EMPAVELI®
(pegcetacoplan) injection
1080 mg/20 mL solution

If you're like Angelo, an adult with PNH taking EMPAVELI,

Where will you go next?

Talk to your doctor about whether EMPAVELI is right for you.

What is the **EMPAVELI Injector** all about?

Find out more inside!

PNH=paroxysmal nocturnal hemoglobinuria.

INDICATION AND IMPORTANT SAFETY INFORMATION

What is EMPAVELI® (pegcetacoplan)?

EMPAVELI is a prescription medicine used to treat adults with a disease called paroxysmal nocturnal hemoglobinuria (PNH).

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

EMPAVELI is a medicine that affects your immune system and may lower the ability of your immune system to fight infections.

EMPAVELI increases your chance of getting serious infections caused by encapsulated bacteria such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B. These serious infections may quickly become life-threatening or cause death if not recognized and treated early.

1. You must complete or be up to date with the vaccines against *Streptococcus pneumoniae* and *Neisseria meningitidis* at least 2 weeks before your first dose of EMPAVELI.

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

Explore the compact, wearable EMPAVELI Injector!

The EMPAVELI Injector allows you to self-administer your EMPAVELI when and where works best for you (after receiving proper training).

Each EMPAVELI injection should take approximately 30 to 60 minutes.

Globin'

[glow-bin]

verb; Acting in pursuit of higher hemoglobin levels

Globin' can correlate to higher levels of hemoglobin in your blood. Hemoglobin carries oxygen throughout your body—and oxygen is, you know, the stuff of life.

If you're intrigued by what higher hemoglobin levels could mean for you, ask your doctor about EMPAVELI.

IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about EMPAVELI? (cont'd)

2. If you have not completed your vaccines and EMPAVELI must be started right away, you should receive the required vaccines as soon as possible.
3. If you have not been vaccinated and EMPAVELI must be started right away, you should also receive antibiotics to take for as long as your healthcare provider tells you.
4. If you have been vaccinated against these bacteria in the past, you might need additional vaccines before starting EMPAVELI. Your healthcare provider will decide if you need additional vaccines.

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PNH=paroxysmal nocturnal hemoglobinuria.

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The impact of hemolysis in PNH

Ongoing hemolysis may be causing your PNH symptoms

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare blood disease that involves the body's immune system acting irregularly.

In PNH, the immune system attacks and destroys its own red blood cells in a process called hemolysis.

If hemolysis is not addressed, it can cause lower than normal levels of red blood cells and hemoglobin (Hb) in your blood.

This may cause ongoing PNH symptoms, like fatigue, that force you to make compromises in your daily life.

Also, with anemia caused by low Hb levels, people with PNH may need to get frequent transfusions, which can take a toll on the body over time.

Findings from a US survey of people with PNH taking C5i treatment

- 122 people taking a C5i treatment for their PNH were surveyed (35 received eculizumab, 87 received ravulizumab)
- Most people surveyed (97%) had been taking C5i treatment for ≥3 months

Possible limitations of the survey

- A small number of people surveyed
- People not satisfied with their current C5i treatment may have been more motivated to participate
- Responses being subjective due to how people interpreted and reported their experiences
- The results cannot be generalized to all people with PNH

With C5i treatments, some people with PNH may continue to have symptoms

According to this survey, some people continued to have low Hb levels, ongoing fatigue, and the need for transfusions.

This could mean hemolysis is not under control.

In this survey, people reported:

Not achieving Hb levels ≥10.5 g/dL*	**63%** on eculizumab (20/32)	**57%** on ravulizumab (47/82)
Ongoing fatigue†	**89%** on eculizumab (31/35)	**75%** on ravulizumab (65/87)
Ongoing need for transfusions‡	**52%** on eculizumab (12/23)	**23%** on ravulizumab (7/31)

C5i=C5 inhibitor.

*Based on responses from 114 of the 122 survey participants who reported their Hb levels.

†Fatigue was measured using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale, which is a type of survey that collects information about the impact of fatigue on different parts of daily life. The scale ranges from 0 to 52. Higher scores mean less fatigue.

‡In patients who had a lifetime history of a transfusion and were on C5i treatment for at least 1 year. The need for transfusions was defined as 1 or more transfusions in the past 12 months.

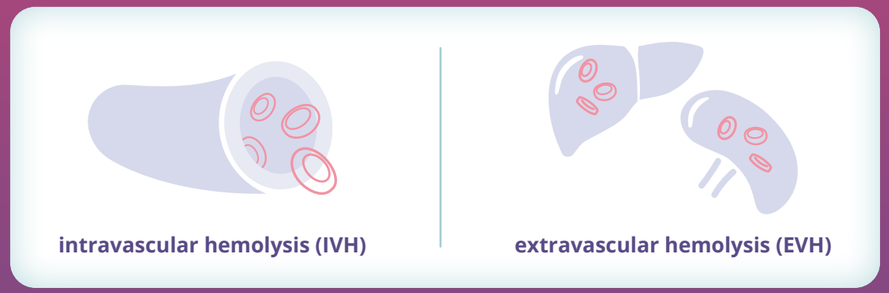
Don't delay!

Talk to your healthcare provider about your ongoing PNH symptoms and available treatment options.

How EMPAVELI works in PNH

EMPAVELI® (pegcetacoplan) injection 1080 mg/20 mL solution

EMPAVELI is the first and only C3i treatment for PNH that controls both types of hemolysis



The complement system is a part of your immune system and helps the body fight off infections. Certain proteins in the complement system work together and create a chain reaction.

This chain reaction is called the complement cascade.

C3i=C3 inhibitor.

IMPORTANT SAFETY INFORMATION (cont'd)

