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RESEARCH**

APPLICATION NUMBER:

761388Orig1s000

REMS

Risk Evaluation and Mitigation Strategy (REMS) Document

PIASKY (crovalimab-akkz) REMS

I. Administrative Information

Risk: Serious meningococcal infections

Application Number: BLA 761388

Application Holder: Genentech, Inc.

Initial REMS Approval: 06/2024

II. REMS Goal

The goal of the PIASKY REMS is to mitigate the risk of serious meningococcal infections.

1. Patients are vaccinated against meningococcal infections caused by *Neisseria meningitidis* serogroups A, C, W, Y, and B prior to starting therapy according to the current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving complement inhibitors and receive antibacterial drug prophylaxis if needed.
2. Patients are aware of early signs and symptoms of meningococcal infection and the need for immediate medical evaluation.
3. Prescribers are aware of early signs and symptoms of meningococcal infection and the need for immediate medical evaluation.

III. REMS Requirements

Genentech, Inc. must ensure that healthcare providers, patients, pharmacies, and wholesalers-distributors comply with the following requirements:

1. Healthcare Providers who prescribe PIASKY must:	
To become certified to prescribe	1. Review the drug's Prescribing Information. 2. Review the Patient Safety Card, Patient Guide, and Healthcare Provider Safety Brochure. 3. Enroll by completing and submitting the Prescriber Enrollment Form to the REMS.
Before treatment initiation	4. Assess the patient for unresolved meningococcal infection. 5. For patients with unresolved serious meningococcal infection: Not initiate PIASKY. 6. Assess the patient's vaccination status for meningococcal serogroups A, C, W, Y, and B and vaccinate as needed according to the current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccinations in patients receiving a complement inhibitor. 7. For patients who are not up to date with meningococcal vaccines at least two weeks prior to initiation of treatment and who must start PIASKY urgently: Provide the patient with a prescription for antibacterial drug prophylaxis. 8. Counsel the patient using the Patient Guide and Patient Safety Card. Provide a copy of the materials to the patient. 9. Counsel the patient on the need to carry the Patient Safety Card at all times during treatment and for 11 months following treatment with PIASKY.

During treatment	10. Assess the patient for early signs and symptoms of meningococcal infection and evaluate immediately, if infection is suspected. 11. Vaccinate patients as needed according to the current ACIP recommendations for meningococcal vaccinations for patients receiving a complement inhibitor.
At all times	12. Report adverse events suggestive of meningococcal infection, including the patient's clinical outcomes, to Genentech, Inc.

2. Patients who are prescribed PIASKY:

Before treatment initiation	1. Get meningococcal vaccines for serogroups A, C, W, Y, and B as directed by your prescriber. 2. Take antibiotics as directed by your prescriber if you have to start PIASKY right away. 3. Receive counseling from your prescriber using the Patient Safety Card and Patient Guide. 4. Get the Patient Guide and Patient Safety Card from your prescriber.
During treatment	5. Get additional meningococcal vaccines as directed by your prescriber.
At all times during treatment and for 11 months after the last PIASKY dose	6. Inform your prescriber or get emergency medical care right away if you experience any of the following: fever; fever and a rash; fever with high heart rate; headache with nausea or vomiting; headache and fever; headache with stiff neck or stiff back; confusion; eyes sensitive to light; muscle aches with flu-like symptoms. 7. Have the Patient Safety Card with you.

3. Pharmacies that dispense PIASKY must:

To become certified to dispense	1. Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS on behalf of the pharmacy. 2. Have the Authorized Representative review the Healthcare Provider Safety Brochure. 3. Have the Authorized Representative enroll by completing and submitting the Pharmacy Enrollment Form to the REMS. 4. Train all relevant staff involved in dispensing PIASKY using the Healthcare Provider Safety Brochure. 5. Establish processes and procedures to contact the prescriber to assess the patient's vaccination status for up to date meningococcal vaccines for serotypes A, C, W, Y, and B according to the current Advisory Committee on Immunization Practices (ACIP) recommendations including antibacterial drug prophylaxis, if needed before treatment initiation, and document the findings. 6. For patients who are not up to date with meningococcal vaccines when starting treatment: Establish processes and procedures to assess the patient's vaccination status for up to date meningococcal vaccines including antibacterial drug prophylaxis, if needed, before dispensing prescriptions up to 6 months after the first dose and document the findings.
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Before dispensing, first dose	- Obtain authorization to dispense each prescription by contacting the REMS to verify that the prescriber is certified. - Assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y and B including antibacterial drug prophylaxis, if needed, by contacting the prescriber and document the findings through the processes and procedures established as a requirement of the REMS.
Before dispensing, up to 6 months after the first dose	- Obtain authorization to dispense each prescription by contacting the REMS to verify the prescriber is certified. - For patients who are not initially up to date with meningococcal vaccines when starting treatment: Assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y, and B including antibacterial drug prophylaxis, if needed, by contacting the prescriber and document the findings through the processes and procedures established as a requirement of the REMS.
Before dispensing, 6 months after the first dose and thereafter	Obtain authorization to dispense each prescription by contacting the REMS to verify the prescriber is certified.
To maintain certification to dispense	If the Authorized Representative changes, have the new Authorized Representative enroll in the REMS by completing and submitting the Pharmacy Enrollment Form to the REMS.
At all times	- Report adverse event suggestive of meningococcal infections to Genentech, Inc. - Not distribute, transfer, loan, or sell PIASKY, except to certified pharmacies. - Maintain records of staff's completion of REMS training. - Maintain records that show all processes and procedures are in place and are being followed. - Comply with audits carried out by Genentech, Inc. or a third party acting on behalf of Genentech, Inc. to ensure that all processes and procedures are in place and are being followed.

