You’ve been a warrior in fighting sickle cell disease

**ADAKVEO gives you the power of protection against pain crises**

ADAKVEO® (crizanlizumab-tmca) reduced pain crises by nearly half (45%) vs placebo in a 1-year study (based on a median annual rate of 1.63 pain crises with ADAKVEO vs 2.98 with placebo)*

*Pain crises were defined as painful episodes leading to a health care visit (ER, clinic, hospital, or local physician visit). Results were based on 132 patients with sickle cell disease. The median is the number that is exactly in the middle of all results seen in the 1-year study.

**What is ADAKVEO® (crizanlizumab-tmca)?**

ADAKVEO is used
- in people 16 years of age and older who have sickle cell disease
- to help reduce how often certain episodes (crises) happen

It is not known if ADAKVEO is safe and effective in children under 16 years of age.

**IMPORTANT SAFETY INFORMATION**

**What is the most important information I should know about ADAKVEO?**

ADAKVEO may cause serious side effects, including infusion reactions.

Please see additional Important Safety Information on pages 20-21, and throughout this brochure, and the Summary of Important Information on pages 22-23.
WHAT YOU NEED TO KNOW

As someone with sickle cell disease, you know it’s necessary to be empowered with information that can help in your fight.

Talk to your doctor today about how ADAKVEO® (crizanlizumab-tmca) may play an essential role in your plan to manage painful episodes (crises) in sickle cell disease.

WHAT IS ADAKVEO?

ADAKVEO [uh-dak-vee-oh] is a prescription medication that is:

- The first and only FDA-approved, once-monthly medication to reduce the number of pain crises in sickle cell disease*
- A biologic (also known as a monoclonal antibody), which is a protein-based medication that is made from living sources. ADAKVEO is taken by IV infusion
- A kind of therapy called a targeted biologic, which means it works within your body by attaching to P-selectin—a key sticky factor in the blood

*You will be given the first IV infusion at Week 0 and the second IV infusion 2 weeks later (Week 2). After that, you will be given an IV infusion every 4 weeks.

Important Safety Information (continued)

Infusion reactions. Infusion reactions may happen within 24 hours of receiving an infusion of ADAKVEO. Tell your health care provider right away if you get any of the following signs and symptoms of an infusion reaction:

- fever
- chills or shivering
- nausea
- vomiting
- tiredness
- shortness of breath or wheezing
- dizziness
- sweating
- hives
- itching
- shortness of breath or wheezing

Your doctor or health care provider may monitor you for signs and symptoms of infusion reactions.

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**The History of ADAKVEO**

The discovery of ADAKVEO® (crizanlizumab-tmca) was decades in the making for people with sickle cell disease:

- **1989**: A scientific team discovers a biologic that attaches to P-selectin (a key sticky factor in the blood) and learns that sickle cell disease involves more than sickled red blood cells.

- **1990**: The monoclonal antibody crizanlizumab-tmca is shown to attach to P-selectin, blocking connections between other cells.

- **2000**: The clinical study for crizanlizumab-tmca, also known as the SUSTAIN study, enrolls a diverse population of nearly 200 patients.

- **2013**: The 1-year SUSTAIN study of crizanlizumab-tmca is completed.

- **2016**: The FDA approves ADAKVEO® (crizanlizumab-tmca) for use in people 16 years of age and older, who have sickle cell disease, to help reduce how often certain episodes (crises) happen.

- **2019**: The scientific team continues research and focuses on one specific monoclonal antibody.

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**Important Safety Information (continued)**

ADAKVEO may interfere with a blood test.

Tell your health care provider that you are receiving ADAKVEO before having any blood tests. ADAKVEO may interfere with a laboratory test to measure your platelet counts.
THERE IS MORE TO THE STORY THAN SICKLED RED BLOOD CELLS

Stickiness

- Your blood vessels are damaged by sickled red blood cells and the breaking apart of red blood cells, which is called hemolysis.
- This damage makes blood vessels inflamed and irritated, activating molecules in the blood called selectins [si-lekt-ins], such as P-selectin. You can think of selectins as “sticky factors.”

Clusters

- These sticky factors can cause blood cells to stick to blood vessel walls and to each other, forming clusters in the bloodstream.