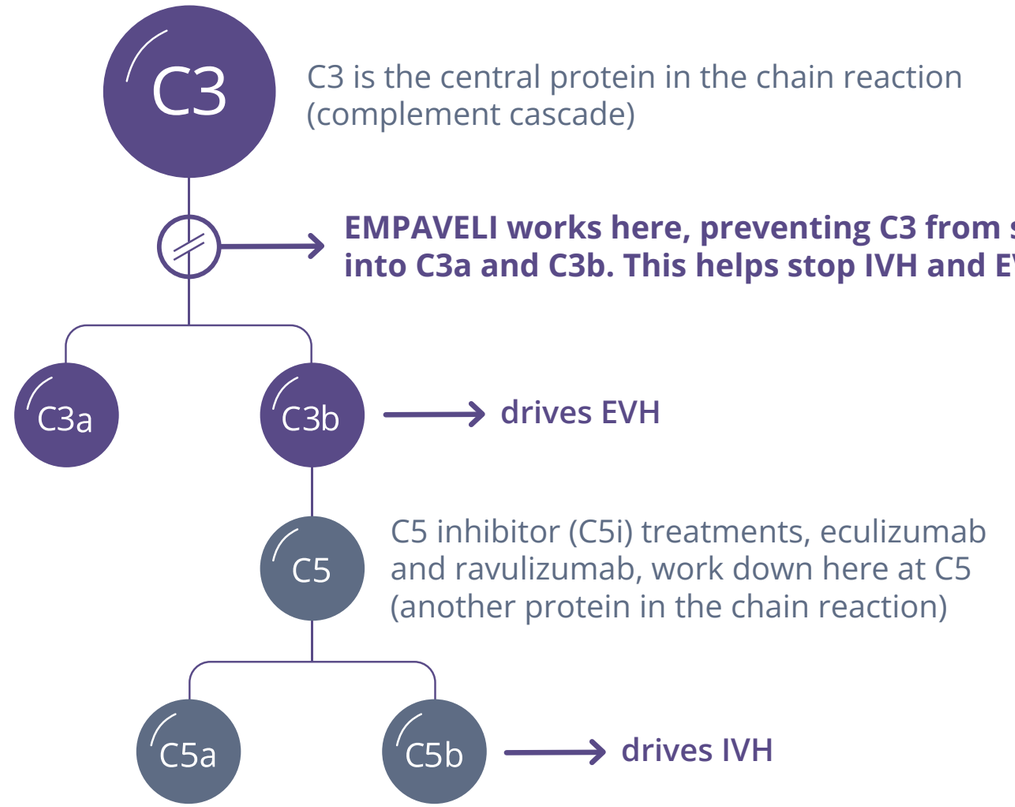
What is the most important information I should know about EMPAVELI? (cont'd)

5. Vaccines do not prevent all infections caused by encapsulated bacteria. **Call your healthcare provider or get emergency medical care right away if you get any of these signs and symptoms of a serious infection:**

- fever with or without shivers or the chills
- fever with chest pain and cough
- fever with high heart rate
- headache and a fever
- confusion
- clammy skin
- fever and a rash
- fever with breathlessness or fast breathing
- headache with nausea or vomiting
- headache with a stiff neck or stiff back
- body aches with flu-like symptoms
- eyes sensitive to light

EMPAVELI acts differently than other PNH treatments

EMPAVELI works higher in the complement system than C5i treatments



PNH=paroxysmal nocturnal hemoglobinuria.

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How EMPAVELI was studied

EMPAVELI was studied in two Phase 3 clinical trials for PNH:

- The PEGASUS study, which included adults with previous C5i treatment (eculizumab)
- The PRINCE study, which included adults without any previous complement inhibitor treatment

See how EMPAVELI was studied in PEGASUS

In the PEGASUS clinical trial, EMPAVELI was compared to the C5i treatment eculizumab

80 adults with PNH

On a steady dose of **eculizumab for at least 3 months**

With low hemoglobin (Hb) levels **(less than 10.5 g/dL)**

The study consisted of 3 parts:

4 weeks

Part 1

All participants received both eculizumab and EMPAVELI

16 weeks

Part 2

They were then split into 2 groups:

- Group 1 received only EMPAVELI for 16 weeks (n=41)
- Group 2 received only eculizumab for 16 weeks (n=39)

32 weeks

Part 3

- Group 1 continued EMPAVELI for 32 more weeks
- Group 2 transitioned to EMPAVELI for 32 weeks*

*The transition time for Group 2 was 4 weeks and involved taking both eculizumab and EMPAVELI, before receiving EMPAVELI only.

Main goals of PEGASUS

- Primary goal: explore changes in Hb levels from the beginning of the study
- Safety: monitor the occurrence of side effects

Selected secondary goals and analyses

- See how many people could become transfusion-free†
- Explore changes in absolute reticulocyte count (ARC) from the beginning of the study†
- Explore changes in lactate dehydrogenase (LDH) from the beginning of the study†
- Explore changes in fatigue from the beginning of the study
- Measure the proportion of people who achieved normalization of Hb or LDH

C5i=C5 inhibitor; PNH=paroxysmal nocturnal hemoglobinuria.

†Noninferiority tests were used for these secondary goals. These tests determined if EMPAVELI was no worse than a C5i (eculizumab) compared from the beginning of the study.

IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about EMPAVELI? (cont'd)

Your healthcare provider will give you a Patient Safety Card about the risk of serious infections. Carry it with you at all times during treatment and for 2 months after your last EMPAVELI dose. Your risk of serious infections may continue for several weeks after your last dose of EMPAVELI. It is important to show this card to any healthcare provider who treats you. This will help them diagnose and treat you quickly.

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

See how EMPAVELI was studied in PRINCE

The PRINCE clinical trial compared people taking EMPAVELI to people in a control arm, which meant they were not taking EMPAVELI or any type of complement inhibitor treatment. People in the control arm continued their non–complement inhibitor medications, if they were taking any.

53 adults with PNH were randomly divided into **2 groups** and studied for **26 weeks**

1st group

received EMPAVELI (n=35)

2nd group

(the control arm) continued their PNH treatment without EMPAVELI or any other complement inhibitor (n=18)

These people had **never received complement inhibitor treatment** for their PNH before entering the trial. People entering the trial had an Hb level below normal.

Most people in the trial had been getting frequent blood transfusions to make up for low Hb levels. People entering the PRINCE trial had received an **average of 4 transfusions in the preceding year**.

Hb=hemoglobin; LDH=lactate dehydrogenase; PNH=paroxysmal nocturnal hemoglobinuria.

IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about EMPAVELI? (cont'd)

EMPAVELI is only available through a program called the EMPAVELI Risk Evaluation and Mitigation Strategy (REMS). Before you can take EMPAVELI, your healthcare provider must enroll in the EMPAVELI REMS program, counsel you about the risk of serious infections caused by certain bacteria, give you information about the symptoms of serious infections, make sure that you are vaccinated against serious infections caused by encapsulated bacteria and that you receive antibiotics if you need to start EMPAVELI right away and you are not up to date on your vaccines, and give you a Patient Safety Card about your risk of serious infections.

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Monica is an adult with PNH who's taken EMPAVELI.