4. Wholesalers-distributors that distribute PIASKY must:

To be able to distribute	- Establish processes and procedures to ensure that the drug is distributed only to certified pharmacies. - Train relevant staff involved in distributing PIASKY on the REMS requirements.
At all times	- Distribute only to certified pharmacies. - Maintain records of PIASKY distributions. - Comply with audits carried out by Genentech, Inc. or a third party acting on behalf of Genentech, Inc. to ensure that all processes and procedures are in place and are being followed.

Genentech, Inc. must provide training to healthcare providers who prescribe PIASKY.

The training includes the following educational materials: **Healthcare Provider Safety Brochure**, **Patient Guide**, and **Patient Safety Card**. The training must be available online and via email and fax.

Genentech, Inc. must provide training to pharmacies that dispense PIASKY.

The training includes the following educational material: [Healthcare Provider Safety Brochure](#). The training must be available online and via email and fax.

To inform healthcare providers about the REMS and the risks and safe use of PIASKY, Genentech, Inc. must disseminate REMS communication materials according to the table below:

Target Audience	Communication Materials & Dissemination Plans
Healthcare providers who are certified to prescribe PIASKY	REMS Letters: Vaccination Reminder Letter 1. Fax or email annually

To support REMS operations, Genentech, Inc. must:

1. Establish and maintain a REMS website, www.PIASKYREMS.com. The REMS website must include the capability to complete prescriber and enrollment online, and the option to print the Prescribing Information, Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS website. The REMS website must not link back to the promotional product website(s).
2. Make the REMS website fully operational and all REMS materials available through the REMS website and Call Center by the date PIASKY is first commercially distributed.
3. Establish and maintain a REMS call center at 1-866-4My-Skyy (469-7599).
4. Establish and maintain a validated, secure database of all enrolled participants in the PIASKY REMS.
5. Ensure that pharmacies are able to obtain authorization to dispense by phone and online.
6. Ensure that prescribers are able to enroll in the REMS by fax and online.
7. Ensure that pharmacies are able to enroll in the REMS by fax only.
8. Ensure that prescribers and pharmacies are able to report adverse events suggestive of meningococcal infections by contacting Genentech, Inc. by phone and email.
9. Ensure that once a report suggestive of meningococcal infection is received, Genentech, Inc. will follow up with the healthcare providers to obtain all required data. This requirement does not affect Genentech, Inc.'s other reporting and follow-up requirements under the FDA regulations.
10. Provide the [Healthcare Provider Safety Brochure](#), [Prescriber Enrollment Form](#), [Patient Guide](#), [Patient Safety Card](#), Prescribing Information, and the Medication Guide to healthcare providers who (1) attempt to prescribe PIASKY and are not yet certified or (2) inquire about how to become certified.
11. Provide the [Healthcare Provider Safety Brochure](#) and [Pharmacy Enrollment Form](#) to pharmacies that (1) attempt to order or dispense PIASKY and are not yet certified or (2) inquire about how to become certified.
12. Notify prescribers and pharmacies within 2 business days after they become certified in the REMS.
13. Provide certified prescribers access to the database of certified pharmacies.
14. Provide certified pharmacies access to the database of certified prescribers.
15. Provide authorized wholesalers-distributors access to a database of certified pharmacies.

To ensure REMS participants' compliance with the REMS, Genentech, Inc. must:

16. Verify annually that the Authorized Representative's name and contact information correspond to those of the current designated Authorized Representative for the pharmacy. If different, the pharmacy must be required to re-certify with a new Authorized Representative.
17. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: PIASKY distribution and dispensing; certification of prescribers and pharmacies; and audits of REMS participants. These records must be readily available for FDA inspections.
18. Establish and maintain a plan for addressing noncompliance with REMS requirements.
19. Monitor prescribers and pharmacies on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if noncompliance is identified, including de-certification.
20. Audit each pharmacy no later than 180 days after the pharmacy receives their first shipment and annually thereafter to ensure that all REMS processes and procedures are in place, functioning, and comply with the REMS requirements.
21. Audit each wholesaler-distributor no later than 180 days after the wholesaler-distributor has initiated their first commercial distribution of PIASKY and annually thereafter to ensure that all REMS processes and procedures are in place, functioning, and comply with REMS requirements.
22. Take reasonable steps to improve operations of and compliance with the requirements of the PIASKY REMS based on monitoring and evaluation of the PIASKY REMS.

