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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:	1.0
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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**.

VI. 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.

VI.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 adult patients with paroxysmal nocturnal haemoglobinuria who have residual haemolytic anaemia. 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.

VI.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.

VI.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 (eg, on the long-term use of the medicine);

Table VI-1 List of important risks and missing information

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

VI.2.2 Summary of important risks

Table VI-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.
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 Signs and symptoms of meningococcal infection and steps to be taken should any of these occur are detailed in SmPC section 4.4 and the PL section 2. 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. Subject to restricted medical prescription

Table VI-2 Important potential risk: Meningococcal infection

Additional pharmacovigilance activities	Additional pharmacovigilance activities: ALX-PNH-502 See section VI.2.3 of this summary for an overview of the post-authorisation development plan.

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

Table VI-3 Important potential risk: Serious infections

Evidence for linking the risk to the medicine	This important potential risk is based on danicopan mode of action, experience from individuals with inherited alternative pathway deficiencies, including partial or complete FD deficiency (Biesma et al 2001, Hiemstra et al 1989, Kluin-Nelemans et al 1984, Ram et al 2010, Sprong et al 2006, Weiss et al 1998), and terminal complement inhibitors, eculizumab and ravulizumab (Röth et al 2018). Since a causal relationship of serious infections to danicopan therapy has not been confirmed in clinical trials, this remains a potential risk.
Risk factors and risk groups	The general risk factors for development of infections include any immunodeficiency, either acquired or due to underlying condition. PNH patients are at increased risk of infections, especially those who experience bone marrow failure (aplastic anaemia, myelodysplastic syndrome).
Risk minimisation measures	Routine risk minimisation measure: SmPC section 4.4 PL sections 2 and 4 Subject to restricted medical prescription
Additional pharmacovigilance activities	Additional pharmacovigilance activities: ALX-PNH-502 See section VI.2.3 of this summary for an overview of the post-authorisation development plan.

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

Table VI-4 Important potential risk: Malignancies and haematologic abnormalities

Evidence for linking the risk to the medicine	Malignancies and hematologic abnormalities are monitored as an important potential risk with C5 inhibitor ravulizumab therapy, though a causal relationship to ravulizumab has not yet been confirmed. Since a causal relationship of malignancies and hematologic abnormalities to danicopan therapy also has not been confirmed in clinical trials, this remains a potential risk. Additionally, as the natural evolution of PNH makes PNH patients more prone to development of haematologic abnormalities or malignancies (de Latour, 2008; Hillmen, 1995; Socié, 1996), the role of danicopan remains unknown.
Risk factors and risk groups	Patients with underlying myelodysplastic syndrome or other pre-leukaemic syndromes are at risk of leukaemia acutisation.

Table VI-4 Important potential risk: Malignancies and haematologic abnormalities

Risk minimisation measures	Routine risk minimisation measure: Subject to restricted medical prescription
Additional pharmacovigilance activities	Additional pharmacovigilance activities: ALX-PNH-502 See section VI.2.3 of this summary for an overview of the post-authorisation development plan.

C5, complement component 5; PNH, paroxysmal nocturnal haemoglobinuria

Table VI-5 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. Subject to restricted medical prescription
Additional pharmacovigilance activities	Additional pharmacovigilance activities: ALX-PNH-502 See section VI.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 VI-6 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 Subject to restricted medical prescription
Additional pharmacovigilance activities	Additional pharmacovigilance activities: ALX-PNH-502 See section VI.2.3 of this summary for an overview of the post-authorisation development plan.

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

Table VI-7 Missing information: Long-term safety

Risk minimisation measures	Routine risk minimisation measure: Subject to restricted medical prescription
Additional pharmacovigilance activities	Additional pharmacovigilance activities: ALX-PNH-502 ALXN2040-PNH-301 ALXN2040-PNH-303 See section VI.2.3 of this summary for an overview of the post-authorisation development plan.

PNH, paroxysmal nocturnal haemoglobinuria.

VI.2.3 Post-authorisation development plan

VI.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.

VI.2.3.2 Other studies in post-authorisation development plan

ALX-PNH-502

Purpose of the study: This is a post-authorisation non-interventional cohort study to evaluate the safety of danicopan as an add-on to ravulizumab or eculizumab in adult patients with PNH who have residual haemolytic anaemia.

There are limited data on danicopan long-term safety and the safety of danicopan in pregnant and breastfeeding women and patients with severe hepatic impairment. Further, the safety profile of danicopan including the risk of meningococcal infection in treated patients has not been characterised in real-world settings.

This study seeks to characterise the safety profile of danicopan as an add-on to ravulizumab or eculizumab in adult participants with PNH. The study's primary objectives are to:

- Characterise the long-term safety profile of danicopan as add-on therapy to ravulizumab/eculizumab in participants with PNH
- Describe and compare the incidence of meningococcal infection in participants with PNH treated with 1) danicopan as add-on therapy to ravulizumab/eculizumab and 2) ULTOMIRIS or SOLIRIS monotherapy
- Describe and compare the incidence of serious infection in participants with PNH treated with 1) danicopan as add-on therapy to ravulizumab/eculizumab and 2) ULTOMIRIS or SOLIRIS monotherapy

- Describe and compare the incidence of malignancies and haematologic abnormalities in participants with PNH treated with 1) danicopan as add-on therapy to ravulizumab/eculizumab and 2) ULTOMIRIS or SOLIRIS monotherapy

- Characterise the safety profile of danicopan as add-on therapy to ravulizumab/eculizumab in participants with severe hepatic impairment

The study's secondary objectives are to:

- Characterise the safety profile of danicopan as add-on therapy to ravulizumab/eculizumab in pregnant participants, pregnant partners of participants, or participants who are breastfeeding

- Describe the demographic and clinical profile at treatment initiation in participants with PNH treated with danicopan as add-on therapy to ravulizumab/eculizumab

- Assess danicopan as add-on therapy to ravulizumab/eculizumab treatment discontinuation patterns among participants with PNH

ALXN2040-PNH-301

Purpose of the study: This pivotal Phase 3 study aims to evaluate the efficacy and safety of danicopan as an add-on therapy to a C5 inhibitor (eculizumab or ravulizumab) to treat clinically-evident EVH.

Additionally, the study aims to evaluate the safety of danicopan as add-on therapy to a C5 inhibitor during the long-term extension (LTE) period.

ALXN2040-PNH-303

Purpose of the study: The purpose of this LTE study is to characterise the long-term safety and efficacy of danicopan as an add-on therapy to C5 inhibitor in patients with PNH who were previously treated with danicopan in an Alexion-sponsored clinical study.