Main goals of PRINCE

- Explore achieving stabilization of Hb levels
- Explore changes in LDH from the beginning of the study
- Safety: monitor the occurrence of side effects

Selected secondary goals and analyses

- See how many people could become transfusion-free
- Measure the proportion of people who achieved normalization of Hb
- Measure the proportion of people who achieved normalization of LDH

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Increased hemoglobin with EMPAVELI

Superior improvements in hemoglobin (Hb) in people who had previously received a C5i: results at Week 16

Primary goal in the PEGASUS study: to explore whether EMPAVELI was better at improving Hb levels than a C5i (eculizumab) in people living with paroxysmal nocturnal hemoglobinuria (PNH)

In people who had previously received a C5i (PEGASUS)

People taking EMPAVELI had a
2.37 g/dL Hb INCREASE

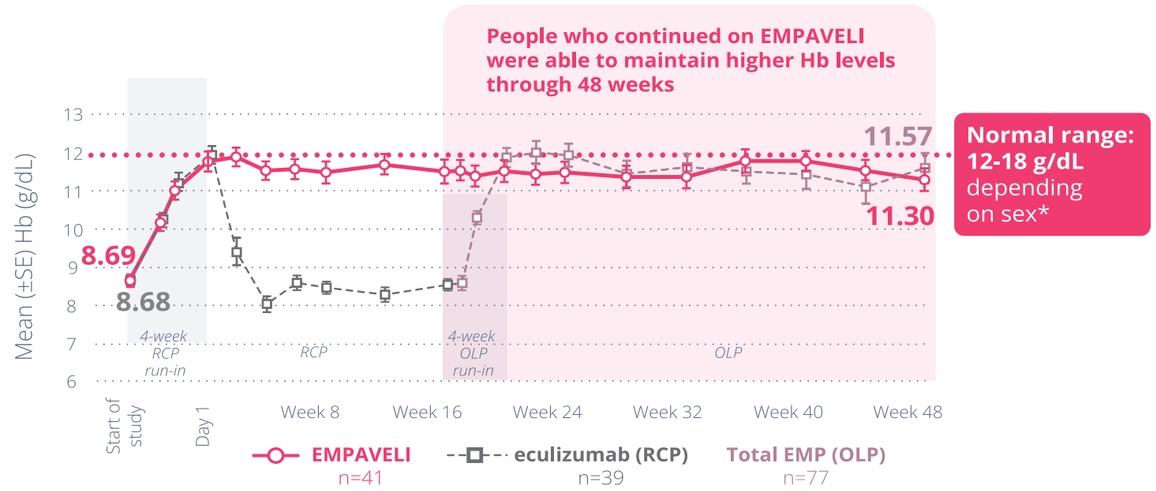
People taking eculizumab had a
1.47 g/dL Hb DECREASE

SUPERIOR Hb DIFFERENCE
of 3.84 g/dL with EMPAVELI
compared to eculizumab
(P<0.0001)

Peg is an adult with PNH who's taken EMPAVELI.

Hb improvement was maintained through the 48-week study

Average change in Hb levels from beginning to Week 48



Normal range: 12-18 g/dL depending on sex*

*12-16 g/dL for females, 13.6-18 g/dL for males.

IMPORTANT SAFETY INFORMATION (cont'd)

Who should NOT take EMPAVELI?

Do not take EMPAVELI if you:

- are allergic to pegcetacoplan or any of the ingredients in EMPAVELI.
- have a serious infection caused by encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B when you are starting EMPAVELI treatment.

C5i=C5 inhibitor; EMP=EMPAVELI; OLP=open-label period; RCP=randomized control period; SE=standard error.

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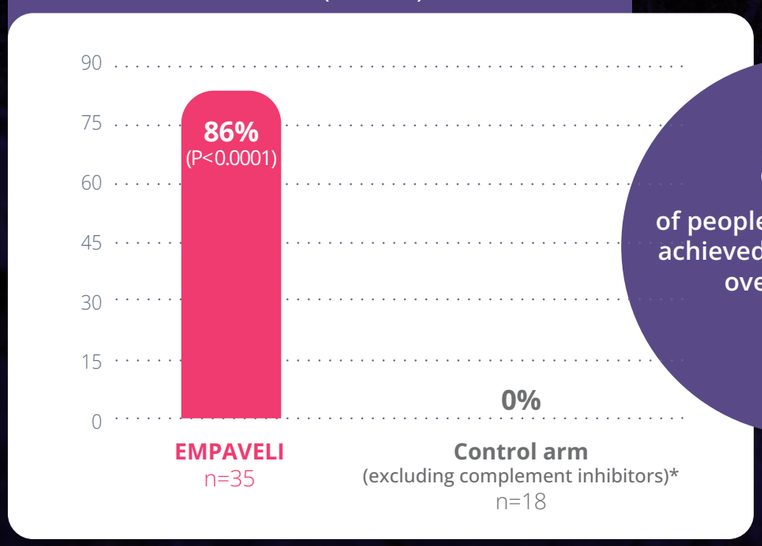
Stabilized hemoglobin with EMPAVELI

Stabilized hemoglobin (Hb) levels in people who had never received a complement inhibitor: results at Week 26*

One of the primary goals in the PRINCE study: to explore whether EMPAVELI stabilized hemoglobin in people living with PNH not previously treated with a complement inhibitor

In people who had never received a complement inhibitor (PRINCE)



86%
of people taking EMPAVELI achieved Hb stabilization over 26 weeks

*Hb stabilization means avoiding a >1 g/dL decrease in Hb levels throughout the study.

PNH=paroxysmal nocturnal hemoglobinuria.

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

Stacey is an adult with PNH who's taken EMPAVELI.

IMPORTANT SAFETY INFORMATION (cont'd)

Before you take EMPAVELI, tell your healthcare provider about all of your medical conditions, including if you:

- have an infection or fever.
- are pregnant or plan to become pregnant. EMPAVELI may harm your unborn baby. Females who are able to become pregnant should have a pregnancy test before starting treatment with EMPAVELI and use an effective method of birth control during treatment with EMPAVELI and for 40 days after the last dose.
- are breastfeeding or plan to breastfeed. It is not known if EMPAVELI passes into your breast milk. You should not breastfeed during treatment with EMPAVELI and for 40 days after the last dose.

Avoiding the need for transfusions with EMPAVELI

Becoming transfusion-free with EMPAVELI vs eculizumab—in people who had previously received a C5i

At Week 16 in PEGASUS, EMPAVELI was no worse than a C5i (eculizumab) in helping people with PNH become transfusion-free.

In people who had previously received a C5i (PEGASUS)

85%
of people taking EMPAVELI were **transfusion-free**

15%
of people taking a C5i (eculizumab) were **transfusion-free**

Becoming transfusion-free with EMPAVELI vs control arm—in people who had never received a complement inhibitor

At Week 26 in PRINCE, most people taking EMPAVELI were transfusion-free.

In people who had never received a complement inhibitor (PRINCE)

91%
of people taking EMPAVELI were **transfusion-free**

6%
of people in the control arm (excluding complement inhibitors) were **transfusion-free**

IMPORTANT SAFETY INFORMATION (cont'd)

Tell your healthcare provider about all the vaccines you receive and medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements which could affect your treatment.

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"I have not needed a transfusion since I switched to EMPAVELI."

Individual experiences may vary.

Jillian is an adult with PNH who's taken EMPAVELI.

