Resistance Protein (BCRP) inhibitor and may increase plasma concentrations of BCRP substrates. Danicopan is P-glycoprotein inhibitor and may increase the plasma concentration of P-gp substrates. Danicopan significantly increased rosuvastatin exposure and rosuvastatin dose should not exceed 10mg/day when concomitantly used with danicopan

PLACE IN THERAPY	DRUG	VANF	CFU	FDA	GUIDELINES
	Ravulizumab	No	Yes	Yes	CFU_Ravulizumab_Ultomiris_CFU_Rev_March_2023.pdf (va.gov)
	Eculizumab	No	Yes	Yes	CFU_Eculizumab_Soliris_for_PNH_CFU_rev_June_2023.pdf (va.gov)
	Danicopan	TBD	TBD	Yes	TBD

VHA PLACE IN THERAPY		
	Potential Use in VHA	1. PNH is a rare condition (1 to 10 per million) with primary treatment for past 2 decades being C5 inhibitors (e.g. eculizumab or ravulizumab). However, 20-30% of patients treated with anti-C5 therapy will have breakthrough hemolysis and/or extravascular hemolysis with danicopan demonstrating benefit in patients with clinically significant extravascular hemolysis despite anti-C5 treatment in the ALPHA trial. There have been multiple drugs recently released for PNH (danicopan, iptacopan, pegcetacoplan) which all fill a similar niche. All treatments cost $300-400k per year (see table below)

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References

1 VOYDEYA (DANICOPAN) 50mg, 100mgral tablets [prescribing information online]. Bostan, Massachusetts: Alexion. Available at: voydeya_uspi (alexion.com). Accessed June 2024.
2 Lee JW, et. Al.,; ALXN2040-PNH-301 Investigators. Addition of danicopan to ravulizumab or eculizumab in patients with paroxysmal nocturnal haemoglobinuria and clinically significant extravascular haemolysis (ALPHA): a double-blind, randomised, phase 3 trial. Lancet Haematol. 2023 Dec;10(12):e955-e965. PMID: 38030318.