IV. REMS Assessment Timetable

Genentech, Inc. must submit REMS Assessments at 6 months and 18 months from the date of the initial approval of the REMS (06/20/2024), and every 12 months thereafter from the date of the 18 month submission. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Genentech, Inc. must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the PIASKY REMS:

Enrollment Forms

Prescriber:

1. [Prescriber Enrollment Form](#)

Pharmacy:

2. [Pharmacy Enrollment Form](#)

Training and Educational Materials

Prescriber:

3. [Healthcare Provider Safety Brochure](#)

Patient:

4. [Patient Guide](#)
5. [Patient Safety Card](#)

Pharmacy:

6. [Healthcare Provider Safety Brochure](#)

Communication Materials

7. [REMS Letter: Vaccination Reminder Letter](#)

Other Materials

8. [REMS website](#)

VI. Statutory Elements

This REMS is approved under section 505-1 of the Federal Food, Drug and Cosmetic Act (FD&C Act) (21 U.S.C. 355-1) and consists of the following elements:

1. Elements to Assure Safe Use:
 - Healthcare providers who prescribe PIASKY are specially certified under 505-1(f)(3)(A).
 - Pharmacies that dispense PIASKY are specially certified under 505-1(f)(3)(B).
 - PIASKY is dispensed to patients with evidence or other documentation of safe-use conditions under 505-1(f)(3)(D).
2. Implementation System
3. Timetable for Submission of Assessments

www.PIASKYREMS.com and 1-866-4MySkyy (469-7599)

Because of the risk of serious meningococcal infections, PIASKY® (crovalimab-akkz) is available only through a restricted distribution program called the PIASKY Risk Evaluation and Mitigation Strategy (REMS). Healthcare providers must become certified in the PIASKY REMS in order to prescribe PIASKY.

To become certified in the PIASKY REMS, prescribers must:

1. Review the PIASKY Prescribing Information, **Healthcare Provider Safety Brochure, Patient Safety Card, and Patient Guide.**
2. Enroll by completing and submitting this **Prescriber Enrollment Form** to the REMS.
 - Online at www.PIASKYREMS.com
 - By fax at 1-833-670-4840

Prescriber Agreement

By completing, signing, and submitting this form, I acknowledge and agree that:

- I have read and understand the PIASKY Prescribing Information (PI), **Healthcare Provider Safety Brochure, Patient Safety Card** and **Patient Guide.**
- I understand the:
 - Risk of serious meningococcal infections associated with PIASKY.
 - Early signs and symptoms of meningococcal infections and the need for immediate medical evaluation.
- Before treatment initiation, I must:
 - Assess the patient for unresolved meningococcal infection.
 - For patients with an unresolved serious meningococcal infection: Not initiate PIASKY.
 - Assess the patient's vaccination status for meningococcal serogroups A, C, W, Y, and B and vaccinate as needed according to the current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving a complement inhibitor.
 - For patients who are not up to date with meningococcal vaccines at least two weeks prior to initiation of treatment and who must start PIASKY urgently: Provide the patient with a prescription for antibacterial drug prophylaxis.
 - Counsel the patient using the **Patient Safety Card** and **Patient Guide.** Provide a copy of these materials to the patient.
 - Counsel the patient on the need to carry the **Patient Safety Card** at all times and for 11 months after their last dose of PIASKY.
- During treatment, I must:
 - Assess the patient for early signs and symptoms of meningococcal infection and evaluate immediately if infection is suspected.
 - Vaccinate patients as needed according to the current ACIP recommendations for meningococcal vaccinations for patients receiving a complement inhibitor.
- At all times, I must:
 - Report any adverse events suggestive of meningococcal infections, including the patient's clinical outcomes to Genentech, Inc. at 888-835-2555 or by email to us_drug.safety@gene.com.

- I understand that if I do not maintain compliance with the requirements of the REMS, I will no longer be able to prescribe PIASKY.
- I understand that the PIASKY REMS and its agents or contractors may contact me to support the administration of the REMS.
- I understand that Genentech or its agents or contractors may use and disclose my information in accordance with the Genentech Privacy Notice, available at www.genentech.com/legal#privacy, including to support the administration of the PIASKY REMS.

Prescriber Information (* fields required)

*First Name: _____ *Last Name: _____

*National Provider Identifier (NPI): _____ *Email: _____

Clinic / Practice Name: _____

*Address Line 1: _____

Address Line 2: _____

*City: _____ *State: _____ *Zip Code: _____

*Phone Number: _____ *Fax Number: _____

*Credentials: ☐ MD ☐ DO ☐ APRN ☐ PA ☐ Other (please specify): _____

*Medical Specialty:

☐ Hematology/Oncology ☐ Immunology ☐ Internal Medicine ☐ Nephrology
☐ Neurology ☐ Rheumatology ☐ Other (please specify): _____

*Prescriber's Signature

*Date (MM/DD/YYYY)

www.PIASKYREMS.com and 1-866-4MySkyy (469-7599)

Because of the risk of serious meningococcal infections, PIASKY® (crovalimab-akkz) is available only through a restricted distribution program called the PIASKY Risk Evaluation and Mitigation Strategy (REMS). Pharmacies must become certified in the PIASKY REMS in order to dispense PIASKY.

To become certified in the PIASKY REMS, pharmacies must designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS on behalf of the pharmacy. The Authorized Representative must:

1. Review the **Healthcare Provider Safety Brochure**.
2. Enroll by completing and submitting this Pharmacy Enrollment Form to the REMS, by fax at 1-833-670-4840.

Authorized Representative Agreement

As the pharmacy's Authorized Representative, to become certified to dispense, I must:

- Review the **Healthcare Provider Safety Brochure**.
- Enroll by completing and submitting this **Pharmacy Enrollment Form** to the REMS.
- Establish processes and procedures to contact the prescriber to assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y, and B according to the current Advisory Committee on Immunization Practices (ACIP) recommendations including antibacterial drug prophylaxis, if needed, before treatment initiation, and document the findings.
- For patients who are not up to date with meningococcal vaccines when starting treatment: Establish processes and procedures to assess the patient's vaccination status for up to date meningococcal vaccines including antibacterial drug prophylaxis, if needed, before dispensing prescriptions up to 6 months after the first dose and document the findings.
- Train all relevant staff involved in dispensing PIASKY using the **Healthcare Provider Safety Brochure**.