In people who had previously received a C5i (PEGASUS)

Reduced ARC

At Week 16 in PEGASUS, EMPAVELI was no worse than a C5i (eculizumab) in helping people with PNH reduce their ARC.

Average changes in ARC with EMPAVELI vs eculizumab—in people who had previously received a C5i

- People taking EMPAVELI saw their ARC **reduced by 136 x 10^9 cells/L**
- People taking a C5i (eculizumab) saw an **increase in their ARC of 28 x 10^9 cells/L**

ARC=absolute reticulocyte count; C5i=C5 inhibitor; PNH=paroxysmal nocturnal hemoglobinuria.

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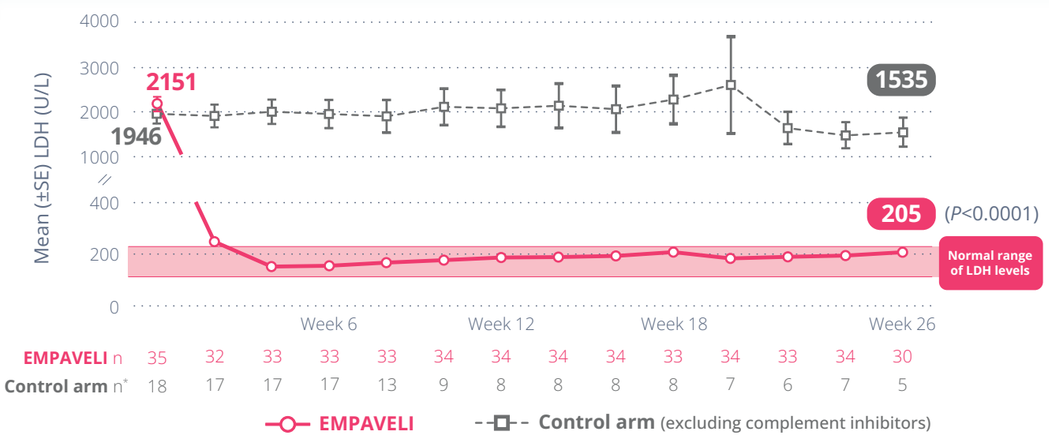
Changes in LDH with EMPAVELI

Rapid and sustained LDH reductions with EMPAVELI vs control arm—in people who had never received a complement inhibitor

One of the primary goals in the PRINCE study: to explore whether EMPAVELI reduced LDH in people living with PNH not previously treated with a complement inhibitor

By Week 2 in PRINCE, average LDH levels in the EMPAVELI group had dropped from baseline and remained there through 26 weeks.

In people who had never received a complement inhibitor (PRINCE)



*Control arm (excluding complement inhibitors) only includes data on or before escape (switching to EMPAVELI).

At Week 26, average reductions in LDH levels were:

- -1870 U/L in the EMPAVELI group
- -400 U/L in the control arm (excluding complement inhibitors)

Changes in LDH levels with EMPAVELI vs eculizumab—in people who had previously received a C5i (PEGASUS)

At Week 16 in PEGASUS, it could not be determined if EMPAVELI was any worse than C5i (eculizumab) in reducing LDH.

C5i=C5 inhibitor; LDH=lactate dehydrogenase; PNH=paroxysmal nocturnal hemoglobinuria; SE=standard error.

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IMPORTANT SAFETY INFORMATION (cont'd)

If you stop taking EMPAVELI, your healthcare provider will need to monitor you closely for at least 8 weeks after stopping EMPAVELI. Stopping treatment with EMPAVELI may cause a breakdown of red blood cells due to PNH.

Symptoms or problems that can happen due to red blood cell breakdown include:

- decreased hemoglobin level in your blood
- blood in your urine
- shortness of breath
- trouble swallowing
- tiredness
- pain in the stomach (abdomen)
- blood clots
- erectile dysfunction (ED)

Changes in fatigue

Changes in fatigue with EMPAVELI vs eculizumab—in people who had previously received a C5i (PEGASUS)

Although it was not formally tested, people in the study were asked to report their changes in levels of fatigue at Week 16.

Measuring fatigue improvement

Fatigue was measured using the FACIT-Fatigue scale, a 13-question survey. In the survey, participants rated the level of impact they felt that their fatigue had on daily activities and function.

This information is for observation only and no conclusions can be made on the effect of EMPAVELI on fatigue. No comparisons can be made between those taking EMPAVELI and those taking eculizumab.

People taking EMPAVELI **showed an improvement of**

9.2 points

compared to their fatigue levels at the beginning of the study

People taking C5i (eculizumab) **showed a decrease of**

-2.7 points

compared to their fatigue levels at the beginning of the study

An increase of 5 or more points is seen as a clinically meaningful improvement.

IMPORTANT SAFETY INFORMATION (cont'd)

What are the possible side effects of EMPAVELI?

EMPAVELI can cause serious side effects including allergic reactions. Allergic reactions can happen during your EMPAVELI infusion. Stop your EMPAVELI infusion and tell your healthcare provider or get emergency medical care right away if you get any of these symptoms during your EMPAVELI infusion:

- chest pain
- trouble breathing or shortness of breath
- swelling of your face, tongue, or throat
- feel faint or pass out

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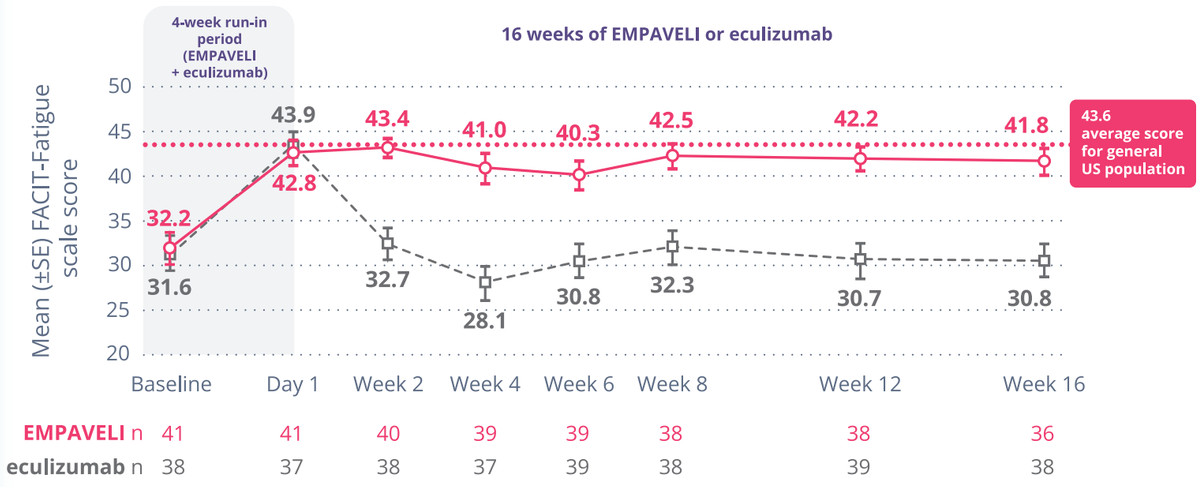
Average FACIT-Fatigue scores from beginning of study through Week 16



The FACIT-Fatigue scale ranges from 0 to 52.
Higher scores mean less fatigue.