Blockages

- Clusters build up and become blockages, making it difficult for blood and oxygen to flow normally in the vessels.
- This process of clusters forming and becoming blockages in the blood vessel can happen throughout the body at any time. Your doctor may refer to these blockages as “vaso-occlusion” [vey-soh uh-klo-zhun].

HOW DOES ADAKVEO WORK?

ADAKVEO works by making blood vessels and certain blood cells less sticky

ADAKVEO® (crizanlizumab-tmca) attaches to P-selectin, a sticky factor that plays a key role in blockages, also known as vaso-occlusion.

By attaching to P-selectin, ADAKVEO blocks connections between certain cells, such as red blood cells, white blood cells, and platelets.

Important Safety Information (continued)

Before receiving ADAKVEO, tell your health care provider about all of your medical conditions, including if you

- are pregnant or plan to become pregnant. It is not known if ADAKVEO may harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if ADAKVEO passes into your breast milk. You and your health care provider should decide the best way to feed your baby during treatment with ADAKVEO.

Tell your health care provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Please see additional Important Safety Information on pages 20-21, and throughout this brochure, and the Summary of Important Information on pages 22-23.
The safety and effectiveness of ADAKVEO® (crizanlizumab-tmca) were studied in 198 people with sickle cell disease who were 16 to 63 years old.

67 people received ADAKVEO and 65 people received placebo at study centers primarily across the United States.

In the 1-year SUSTAIN study, pain crises were defined as painful episodes that led to a health care visit (ER, clinic, hospital, or local physician visit). Your doctor or health care provider may refer to pain crises as “vaso-occlusive crises” [vey-soh uh-kloo-siv], or VOCs. The following health conditions were also considered pain crises if they led to a health care visit:

- Respiratory issues, or acute chest syndrome
- Reduced blood flow or cell trapping in the liver, or hepatic sequestration
- Reduced blood flow or cell trapping in the spleen, or splenic sequestration
- Prolonged erections, or priapism

The clinical study of ADAKVEO included people:

- Who were of African, Hispanic, Caucasian, and other ancestries
- Across all genotypes of sickle cell disease, including HbSS, HbSC, HbSβ−thalassemia, HbSβ+-thalassemia, and others
- Who had either 2-4 or 5-10 pain crises in the last 12 months
- Who were also on hydroxyurea, and people who were not

Please see Important Safety Information on pages 20-21, and throughout this brochure, and the Summary of Important Information on pages 22-23.
HOW MAY ADAKVEO HELP?

ADAKVEO REDUCED PAIN CRISISSES BY NEARLY HALF

45% vs placebo (based on a median annual rate of 1.63 pain crises vs 2.98) in a 1-year study*

67 people taking ADAKVEO® (crizanlizumab-tmca) experienced a median annual rate of 1.63 pain crises compared with 2.98 pain crises in 65 people taking placebo—a 45% reduction. The median is the number that is exactly in the middle of all results seen in the 1-year study.*

ADAKVEO reduced the number of pain crises people had regardless of whether or not they were taking hydroxyurea

*Pain crises were defined as painful episodes leading to a health care visit (ER, clinic, hospital, or local physician visit). Results were based on 132 patients with sickle cell disease.

Important Safety Information (continued)
The most common side effects of ADAKVEO include:

- nausea
- back pain
- joint pain
- fever

These are not all of the possible side effects of ADAKVEO. For more information, ask your health care provider or pharmacist.

Call your doctor for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

PEOPLE TREATED WITH ADAKVEO SPENT FEWER DAYS IN THE HOSPITAL (vs placebo)

67 people taking ADAKVEO experienced a median annual rate of 4.0 days in the hospital vs 6.87 days for 65 people taking placebo—a 42% reduction. The median is the number that is exactly in the middle of all results seen in the 1-year study.* The annual number of days a patient was hospitalized included those days related to pain crises.

More than one-third of people had no pain crises with ADAKVEO in the clinical study

36% of people taking ADAKVEO had no pain crises vs 17% of people taking placebo

A total of 24 out of 67 people taking ADAKVEO had no pain crises compared with 11 out of 65 people taking placebo. These results include some people who did not complete the study.

Please see additional Important Safety Information on pages 20-21, and throughout this brochure, and the Summary of Important Information on pages 22-23.
WHAT SHOULD YOU KNOW ABOUT THE SIDE EFFECTS OF ADAKVEO?