Before dispensing the first dose, all pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the REMS to verify that the prescriber is certified.
- Assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y, and B including antibacterial drug prophylaxis, if needed, by contacting the prescriber and document the findings through the processes and procedures established as a requirement of the REMS.

Before dispensing, up to 6 months after the first dose, all pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the REMS to verify that the prescriber is certified.
- For patients who are not initially up to date with meningococcal vaccines when starting treatment: Assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y, and B including antibacterial drug prophylaxis, if needed, by contacting the prescriber and document the findings through the processes and procedures established as a requirement of the REMS.

Before dispensing, 6 months after the first dose and thereafter, all pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the REMS to verify that the prescriber is certified.

To maintain certification to dispense, any new Authorized Representative must:

- Enroll by completing and submitting this **Pharmacy Enrollment Form** to the REMS.

At all times, all pharmacy staff must:

- Report adverse events suggestive of meningococcal infections to Genentech, Inc. at 888-835-2555 or by email to us_drug.safety@gene.com.
- Not distribute, transfer, loan, or sell PIASKY, except to certified pharmacies.
- Maintain records that all processes and procedures are in place and are being followed.
- Maintain records of staff's completion of REMS training.
- Comply with audits carried out by Genentech, Inc. or a third party acting on behalf of Genentech, Inc. to ensure that all processes and procedures are in place and are being followed.

I understand that if this pharmacy does not maintain compliance with the requirements of the REMS, the pharmacy will no longer be able to dispense PIASKY.

I understand that the PIASKY REMS and its agents or contractors may contact me to support the administration of the REMS.

I understand that Genentech, Inc. or its agents or contractors may use and disclose my information in accordance with the Genentech, Inc. Privacy Notice, available at www.genentech.com/legal#privacy, including to support the administration of the PIASKY REMS.

Pharmacy Information (*fields required)☐ Initial pharmacy enrollment☐ Change of information for enrolled pharmacy☐ Change of Authorized Representative**Authorized Representative Information**

*First Name: _____ *Last Name: _____

*Title/Position: ☐ Pharmacist ☐ Nurse ☐ Other (please specify): _____

*Authorized Representative National Provider Identifier (NPI): _____

*Email: _____ *Preferred Method of Contact: ☐ Phone ☐ Email

Pharmacy Information

*Pharmacy Name: _____

*Address Line 1: _____

Address Line 2: _____

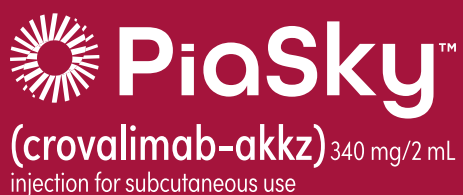
*City: _____ *State: _____ *Zip Code: _____

*Phone Number: _____ *Fax Number: _____

*Pharmacy National Provider Identifier (NPI): _____

***Authorized Representative's Signature**

***Date (MM/DD/YYYY)**



Risk Evaluation and Mitigation Strategy (REMS)

Healthcare Provider Safety Brochure

This brochure provides information for healthcare providers who will prescribe or dispense PIASKY® (crovalimab-akkz). It describes :

- What is PIASKY?
- What is the PIASKY REMS?
- Prescriber Requirements
- Pharmacy Requirements
- PIASKY REMS Resources
- Adverse Event Reporting

Please see the Prescribing Information, including the BOXED WARNING, for more detailed safety information about PIASKY.

What is PIASKY?

PIASKY (crovalimab-akkz) is a complement inhibitor indicated for the treatment of adult and pediatric patients 13 years and older with paroxysmal nocturnal hemoglobinuria (PNH).

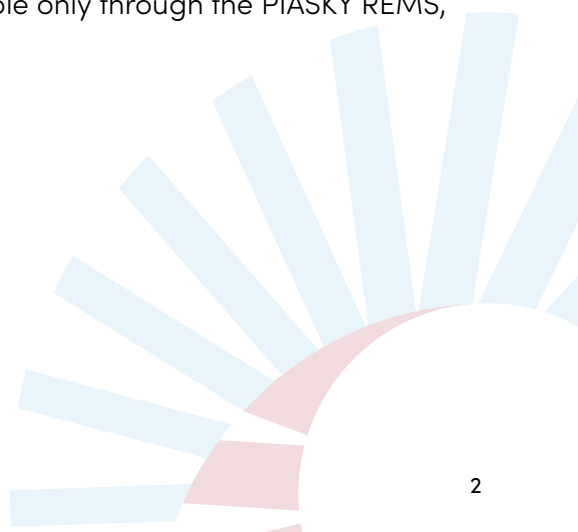
Risk of Serious Meningococcal Infections

- PIASKY, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by meningococcal bacteria (meningococcemia and/or meningitis) in any serogroup, including non-groupable strains.
- Life-threatening and fatal meningococcal infections have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors.
- The initiation of PIASKY is contraindicated in patients with serious unresolved *Neisseria meningitidis* infection.
- Completed or update meningococcal vaccination (for serogroups A, C, W, Y, and B) at least 2 weeks prior to administration of the first dose of PIASKY, according to current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving a complement inhibitor.
- If urgent PIASKY therapy is indicated in a patient who is not up to date with meningococcal vaccines according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer meningococcal vaccines as soon as possible.
- Vaccination does not eliminate the risk of serious meningococcal infections, despite development of antibodies following vaccination.
- Closely monitor patients for early signs of meningococcal infection and evaluate patients immediately if infection is suspected. Promptly treat known infections.
- Meningococcal infections may rapidly become life-threatening or fatal if not recognized and treated early.
- Inform patients on the signs and symptoms of meningococcal infection and instruct patients to seek immediate medical care if any of these signs and symptoms occur.
- Consider interruption of PIASKY in patients who are undergoing treatment for serious meningococcal infection.