These data include people who did and did not get a transfusion during the study.

Andrea is an adult with PNH who's taken EMPAVELI.

C5i=C5 inhibitor; FACIT=Functional Assessment of Chronic Illness Therapy; PNH=paroxysmal nocturnal hemoglobinuria; SE=standard error.

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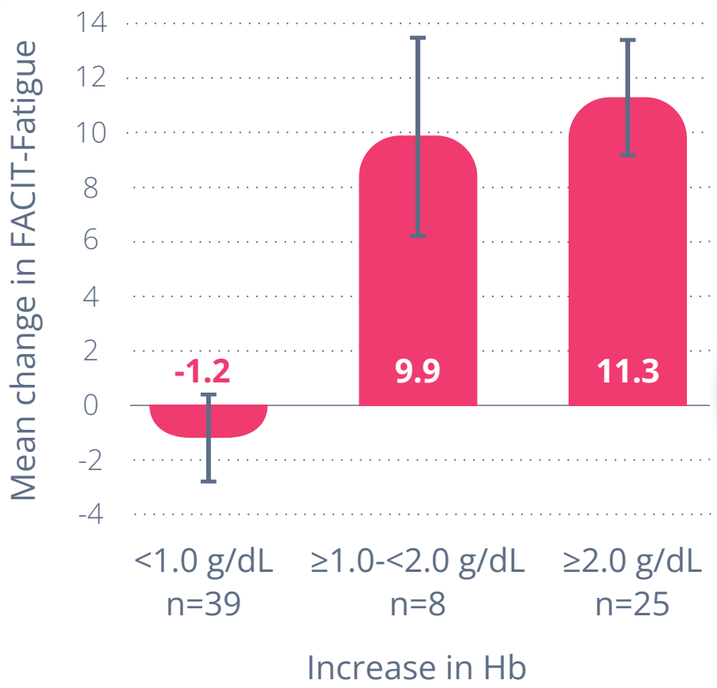
A post hoc analysis of PEGASUS data found a link between Hb and fatigue

In people who had previously received a C5i (PEGASUS)



People with greater **improvements in Hb** showed larger **reductions in fatigue**

People with PNH who had an **Hb improvement of 1 g/dL** or more had an **average fatigue improvement of ~10 points**.

- A post hoc analysis gathers additional findings after a study has ended. It is not considered as scientifically strong as an analysis that was planned before the study began
- This analysis included people receiving EMPAVELI and people receiving eculizumab

C5i=C5 inhibitor; FACIT=Functional Assessment of Chronic Illness Therapy; Hb=hemoglobin; PNH=paroxysmal nocturnal hemoglobinuria.

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"I love leisurely walks and vacations with my family. With my increase in Hb levels and energy, I don't have to miss out."

Individual experiences may vary.

Andrea is an adult with PNH who's taken EMPAVELI.

IMPORTANT SAFETY INFORMATION (cont'd)

What are the possible side effects of EMPAVELI? (cont'd)

The most common side effects in people with PNH treated with EMPAVELI include injection-site reactions; infections; diarrhea; pain in the stomach (abdomen); respiratory tract infection; pain in the arms, hands, legs, or feet; low potassium in blood; tiredness; viral infection; cough; joint pain; dizziness; headache; and rash.

Getting to normalization of lab values

What is normalization? How is it different than stabilization?

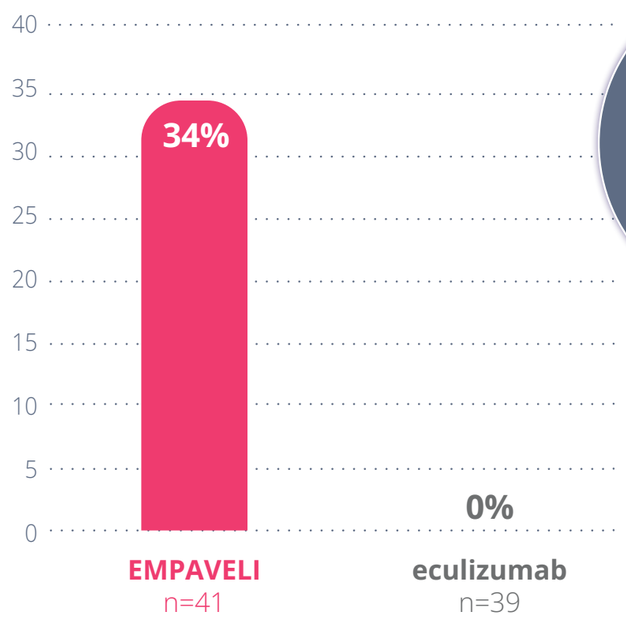
Normalization means lab values improved to levels like those of adults who don't have PNH. This is different than stabilization, which generally means that lab values did not get worse.

Hemoglobin (Hb) normalization in people with and without previous complement inhibitor treatment

This information is for observation only and no conclusions can be made on the effect of EMPAVELI on Hb normalization. No comparisons can be made between those taking EMPAVELI and those taking eculizumab in PEGASUS or those in the control arm (excluding complement inhibitors) in PRINCE.

In people who had previously received a C5i (PEGASUS)

At Week 16 in PEGASUS



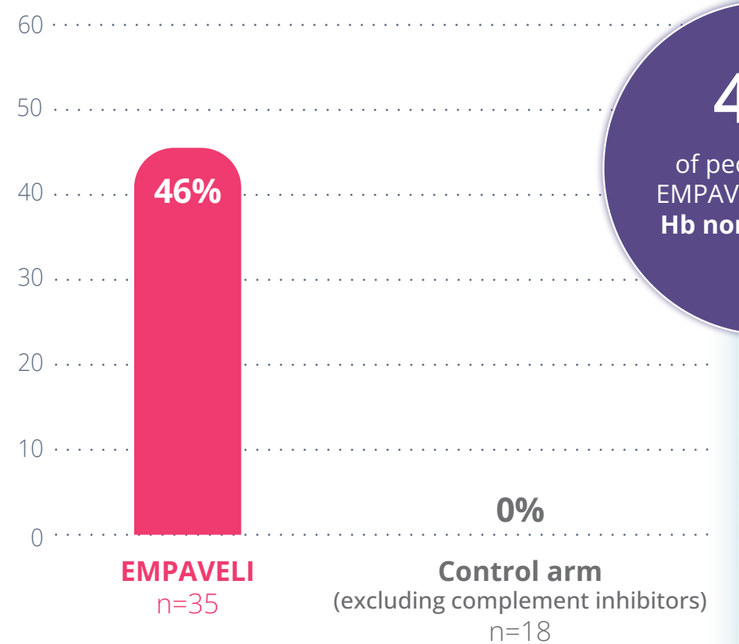
34% of people taking EMPAVELI achieved **Hb normalization**

Hb normalization means their Hb got to within the normal range (12-16 g/dL for females, 13.6-18 g/dL for males).

