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Voydeya Film-coated tablet
Swissmedic Authorisation Number: 69301

Swiss Summary of the Risk Management Plan for Voydeya® (Danicopan)

Based on EU-RMP version number:	0.1
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Disclaimer:

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of **Voydeya** is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of **Voydeya** in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. **Alexion Pharma GmbH** is fully responsible for the accuracy and correctness of the content of the published summary RMP of **Voydeya**.

Part VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for VOYDEYA (danicopan)

This is a summary of the risk management plan (RMP) for VOYDEYA. The RMP details important risks of VOYDEYA, how these risks can be minimised, and how more information will be obtained about VOYDEYA risks and uncertainties (missing information).

VOYDEYA summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how VOYDEYA should be used.

This summary of the RMP for VOYDEYA should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of VOYDEYA RMP.

I.1 THE MEDICINE AND WHAT IT IS USED FOR

VOYDEYA is indicated as an add-on therapy to ravulizumab or eculizumab for the treatment of signs or symptoms of extravascular haemolysis in adult patients with paroxysmal nocturnal haemoglobinuria. It contains danicopan as the active substance and it is given by oral route of administration.

Further information about the evaluation of VOYDEYA's benefits can be found in VOYDEYA's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

I.2 RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of VOYDEYA, together with measures to minimise such risks and the proposed studies for learning more about VOYDEYA risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (eg, with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation measures*.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Report assessment so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of VOYDEYA is not yet available, it is listed under 'missing information' below.

I.2.1 List of important risks and missing information

Important risks of VOYDEYA are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of VOYDEYA. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e. g, on the long-term use of the medicine);

Table I-1 List of important risks and missing information

Important identified risks	None
Important potential risks	Meningococcal infection
Missing Information	Use in pregnant and breastfeeding women Use in patients with severe hepatic impairment Long-term safety

I.2.2 Summary of important risks

Table I-2 Important potential risk: Meningococcal infection

Evidence for linking the risk to the medicine	This important potential risk is based on danicopan mode of action, experience from individuals with complement deficiencies (Biesma et al 2001, Figueroa and Densen 1991, Hiemstra et al 1989, Sprong et al 2006), and terminal complement inhibitors, eculizumab and ravulizumab (Röth et al 2018). The link between terminal complement components deficiency states and (serious) infections caused by *Neisseria meningitidis* is firmly established and evidenced by the scientific literature (Figueroa and Densen 1991, Lewis and Ram 2014, Ram et al 2010, Ross and Densen 1984). However, this risk remains potential for FD inhibitors since classical and lectin pathways of complement are not inhibited by FD blockade.

Table I-2 Important potential risk: Meningococcal infection

Risk factors and risk groups	No risk factors specific to danicopan were identified. General risk factors for meningococcal infection include the following: • Underlying disease (eg, splenectomised patients with sickle cell disease), genetic complement deficiency or therapeutic inhibition of complement (eg, C5 inhibitors eculizumab and ravulizumab) • Lack of commercially available vaccine against certain meningococcus serogroup • (Partial) resistance of meningococcal strain to prophylactic antibiotics • Professionals who are exposed to environments of greater risk for meningococcal disease • Research, industrial, and clinical laboratory personnel who are routinely exposed to *N meningitidis* • Military personnel during recruit training (military personnel may be at increased risk of meningococcal infection when accommodated in close quarters) • Day-care centre workers • Living on a college or university campus • Travelling to endemic areas for meningococcal meningitis (eg, India, Sub Saharan Africa, pilgrimage to Saudi Arabia for Hajj).
Risk minimisation measures	Routine risk minimisation measure: SmPC sections 4.3 and 4.4 PL sections 2 and 4 The need for a vaccination (including the need for antibiotic prophylaxis until 2 weeks after vaccination) is stated in SmPC section 4.4. and PL section 2.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Safety of Danicopan as an Add-on to Ravulizumab or Eculizumab in Patients with PNH: A Registry Based Study See section **I.2.3** of this summary for an overview of the post-authorisation development plan.