What is the PIASKY REMS?

A Risk Evaluation and Mitigation Strategy (REMS) is a program required by the Food and Drug Administration (FDA) to help ensure that the benefits of a drug outweigh its risks.

Because of the risk of serious meningococcal infections, PIASKY is available only through the PIASKY REMS, a restricted distribution program.



Prescriber Requirements

What Do Prescribers Need to Do When Prescribing PIASKY?

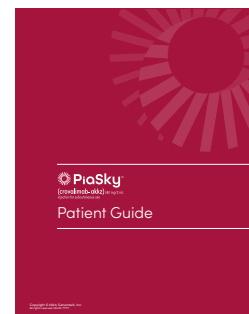
Healthcare providers who prescribe PIASKY must be certified in the REMS to prescribe PIASKY. To become certified, healthcare providers must:

- Review the PIASKY Prescribing Information, **Healthcare Provider Safety Brochure Patient Safety Card**, and **Patient Guide**.
- Enroll by completing and submitting the **Prescriber Enrollment Form** to the REMS.
 - Online at www.PIASKYREMS.com
 - By fax at 1-833-670-4840
- The **Prescriber Enrollment Form** is available online at www.PIASKYREMS.com or by calling 1-866-4MySkyy (469-7599).
- Prescribers will be notified within 2 business days after submission of the form that they are certified in the REMS and can prescribe PIASKY.

Before initiating treatment with PIASKY, prescribers must:

- Assess the patient for unresolved meningococcal infection.
- For patient with an unresolved serious meningococcal infection: Not initiate PIASKY.
- Assess the patient's vaccination status for meningococcal serogroups A, C, W, Y, and B and vaccinate as needed according to the current ACIP recommendations for patients receiving a complement inhibitor.
- For patients who are not up to date with meningococcal vaccines at least two weeks prior to initiation of treatment and who must start PIASKY urgently: Provide the patient with a prescription for antibacterial drug prophylaxis.
- Counsel the patient using the **Patient Safety Card** and **Patient Guide**. Provide a copy of these materials to the patient.
 - The **Patient Guide** provides information for your patients about the risk of serious meningococcal infections including:
 - The need to complete or update their meningococcal vaccines for serotypes A, C, W, Y, and B at least 2 weeks prior to receiving the first dose of PIASKY or receive antibacterial drug prophylaxis if PIASKY must be initiated immediately, and they have not previously been vaccinated.
 - Additional vaccines may be necessary during treatment with PIASKY.
 - Meningococcal vaccines do not prevent all meningococcal infections.
 - The **Patient Safety Card** has important safety information for both patients and any healthcare providers that may see or treat your patient. It describes the following signs and symptoms which, if experienced, should prompt the patient to seek immediate medical care:

▪ Fever	▪ Headache with a stiff neck or stiff back
▪ Fever and a rash	▪ Confusion
▪ Headache with nausea and vomiting	▪ Muscle aches, with flu-like symptoms
▪ Fever with a high heart rate	▪ Eyes sensitive to light
▪ Headache and a fever	
- Counsel the patient on the need to carry the **Patient Safety Card** at all times and for 11 months after their last dose of PIASKY and show the card to any healthcare provider involved in their care.



Prescriber Requirements (continued)

During PIASKY treatment, prescribers must:

- Assess the patient for early signs and symptoms of meningococcal infection and evaluate immediately if infection is suspected.
- Vaccinate patients as needed according to the current ACIP recommendations for meningococcal vaccinations for patients receiving a complement inhibitor.

At all times, prescribers must:

- Comply with all REMS requirements to maintain certification to prescribe PIASKY.
- Report all adverse events suggestive of meningococcal infections, including the patient's clinical outcomes, to Genentech, Inc. at 888-835-2555 or by email to us_drug.safety@gene.com.

Pharmacy Requirements

What Do Pharmacies Need to Do When Dispensing PIASKY?

PIASKY may only be dispensed by pharmacies that are certified in the REMS. To become certified in the REMS, the pharmacy must designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS on behalf of the pharmacy. The Authorized Representative must:

- Review the **Healthcare Provider Safety Brochure** (this document).
- Enroll by completing and submitting the **Pharmacy Enrollment Form** to the REMS, by fax at 1-833-670-4840.

By completing and submitting the Pharmacy Enrollment Form, the pharmacy's Authorized Representative agrees to:

- Train all staff involved in dispensing PIASKY using the **Healthcare Provider Safety Brochure**.
- Establish processes and procedures to contact the prescriber to assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y, and B according to the current Advisory Committee on Immunization Practices (ACIP) recommendations including antibacterial drug prophylaxis, if needed, before treatment initiation, and document the findings.
- For patients who are not up to date with meningococcal vaccines when starting treatment: Establish processes and procedures to assess the patient's vaccination status for up to date meningococcal vaccines including antibacterial drug prophylaxis, if needed, before dispensing prescriptions up to 6 months after the first dose and document the findings.