These data include only people who did not require a transfusion during the study.

In people who had never received a complement inhibitor (PRINCE)

At Week 26 in PRINCE



46% of people taking EMPAVELI achieved **Hb normalization**

Hb normalization means their Hb got to within the normal range (12-16 g/dL for females, 13.6-18 g/dL for males).

These data include only people who did not require a transfusion during the study.

C5i=C5 inhibitor; PNH=paroxysmal nocturnal hemoglobinuria.

IMPORTANT SAFETY INFORMATION (cont'd)

What are the possible side effects of EMPAVELI? (cont'd)

These are not all of the possible side effects of EMPAVELI. Tell your healthcare provider about any side effect that bothers you or that does not go away.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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Louis is an adult with PNH who's taken EMPAVELI.

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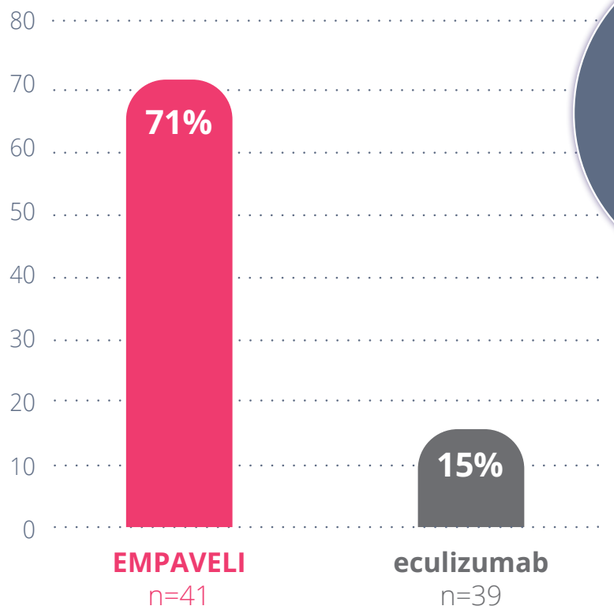
LDH normalization in people with and without previous complement inhibitor treatment

This information is for observation only and no conclusions can be made on the effect of EMPAVELI on LDH normalization. No comparisons can be made between those taking EMPAVELI and those taking eculizumab in PEGASUS or those in the control arm (excluding complement inhibitors) in PRINCE.

The majority of people taking EMPAVELI reduced their LDH levels to within the normal range (113-226 U/L).

In people who had previously received a C5i (PEGASUS)

At Week 16 in PEGASUS



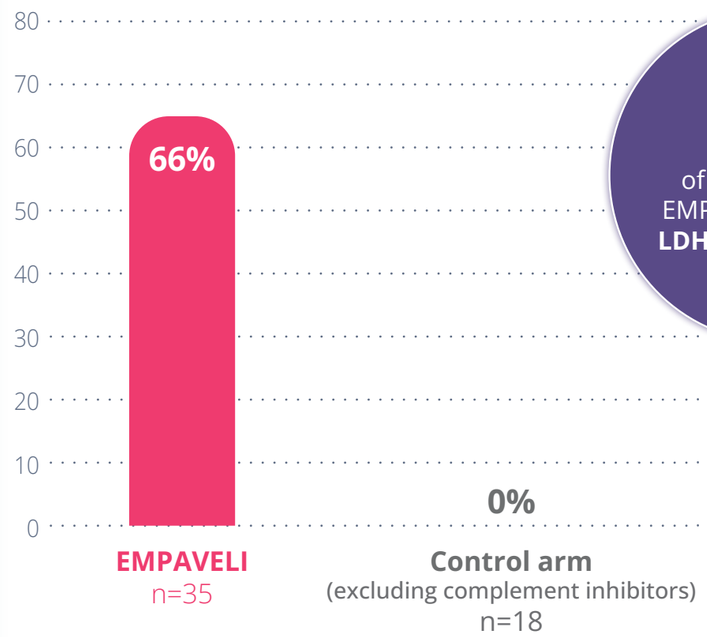
71% of people taking EMPAVELI achieved **LDH normalization**

These data include only people who did not require a transfusion during the study.

Nearly 2/3 of people taking EMPAVELI reduced their LDH levels to within the normal range (113-226 U/L).

In people who had never received a complement inhibitor (PRINCE)

At Week 26 in PRINCE



66% of people taking EMPAVELI achieved **LDH normalization**

These data include only people who did not require a transfusion during the study.

Jillian is an adult with PNH who's taken EMPAVELI.

C5i=C5 inhibitor; Hb=hemoglobin; LDH=lactate dehydrogenase; PNH=paroxysmal nocturnal hemoglobinuria.

IMPORTANT SAFETY INFORMATION

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

EMPAVELI is a medicine that affects your immune system and may lower the ability of your immune system to fight infections.

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 38-39, and the full Prescribing Information and Medication Guide.

Up to 3 years of results from an integrated analysis

Tori is an adult with PNH who's taken EMPAVELI.

An open-label extension study included adults with PNH (N=114) who enrolled and had previously completed the EMPAVELI Phase 3 studies (PEGASUS, PRINCE). Long-term data presented are from an integrated analysis of data in the subset of people who received 1080 mg of EMPAVELI by subcutaneous infusion twice weekly, or every 3 days, for up to 3 years (2.5 years, PRINCE; 3 years, PEGASUS).

An integrated analysis is an analysis of 2 or more sets of clinical trial data.

The goal of this analysis was to evaluate the long-term effectiveness and safety of EMPAVELI in treating adults with PNH.

Limitations:

- Data from this post hoc, integrated analysis are descriptive in nature, collected for observation only
- The analysis included a mixed group of people with PNH—those with previous C5i treatment (PEGASUS) and those without complement inhibitor treatment (PRINCE). Findings may not represent all people with PNH
- Baseline for those not originally assigned EMPAVELI in the trials was defined by when they started receiving EMPAVELI to evaluate the long-term effectiveness and safety of treatment with EMPAVELI

Most common side effects

- The most common adverse events (≥10%) were infections and infestations (75.8%), injection site reactions (36.4%), abdominal pain (18.2%), fatigue (18.2%), headache (16.7%), and cough (12.1%)—consistent with those reported in the original studies)

Serious side effects

- Two serious adverse events deemed related to EMPAVELI occurred: 1 case of biliary sepsis (severe infection of the gallbladder and associated structures) in PEGASUS and 1 case of sepsis (severe, potentially life-threatening infection throughout the body) in PRINCE

Overall, no new or unexpected side effects were identified.