It’s only natural to have concerns about side effects when starting a new treatment. ADAKVEO® (crizanlizumab-tmca) may cause side effects that you are not familiar with. It’s important for you and your health care provider to be aware of possible side effects of treatment with ADAKVEO.

ADAKVEO may cause serious side effects, including infusion reactions.

Infusion reactions may happen within 24 hours of receiving an infusion of ADAKVEO. Your doctor or health care provider may monitor you for signs and symptoms of infusion reactions. Tell your health care provider right away if you get any of the following signs and symptoms of an infusion reaction:

- Fever
- Chills or shivering
- Nausea (feeling sick)
- Vomiting
- Tiredness
- Dizziness
- Sweating
- Hives
- Itching
- Shortness of breath or wheezing

ADAKVEO may interfere with a certain blood test.

Tell your health care provider that you are receiving ADAKVEO before having any blood tests. ADAKVEO may interfere with a laboratory test to measure your platelet counts.

Common side effects

The most common side effects of ADAKVEO include nausea, back pain, joint pain, and fever. In the ADAKVEO study, most side effects were mild to moderate.

These are not all of the possible side effects of ADAKVEO. For more information, ask your health care provider or pharmacist. Call your doctor or health care provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

SOME HELPFUL TIPS

As a person living with sickle cell disease, it’s important to take care of yourself. Whether you are currently receiving ADAKVEO or not, follow these general tips for staying healthy:

- Eat heart-healthy foods such as fruits, vegetables, whole grains, and protein-rich foods and drink 8 to 10 glasses of water a day
- Try to avoid very hot or very cold temperatures
- Wash your hands regularly
- Stay up-to-date with vaccinations (shots)
- Talk to your doctor about how often you should schedule follow-up appointments

Please see Important Safety Information on pages 20-21, and throughout this brochure, and the Summary of Important Information on pages 22-23.
HOW DO YOU RECEIVE ADAKVEO?

ADAKVEO is a 30-minute IV infusion given once per month

- You will be given the first IV infusion at Week 0 and the second IV infusion 2 weeks later (Week 2). After that, you will be given an IV infusion every 4 weeks. If you miss an appointment for infusion, contact your doctor or health care provider as soon as possible to reschedule.

ADAKVEO is an IV infusion. What does that mean for you?

Delivered directly into your vein through an IV for 30 minutes
Given monthly 12 times per year (after your first 2 doses at Week 0 and Week 2)
Does not add to the number of pills you may be taking

WHAT ELSE SHOULD YOU CONSIDER WITH ADAKVEO?

- ADAKVEO® (crizanlizumab-tmca) is intended as a long-term treatment. Your doctor or health care provider will regularly monitor your condition and treatment plan.
- Before receiving ADAKVEO, remember to tell your health care provider about all of your medical conditions, including if you’re pregnant or plan to become pregnant. It is not known if ADAKVEO may harm your unborn baby.
- Tell your health care provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
- ADAKVEO can be taken with or without other treatments such as hydroxyurea.
- Follow your prescribed treatment plan and do not stop taking ADAKVEO unless your doctor or health care provider tells you to do so.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ADAKVEO?

ADAKVEO may cause serious side effects, including infusion reactions.

Infusion reactions. Infusion reactions may happen within 24 hours of receiving an infusion of ADAKVEO. Tell your health care provider right away if you get any of the following signs and symptoms of an infusion reaction:

- fever
- chills or shivering
- nausea
- vomiting
- tiredness
- dizziness
- sweating
- hives
- itching
- shortness of breath or wheezing

Please see additional Important Safety Information on pages 20-21, and throughout this brochure, and the Summary of Important Information on pages 22-23.
HAVE YOU JOINED THE WARRIOR WAY?

If you have started treatment with ADAKVEO® (crizanlizumab-tmca), or have been prescribed ADAKVEO, you are invited to be part of the Warrior Way program, which offers helpful resources for living with sickle cell disease and receiving treatment with ADAKVEO. For those of you who have already joined, welcome! For those of you who have not yet enrolled, find out more below. Being part of the Warrior Way will help you stay informed, feel supported, and get treatment resources that will help guide you on your treatment journey.

ADAKVEO SUPPORT AT PANO

HOW CAN YOU GET THE SUPPORT YOU NEED?