Biesma DH, Hannema AJ, van Velzen-Blad H, Mulder L, van Zwieten R, Kluijt I et al. A family with complement factor D deficiency. J Clin Invest. 2001; 108(2):233-240.

Figueroa JE and Densen P. Infectious diseases associated with complement deficiencies. Clin Microbiol Rev. 1991; 4(3):359-395.

Hiemstra PS, Langeler E, Compier B, Keepers Y, Leijh PC, van den Barselaar MT et al. Complete and partial deficiencies of complement factor D in a Dutch family. J Clin Invest. 1989; 84(6):1957-1961.

Lewis LA and Ram S. Meningococcal disease and the complement system. Virulence. 2014; 5(1):98-126.

Ram S, Lewis LA, Rice PA. Infections of People with Complement Deficiencies and Patients Who Have Undergone Splenectomy. Clin Microbiol Rev. 2010; 23(4):740-780.

Röth A, Hock C, Konik A, Christoph S, Dührsen U. Chronic treatment of paroxysmal nocturnal hemoglobinuria patients with eculizumab: safety, efficacy, and unexpected laboratory phenomena. Int J Hematol. 2011; 93(6):704-714.

Ross SC and Densen P. Complement deficiency states and infection: epidemiology, pathogenesis and consequences of neisserial and other infections in an immune deficiency. Medicine (Baltimore). 1984; 63(5):243-273.

Sprong T, Roos D, Weemaes C, Neeleman C, Geesing CL, Mollnes TE et al. Deficient alternative complement pathway activation due to factor D deficiency by 2 novel mutations in the complement factor D gene in a family with meningococcal infections. Blood. 2006; 107(12):4865-4870.

C5, complement component 5; FD, factor D; PL, Package Leaflet; PNH, paroxysmal nocturnal haemoglobinuria; SmPC, Summary of Product Characteristics.

Table I-3 Missing information: Use in pregnant and breastfeeding women

Risk minimisation measures	Routine risk minimisation measure: SmPC sections 4.6 and 5.3 PL section 2 The recommendation for the use of effective contraception during treatment and until 3 days after discontinuation is included in SmPC section 4.6 and PL section 2.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Safety of Danicopan as an Add-on to Ravulizumab or Eculizumab in Patients with PNH: A Registry Based Study See section **I.2.3** of this summary for an overview of the post-authorisation development plan.

PL, Package Leaflet; PNH, paroxysmal nocturnal haemoglobinuria; SmPC, Summary of Product Characteristics.

Table I-4 Missing information: Use in patients with severe hepatic impairment

Risk minimisation measures	Routine risk minimisation measure: SmPC sections 4.2, 4.4, and 5.2
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Safety of Danicopan as an Add-on to Ravulizumab or Eculizumab in Patients with PNH: A Registry Based Study See section **I.2.3** of this summary for an overview of the post-authorisation development plan.

PNH, paroxysmal nocturnal haemoglobinuria; SmPC, Summary of Product Characteristics.

Table I-5 Missing information: Long-term safety

Risk minimisation measures	None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Safety of Danicopan as an Add-on to Ravulizumab or Eculizumab in Patients with PNH: A Registry Based Study See section **I.2.3** of this summary for an overview of the post-authorisation development plan.

PNH, paroxysmal nocturnal haemoglobinuria.

I.2.3 Post-authorisation development plan

I.2.3.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of VOYDEYA.

I.2.3.2 Other studies in post-authorisation development plan

Safety of Danicopan as an Add-on to Ravulizumab or Eculizumab in Patients with PNH: A Registry-Based Study

Purpose of the study: This is a post-authorisation observational study to evaluate the safety of danicopan as an add-on to ravulizumab or eculizumab in adult patients with PNH with clinically significant EVH. It aims to collect and evaluate safety data specific to the use of danicopan, including the rate of targeted events, the safety profile in subpopulations not exposed to danicopan in clinical trials, and long-term use.