Before dispensing the first dose, all pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the REMS to verify that the prescriber is certified.
- Assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y, and B including antibacterial drug prophylaxis, if needed, by contacting the prescriber and document the findings through the processes and procedures established as a requirement of the REMS.

Pharmacy Requirements (continued)

Before dispensing, up to 6 months after the first dose, all pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the REMS to verify that the prescriber is certified.
- For patients who are not initially up to date with meningococcal vaccines when starting treatment: Assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y, and B including antibacterial drug prophylaxis, if needed, by contacting the prescriber and document the findings through the processes and procedures established as a requirement of the REMS.

Before dispensing, 6 months after the first dose and thereafter, all pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the REMS to verify that the prescriber is certified.

To maintain certification to dispense, any new Authorized Representative must:

- Enroll by completing and submitting this **Pharmacy Enrollment Form** to the REMS.

At all times, all pharmacy staff must:

- Report adverse events suggestive of meningococcal infections to Genentech, Inc. at 888-835-2555 or by email to us_drug.safety@gene.com.
- Not distribute, transfer, loan, or sell PIASKY, except to certified pharmacies.
- Maintain records that show all processes and procedures are in place and are being followed.
- Maintain REMS training records for all staff who play a role in dispensing PIASKY.
- Comply with audits carried out by Genentech, Inc. or a third party acting on behalf of Genentech, Inc. to ensure that all processes and procedures are in place and are being followed.

PIASKY REMS Resources

Visit www.PIASKYREMS.com or call 1-866-4My-Skyy (469-7599) to learn more about the REMS.

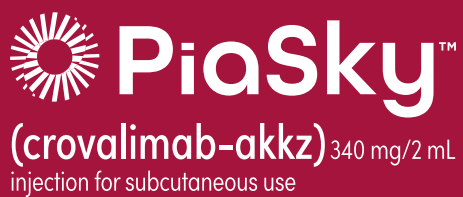
Adverse Event Reporting

Report adverse events suggestive of meningococcal infections, including the patient's clinical outcomes, immediately to Genentech, Inc. at 888-835-2555 or by email to us_drug.safety@gene.com.

You are encouraged to report other adverse reactions of PIASKY to Genentech, Inc. at 888-835-2555 or by email to us_drug.safety@gene.com or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

This guide does not provide complete safety information on PIASKY.

Please see the Prescribing Information, including the BOXED WARNING regarding serious meningococcal infection, for the complete safety information on PIASKY.



Patient Guide

What is PIASKY®?

PIASKY (crovalimab-akkz) is a prescription medicine used to treat paroxysmal nocturnal hemoglobinuria (PNH) in adults and children 13 years of age and older who weigh at least 88 pounds.

What are the serious risks of PIASKY?

PIASKY can lower the ability of your immune system to fight infections.

PIASKY increases your chance of getting serious meningococcal infections caused by *Neisseria meningitidis*. Meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.

Call your doctor or get emergency medical care right away if you have any of these signs and symptoms of a serious meningococcal infection:

- Fever
- Fever and a rash
- Headache with nausea or vomiting
- Fever with a high heart rate
- Headache and a fever
- Headache with a stiff neck or stiff back
- Confusion
- Muscle aches, with flu-like symptoms
- Eyes sensitive to light

What do I need to do before I start PIASKY?

It is important for you to be complete or update your meningococcal vaccinations.

- You will need to be vaccinated **at least 2 weeks before** your first dose of PIASKY.
- Your healthcare provider will review your vaccine history with you.
- Your healthcare provider will let you know which vaccines you need.

Your healthcare provider may decide that you need to start PIASKY earlier than 2 weeks after you are vaccinated. If this happens:

- You still need to get your vaccines as soon as possible.
- Your healthcare provider will prescribe an antibiotic for you to take.
- You will need to take this antibiotic for as long as your healthcare provider tells you.

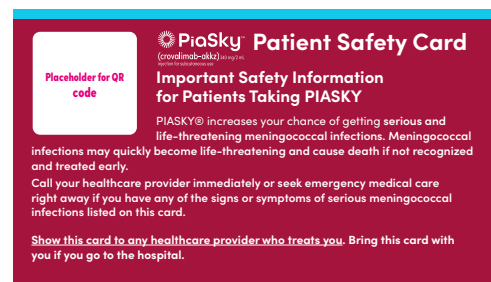
Meningococcal vaccines do not prevent all meningococcal infections. You will still need to watch for signs and symptoms of serious meningococcal infection. They are listed in this brochure and on your **Patient Safety Card**.

What else do I need to do?

Your healthcare provider will give you a **Patient Safety Card** about the risk of serious meningococcal infection.

- Review the card with your healthcare provider.
- Keep this card with you at all times while are receiving treatment with PIASKY and for 11 months following treatment with PIASKY.
- Your risk of serious meningococcal infections may continue for several months after your last dose of PIASKY.
- Show your **Patient Safety Card** to any healthcare provider who treats you. It will help them quickly diagnose and treat a possible meningococcal infection.

Get emergency medical care right away if you have any symptoms of meningococcal infection even if you don't have the **Patient Safety Card** with you.



What is the PIASKY REMS?