The ADAKVEO Support at PANO program may be able to assist you with accessing your medicine—from insurance verification to financial assistance information through a knowledgeable call center.

Novartis is committed to support you as you begin treatment with ADAKVEO, according to your doctor’s prescribed treatment. ADAKVEO Support at PANO offers resources and support designed specifically to help you with the process.*

ADAKVEO Support at PANO offers the following services:

• Help you understand your insurance coverage and financial responsibilities throughout the insurance verification process
• Help identify infusion sites covered by your insurance plan
• Information about financial assistance that may be available*
• Patient Support Counselors who are able to provide information in more than 160 languages
• One single point of contact to help guide you through getting access to ADAKVEO

*Novartis Pharmaceuticals Corporation does not guarantee success in obtaining coverage or financial assistance. Third-party payment for medical products and services is affected by numerous factors, not all of which can be anticipated or resolved.

ADAKVEO Support at PANO Service Request Form

The SRF is a single form with 2 parts:

• One part to be completed by you or your caregiver
• One part to be completed by your doctor

Both parts must be fully completed and submitted to start the process. ADAKVEO Support at PANO will then match the 2 parts and contact your doctor to initiate next steps.

Complete the ADAKVEO Support at PANO SRF today by visiting autosrf.force.com/autosrf.

Please see Important Safety Information on pages 20-21, and throughout this brochure, and the Summary of Important Information on pages 22-23.
How Can You Get the Support You Need?

Case coordinators, who have a background in social work, can provide support to you and your caregivers and connect you to third-party resources as needed.

Case coordinators are able to provide:

Insurance coverage guidance - Inform you and your caregiver about the process for insurance approval and provide status updates. Help educate you and your caregiver on the process for enrolling into ADAKVEO Support at PANO

Patient drug & disease education - Provide education about ADAKVEO and offer disease education

Case management - Suggest local and national resources to help you overcome barriers to disease management

This program does not provide medical advice or replace the care you receive from your health care team. For more information, call 1-800-282-7630.

Universal Co-pay Program

You may be eligible for immediate co-pay savings on your prescriptions.

• Eligible patients with private insurance may pay $0 per month
• Novartis will pay the remaining co-pay, up to $15,000 per calendar year, per product*

*Limitations apply. This offer is only available to patients with private insurance. The program is not available for patients who are enrolled in Medicare, Medicaid, or any other federal or state health care program. Novartis reserves the right to rescind, revoke, or amend this program without notice. For full Terms and Conditions, visit Copay.NovartisOncology.com or call 1-877-577-7756.

To find out if you are eligible for the Universal Co-pay Program, call 1-877-577-7756 or visit Copay.NovartisOncology.com.

Terms and Conditions: The Novartis Oncology Universal Co-pay Program includes the co-pay card, payment card, or rebate with a combined annual limit of $15,000. Patient is responsible for any costs once the limit is reached in a calendar year. This offer is only available to patients with private insurance. The program is not available for patients who: (i) are enrolled in Medicare, Medicaid, TRICARE, VA, DaVita, or any other federal or state health care program; (ii) are not using insurance coverage at all; (iii) are enrolled in an insurance plan that reimburses for the entire cost of the drug; or (iv) where product is not covered by patient’s insurance. The value of this program is exclusively for the benefit of enrolled patients and is intended to be credited toward patient out-of-pocket obligations, including applicable copayments, coinsurance, and deductibles. Proof of purchase may be required. Patient may not seek reimbursement for the value received from this program from other parties, including any health insurance program or plan, flexible spending account, or health care savings account. Patient is responsible for complying with any applicable limitations and requirements of his/her health plan related to the use of the program. Program is not valid where prohibited by law. Valid only in the United States and Puerto Rico. For certain medications, this offer is NOT valid for Massachusetts patients and is only valid for California patients that meet additional eligibility criteria. This program is not health insurance. This program may not be combined with any third-party rebate, coupon, or offer. Novartis reserves the right to rescind, revoke, or amend the program and discontinue support at any time without notice. Patient Instructions: After enrollment in the program, present this card and your insurance card along with a valid prescription at any participating pharmacy or through mail order OR send a completed Co-pay Assistance Request Form, using the information provided on this card, and the documents’ information identified on the request form to the Novartis Claim Processing Center. Patients are responsible for up to the first $0 (specific offer varies by brand). Novartis pays up to $15,000 per calendar year. If patient reaches the maximum annual cap per calendar year of $15,000, patient will be responsible for the difference. When you use this card, you are certifying that you understand and agree to comply with the program Terms and Conditions above. Direct patient questions to: 1-877-577-7756.