C5i=C5 inhibitor; Hb=hemoglobin; LDH=lactate dehydrogenase; PNH=paroxysmal nocturnal hemoglobinuria.

IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about EMPAVELI? (cont'd)

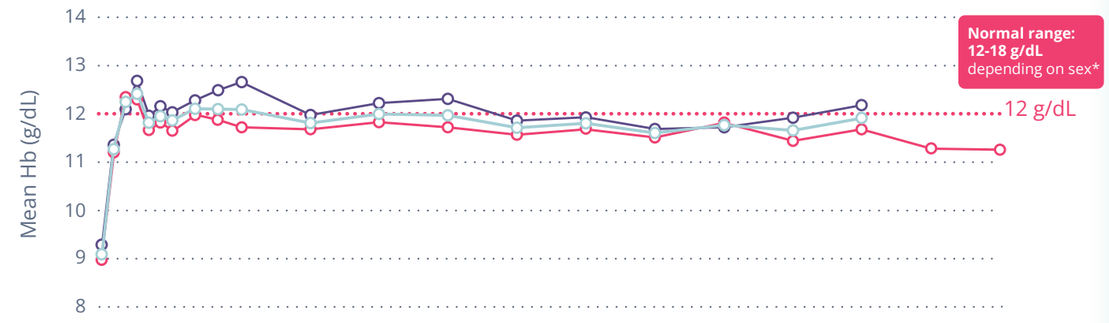
EMPAVELI increases your chance of getting serious infections caused by encapsulated bacteria such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B. These serious infections may quickly become life-threatening or cause death if not recognized and treated early.

1. **You must complete or be up to date with the vaccines against *Streptococcus pneumoniae* and *Neisseria meningitidis* at least 2 weeks before your first dose of EMPAVELI.**

EMPAVELI®
(pegcetacoplan) injection
1080 mg/20 mL solution

Long-term sustained Hb and LDH

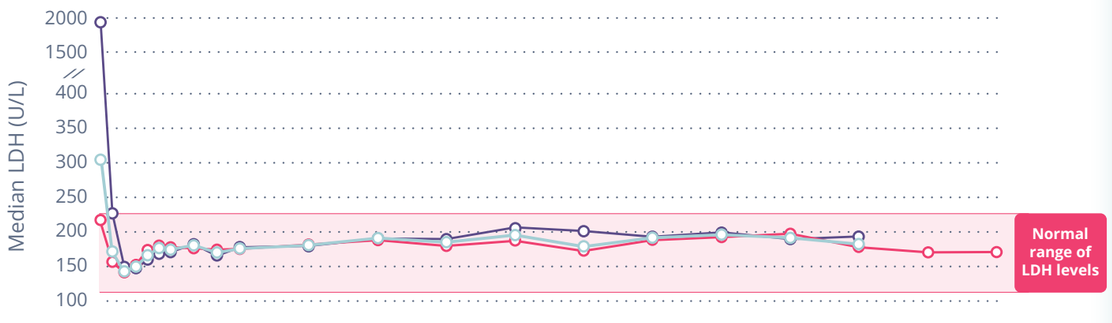
Hb levels up to 3 years



	Baseline	Week 12	Week 36	Week 60	Week 84	Week 108	Week 132	Week 156
PEGASUS n	80	42	68	60	52	44	35	25
PRINCE n	52	47	49	46	45	41	29	
Total n	132	89	117	106	97	85	64	

*12-16 g/dL for females, 13.6-18 g/dL for males.

LDH levels up to 3 years



	Baseline	Week 12	Week 36	Week 60	Week 84	Week 108	Week 132	Week 156
PEGASUS n	80	46	73	63	53	49	39	26
PRINCE n	52	49	50	47	47	42	32	
Total n	132	95	123	110	100	91	71	

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

EMPAVELI®
(pegcetacoplan) injection
1080 mg/20 mL solution

Most common side effects

PEGASUS at Week 16


Injection site reactions


Infections


Diarrhea


Abdominal pain


Respiratory tract infection


Viral infection


Tiredness

- **Serious adverse reactions were reported in 17% of patients treated with EMPAVELI**
  - The most common serious adverse events were infections (5%)
- Injection/infusion site reactions were mild or moderate in severity. Seventeen cases of diarrhea were reported during the 48 weeks. Fifteen of the cases were mild and 2 were moderate
- Breakthrough hemolysis occurred in 10% of those taking EMPAVELI vs 23% of those taking eculizumab at Week 16 in the PEGASUS study. Three people taking EMPAVELI left the study due to hemolysis

PRINCE at Week 26


Injection site reactions


Infections


Viral infection


Pain in extremity


Low potassium


Joint pain


Dizziness


Abdominal pain


Rash


Headache

- **One patient treated with EMPAVELI died due to septic shock**
- **Serious adverse reactions were reported in 13% of patients treated with EMPAVELI**
- Overall, there were no EMPAVELI-related side effects leading to drug or trial discontinuation
- No events of acute hemolysis were observed in either treatment group through Week 26

- **These are not all the possible side effects of EMPAVELI. Be sure to tell your healthcare provider about any side effect that bothers you or that does not go away. Side effects can be reported to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch**
- Two people taking EMPAVELI in the PEGASUS and PRINCE studies had side effects related to blood clots. They were deemed not related to EMPAVELI
- There have been no cases of meningococcal infections in any adults with PNH treated with pegcetacoplan, as of 11/13/2023. They were vaccinated prior to treatment with pegcetacoplan

EMPAVELI REMS program ensures your safety is a top priority

EMPAVELI is only available through a program called the EMPAVELI REMS (Risk Evaluation and Mitigation Strategy).

REMS is a safety program run by the FDA. **Before you can take EMPAVELI, your healthcare provider must enroll in the program and will provide you with the following:**

- Counseling on the risk of serious infections caused by certain bacteria
- Information about the symptoms of serious infections
- Appropriate vaccinations against serious infections caused by encapsulated bacteria
  - You will receive antibiotics if you need to start EMPAVELI right away and are not up to date on your vaccines
- A Patient Safety Card
  - Carry this card with you at all times during treatment and for 2 months after your last EMPAVELI dose
  - Show this card to any healthcare professional to help diagnose and treat you quickly
  - Your risk of serious infection may continue for several weeks after your last dose of EMPAVELI

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

Self-administration with the EMPAVELI® Injector (pegcetacoplan)

EMPAVELI self-administration may fit into your lifestyle

EMPAVELI is a PNH treatment that you give yourself at home or wherever works for you (after receiving proper training).