A Risk Evaluation and Mitigation Strategy (REMS) is a drug safety program that the US Food and Drug Administration (FDA) can require for certain medicines to ensure they are used safely. When there is a REMS, drug companies, healthcare providers, and pharmacies must take extra steps to make sure the benefits of using the drug are greater than the risks.

PIASKY has a REMS because it can increase your chance of getting serious meningococcal infections. Meningococcal infections may quickly become life-threatening or cause death if not recognized and treated early.

How will I get my PIASKY medicine?

Only certain pharmacies can fill your PIASKY prescription. The pharmacies that are part of the PIASKY REMS will contact you to fill your prescription and ship it to your preferred address.

Fold

Fold



Print out, cut along the dotted lines and fold in half and half again.

[Date]

[HCP_Title][HCP_First Name] [HCP_Last_Name]

[HCP_Address_Line1]

[HCP_Address_Line2]

[HCP_City], «HCP_State» «HCP_ZIP»

Dear [HCP_Title][HCP_First Name] [HCP_Last_Name]:

We are sending you this annual reminder because you are enrolled as a prescriber in the PIASKY® Risk Evaluation and Mitigation Strategy (REMS). The REMS is required by the FDA to mitigate the risk of serious meningococcal infections.

Please remember that all patients who are receiving PIASKY (crovalimab-akkz) treatment must be vaccinated against meningococcal infections caused by *Neisseria meningitidis* serogroups A, C, W, Y, and B prior to starting therapy according to the current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving a complement inhibitor. Please assess your patients' vaccine history for meningococcal serogroups A, C, W, Y and B and ensure all are up to date. During treatment, patients may require additional doses of vaccines in order to remain up to date with the recommended vaccinations. Recommendations from ACIP for patients who are receiving a complement inhibitor can be found at the [CDC Website](#).

Be aware that these recommendations may be periodically updated; therefore, please check the latest ACIP recommendations.

These steps are important to mitigate the risk of meningococcal infection for your patients who are receiving treatment with PIASKY.

If you have any questions about the vaccination requirements of the PIASKY REMS, please call 1-866-4MySkyy (469-7599), Monday through Friday, 8:00 am to 8:00 pm ET.

Sincerely,

PIASKY REMS

PIASKY REMS

Public Website Screenshots

Date: June 12, 2024

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2. Home Page

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(crovalimab-akkz) 340 mg/2 mL
injection for subcutaneous use

What is a REMS?

A Risk Evaluation and Mitigation Strategy (REMS) is a safety program required by the Food and Drug Administration (FDA) to help ensure that the benefits associated with a medication outweigh its risks.

What is the goal of the PIASKY REMS?

The goal of the PIASKY REMS is to mitigate the risk of serious meningococcal infections.

- Patients are vaccinated against meningococcal infections caused by *Neisseria meningitidis* serogroups A, C, W, Y, and B prior to starting therapy according to the current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving complement inhibitors and receive antibacterial drug prophylaxis if needed.
- Patients are aware of early signs and symptoms of meningococcal infection and the need for immediate medical evaluation.
- Prescribers are aware of early signs and symptoms of meningococcal infection and the need for immediate medical evaluation.

REMS Requirements

PIASKY is available only through a restricted distributions program under a REMS, called the PIASKY REMS, because of the risk of serious meningococcal infections.

Healthcare providers must become certified in the REMS in order to prescribe PIASKY. Pharmacies must become certified in the REMS in order to dispense PIASKY.

Indication

PIASKY (crovalimab-akkz) is a complement inhibitor indicated for the treatment of adult and pediatric patients with paroxysmal nocturnal hemoglobinuria (PNH).

Report all adverse events, especially meningococcal infections, that occur in patients receiving PIASKY to Genentech, Inc. at 888-835-2555 or by email to us drugsafety@gene.com.

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3. Prescribers Page

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Prescribers

To become certified, the prescriber must:

Step 1

Review the following materials

- [Prescribing Information](#)
- [Patient Safety Card](#)
- [Patient Guide](#)
- [Healthcare Provider Safety Brochure](#)

Step 2

Enroll in the PIASKY REMS by completing and submitting the **Prescriber Enrollment Form**:

- Online
- Fax
 - Fax the completed form to the PIASKY REMS at 1-833-670-4840

[Start Online Prescriber Enrollment →](#)

Or - Print and fax to PIASKY REMS:
[Prescriber Enrollment Form](#)

Key Prescriber Requirements

- Assess the patient for unresolved meningococcal infection.
- For patients with an unresolved serious meningococcal infection: Not initiate PIASKY.
- Assess the patient's vaccination status for meningococcal serogroups A, C, W, Y, and B and vaccinate as needed according to the current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving a complement inhibitor.
- For patients who are not up to date with meningococcal vaccines at least two weeks prior to initiation of treatment and who must start PIASKY urgently: Provide the patient with a prescription for antibacterial drug prophylaxis.
- Counsel the patient using the **Patient Guide** and **Patient Safety Card** and provide a copy of these materials to the patient.
- Counsel the patient on the need to carry the **Patient Safety Card** at all times and for 11 months after their last dose of PIASKY.
- Assess the patient for early signs and symptoms of meningococcal infection and evaluate immediately if infection is suspected.
- Vaccinate patients as needed according to the current ACIP recommendations for meningococcal vaccinations for patients receiving a complement inhibitor.