Please see Important Safety Information on pages 20-21, and throughout this brochure, and the Summary of Important Information on pages 22-23.
IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ADAKEVO® (crizanlizumab-tmca)?

ADAKEVO may cause serious side effects, including infusion reactions.

Infusion reactions. Infusion reactions may happen within 24 hours of receiving an infusion of ADAKEVO. Tell your health care provider right away if you get any of the following signs and symptoms of an infusion reaction:

• fever
• chills or shivering
• nausea
• vomiting
• tiredness

• dizziness
• sweating
• hives
• itching
• shortness of breath or wheezing

Your doctor or health care provider may monitor you for signs and symptoms of infusion reactions.

ADAKEVO may interfere with a blood test.

Tell your health care provider that you are receiving ADAKEVO before having any blood tests. ADAKEVO may interfere with a laboratory test to measure your platelet counts.

Before receiving ADAKEVO, tell your health care provider about all of your medical conditions, including if you

• are pregnant or plan to become pregnant. It is not known if ADAKEVO may harm your unborn baby
• are breastfeeding or plan to breastfeed. It is not known if ADAKEVO passes into your breast milk. You and your health care provider should decide the best way to feed your baby during treatment with ADAKEVO

Tell your health care provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

The most common side effects of ADAKEVO include:

• nausea
• joint pain
• back pain
• fever

These are not all of the possible side effects of ADAKEVO. For more information, ask your health care provider or pharmacist.

Call your doctor for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see Summary of Important Information on pages 22-23.
SUMMARY OF IMPORTANT INFORMATION FOR ADAKVEO

What is ADAKVEO® (crizanlizumab-tmca)?

ADAKVEO is used
• in people 16 years of age and older who have sickle cell disease
• to help reduce how often certain episodes (crises) happen

It is not known if ADAKVEO is safe and effective in children under 16 years of age.

What should I tell my doctor or health care provider before taking ADAKVEO?

Before receiving ADAKVEO, tell your health care provider about all of your medical conditions, including if you
• are pregnant or plan to become pregnant. It is not known if ADAKVEO may harm your unborn baby
• are breastfeeding or plan to breastfeed. It is not known if ADAKVEO passes into your breast milk. You and your health care provider should decide the best way to feed your baby during treatment with ADAKVEO

Tell your health care provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive ADAKVEO?
• Your health care provider will give you ADAKVEO as an infusion into your vein through an intravenous (IV) line over 30 minutes
• You will receive your first infusion, and then a second infusion 2 weeks later. After that, you will receive an infusion every 4 weeks
• Your health care provider may also prescribe other treatments for you to take during treatment with ADAKVEO
• Do not stop receiving ADAKVEO unless your health care provider tells you to
• If you miss an appointment for infusion, call your health care provider as soon as possible to reschedule

What are the possible side effects of ADAKVEO?

ADAKVEO may cause serious side effects, including infusion reactions.

Infusion reactions. Infusion reactions may happen within 24 hours of receiving an infusion of ADAKVEO. Tell your health care provider right away if you get any of the following signs and symptoms of an infusion reaction:
• fever
• dizziness
• chills or shivering
• nausea
• vomiting
• tiredness
• shortness of breath or wheezing

Your doctor or health care provider may monitor you for signs and symptoms of infusion reactions.

ADAKVEO may interfere with a blood test.

Tell your health care provider that you are receiving ADAKVEO before having any blood tests. ADAKVEO may interfere with a laboratory test to measure your platelet counts.

The most common side effects of ADAKVEO include:
• nausea
• joint pain
• back pain
• fever

These are not all of the possible side effects of ADAKVEO. For more information, ask your health care provider or pharmacist.

Call your doctor for medical advice about side effects.

You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of ADAKVEO

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your health care provider or pharmacist for more information about ADAKVEO.
FOR MORE INFORMATION, VISIT ADAKVEO.com.

Please see Important Safety Information on pages 20-21, and throughout this brochure, and the Summary of Important Information on pages 22-23.