Report all adverse events, especially meningococcal infections, that occur in patients receiving PIASKY to Genentech, Inc. at 888-835-2555 or by email to us_drugsafety@gene.com.

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3.1 Online Prescriber Enrollment Page

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Online Prescriber Enrollment

Because of the risk of serious meningococcal infections, PIASKY® (crovalimab-akkz) is available only through a restricted distribution program called the PIASKY Risk Evaluation and Mitigation Strategy (REMS). Healthcare providers must become certified in the REMS in order to prescribe PIASKY.

To become certified in the REMS, prescribers must:

1. Review the PIASKY Prescribing Information, **Healthcare Provider Safety Brochure**, **Patient Safety Card**, and **Patient Guide**.
2. Enroll by completing and submitting this **Prescriber Enrollment Form** to the REMS.

Prescriber Information

Please enter your National Provider Identifier (NPI)# and click "Continue".

* fields required

* National Provider Identifier (NPI)#

[Continue](#)

Report all adverse events, especially meningococcal infections, that occur in patients receiving PIASKY to Genentech, Inc. at 888-835-2555 or by email to us_drugsafety@gene.com.

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3.3 Online Prescriber Enrollment Page Cont. - Conditional Field

* Credentials
☐ MD ☐ DO ☐ APRN ☐ PA ☒ Other (please specify)
* Credentials Other
* Medical Specialty
☐ Hematology/Oncology ☐ Immunology ☐ Internal Medicine ☐ Nephrology ☐ Neurology ☐ Rheumatology ☒ Other (please specify)
* Medical Specialty Other

3.4 Online Prescriber Enrollment Page - Successfully Submitted

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Online Prescriber Enrollment

Thank you for submitting your information to enroll in the PIASKY REMS.
You will receive an enrollment confirmation via email.

For questions regarding the PIASKY REMS, call 1-866-4My-Skyy (1-866-469-7599).

Report all adverse events, especially meningococcal infections, that occur in patients receiving PIASKY to Genentech, Inc. at 888-835-2555 or by email to us_drugsafety@gene.com.

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4. Pharmacies Page

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Pharmacies

Only a limited number of pharmacies will dispense PIASKY. All pharmacies that wish to dispense PIASKY must contract with Genentech, Inc., and must have the Authorized Representative certify by enrolling in the PIASKY REMS.

To become certified to dispense PIASKY, pharmacies must:

Step 1

Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the PIASKY REMS on behalf of the pharmacy.

Step 2

Have the Authorized Representative review the [Healthcare Provider Safety Brochure](#).

Step 3

Have the Authorized Representative enroll by completing and submitting the [Pharmacy Enrollment Form](#) to the REMS by fax.

Pharmacies interested in getting certified in the PIASKY REMS should contact the PIASKY REMS Call Center at 1-866-4MY-Sky (1-866-469-7599).

Step 4

Train all relevant staff involved in dispensing on PIASKY REMS requirements using the [Healthcare Provider Safety Brochure](#).

Step 5

Establish processes and procedures to contact the prescriber to assess the patient's vaccination status for up-to-date meningococcal vaccines for serotypes A, C, W, Y, and B according to the current Advisory Committee on Immunization Practices (ACIP) recommendations including antibacterial drug prophylaxis, if needed before treatment initiation, and document the findings.

Step 6

For patients who are not up to date with meningococcal vaccines when starting treatment: Establish processes and procedures to assess the patient's vaccination status for up-to-date meningococcal vaccines including antibacterial drug prophylaxis, if needed, before dispensing prescriptions up to 6 months after the first dose and document the findings.

Steps pharmacy staff should take prior to dispensing PIASKY, and at all times, are included in the [Healthcare Provider Safety Brochure](#).

Report all adverse events, especially meningococcal infections, that occur in patients receiving PIASKY to Genentech, Inc. at 888-835-2555 or by email to us drugsafety@gene.com.

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5. Forms and Resources Page

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Forms & Resources

Forms

 [PIASKY Prescriber Enrollment Form](#)

 [PIASKY Pharmacy Enrollment Form](#)

Resources

 [Healthcare Provider Safety Brochure](#)

 [Patient Guide](#)

 [Patient Safety Card](#)

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Report all adverse events, especially meningococcal infections, that occur in patients receiving PIASKY to Genentech, Inc. at 888-835-2555 or by email to us_drugsafety@gene.com.

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6. Certified Pharmacy Listing Page

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Certified Pharmacy Listing

The listing below includes only pharmacies that are certified in the PIASKY REMS.

Name ↑	Address	City	State	ZIP Code	Phone Number
ABC Pharmacy	123 Main Street	Philadelphia	PA	99999	555 555-1212
XYZ Pharmacy	416 Broadway	Philadelphia	PA	99999	555 555-3434

Report all adverse events, especially meningococcal infections, that occur in patients receiving PIASKY to Genentech, Inc. at 888-835-2555 or by email to us_drugsafety@gene.com.

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7. Contact Us Page

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injection for subcutaneous use

Contact Us

If you have any questions or require additional information, please contact us using one of the methods listed below.

The PIASKY REMS Contact Center is available Monday through Friday from 8am - 8pm ET.

 Phone: 1-866-4My-Skyy (1-866-469-7599)

 Fax: 1-833-670-4840

 Email: PIASKYREMS@REMSHelp.com

Report all adverse events, especially meningococcal infections, that occur in patients receiving PIASKY to Genentech, Inc. at 888-835-2555 or by email to drugsafety@gene.com.

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