EMPAVELI is self-administered subcutaneously (just under the skin). Self-administering EMPAVELI should take approximately 30 to 60 minutes.

- No intravenous (IV) infusions
- No infusion center visits
- No need to plan around infusion appointments

EMPAVELI can be self-administered using either:

- The EMPAVELI Injector; or
- A commercially available infusion pump with a reservoir of at least 20 mL

PNH=paroxysmal nocturnal hemoglobinuria.

IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about EMPAVELI? (cont'd)

2. If you have not completed your vaccines and EMPAVELI must be started right away, you should receive the required vaccines as soon as possible.
3. If you have not been vaccinated and EMPAVELI must be started right away, you should also receive antibiotics to take for as long as your healthcare provider tells you.
4. If you have been vaccinated against these bacteria in the past, you might need additional vaccinations before starting EMPAVELI. Your healthcare provider will decide if you need additional vaccinations.

EMPAVELI®
(pegcetacoplan) injection
1080 mg/20 mL solution

About the EMPAVELI Injector

- **Push button starts injection and pops up when injection is complete**
- **The needle is never seen**
- **Compact device with no tubing involved**
- **The gauge shows the injection progress**

You will be trained before using the EMPAVELI Injector for the first time. Refer to the EMPAVELI Injector Instructions for Use for more information.

"I love to travel. With EMPAVELI self-administration, I can bring my supplies with me and travel without interrupting my treatment schedule."

Emma is an adult with PNH who's taken EMPAVELI.
Individual experiences may vary.

When traveling, ensure that EMPAVELI stays at 36°F to 46°F (2°C-8°C).

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

How do I take EMPAVELI?

EMPAVELI is self-administered just under the skin using a small, thin needle that you never see with the EMPAVELI Injector.

EMPAVELI is not an IV infusion (into the vein) that requires a healthcare provider to administer it for you.

How often do I take EMPAVELI?

- EMPAVELI is taken 2 times a week*
- The injection takes approximately 30 to 60 minutes

*If there is an increase in your LDH, an enzyme in your blood, your healthcare provider may tell you to take EMPAVELI every 3 days.

1080-mg dose
2x WEEKLY*
For ~30-60 minutes

Scan the QR code to watch the EMPAVELI Injector self-administration video.

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

EMPAVELI®
(pegcetacoplan) injection
1080 mg/20 mL solution

See the EMPAVELI Injector Instructions for Use or, if using an infusion pump, see those specific Instructions for Use.

Avoid intense physical activity and do not bump or knock the EMPAVELI Injector or button during the injection. Keep your stomach totally dry.

If you miss a dose of EMPAVELI, take the missed dose as soon as possible. Take your next dose as regularly planned.

If your healthcare provider decides to stop your treatment with EMPAVELI, follow their instructions for how to stop. Your healthcare provider will monitor you closely for at least 8 weeks after stopping treatment with EMPAVELI for any signs of hemolysis due to PNH.

LDH=lactate dehydrogenase; PNH=paroxysmal nocturnal hemoglobinuria.

IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about EMPAVELI? (cont'd)

5. Vaccines do not prevent all infections caused by encapsulated bacteria. **Call your healthcare provider or get emergency medical care right away if you get any of these signs and symptoms of a serious infection:**

- fever with or without shivers or the chills
- fever with chest pain and cough
- fever with high heart rate
- headache and a fever
- confusion
- clammy skin
- fever and a rash
- fever with breathlessness or fast breathing
- headache with nausea or vomitting
- headache with a stiff neck or stiff back
- body aches with flu-like symptoms
- eyes sensitive to light

What else should I know before starting EMPAVELI?

You get self-administration support from the start

Your healthcare provider will first show you how to self-administer your EMPAVELI.

At Apellis, we understand each person's journey with PNH and EMPAVELI is different. With that in mind, we have designed our support services and self-administration training to fit comprehensive patient needs.

With the ApellisAssist patient support program, you will have the help of an Apellis Care Educator (ACE). ACEs have nursing backgrounds and will provide you with self-administration training. Your ACE can train you in your home or virtually—multiple times, if necessary—to make sure you're comfortable with the process.

They will continue to be by your side throughout your journey with ongoing support, education, and answers to your questions.

ACEs do not give medical advice. Talk to your doctor for treatment-related questions.

Mollie is an Apellis Care Educator.

There are processes for transitioning to EMPAVELI

Your healthcare provider will work with you to transition you to EMPAVELI.

Eculizumab

- For the first 4 weeks, you will receive EMPAVELI and your current dose of eculizumab
- After 4 weeks, STOP eculizumab and only take EMPAVELI

Ravulizumab

- You should start taking EMPAVELI no more than 4 weeks after your last dose of ravulizumab

PNH=paroxysmal nocturnal hemoglobinuria.

EMPAVELI®
(pegcetacoplan) injection
1080 mg/20 mL solution

Certain vaccines are required before starting EMPAVELI

Before starting your treatment journey with EMPAVELI, you will need to get certain vaccines. They help reduce the risk of certain serious infections.

You will be required to receive vaccinations against certain types of bacteria at least 2 weeks before taking your first dose of EMPAVELI.

As part of the ApellisAssist program, a Vaccine Coordinator through our specialty pharmacy, PANTHERx® Rare, can help you with this process.

Your Vaccine Coordinator can help make sure you get the required vaccines by:

- Researching local pharmacies based on your location and insurance coverage
- Creating a list of local options that have all required vaccines in stock along with information on hours of operations and how to make an appointment
- Contacting your pharmacy of choice to transfer any required prescription orders and make sure the pharmacy has all the appropriate information on file for billing the vaccines

When visiting your healthcare provider:

- Bring your vaccination records
- Ask your healthcare provider which vaccines you will need before starting EMPAVELI

Reach out to your healthcare provider if you have any additional questions about starting EMPAVELI.

IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about EMPAVELI? (cont'd)

Your healthcare provider will give you a Patient Safety Card about the risk of serious infections. Carry it with you at all times during treatment and for 2 months after your last EMPAVELI dose. Your risk of serious infections may continue for several weeks after your last dose of EMPAVELI. It is important to show this card to any healthcare provider who treats you. This will help them diagnose and treat you quickly.

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

EMPAVELI®
(pegcetacoplan) injection
1080 mg/20 mL solution

Support every step of the way

The ApellisAssist program is here for you

It takes teamwork to help manage PNH. The ApellisAssist patient support program provides comprehensive support, with helpful resources and experienced people dedicated to making a difference for you.

With the program, you have access to:

- Financial assistance (for those who are eligible)
- Insurance support
- Self-administration training from an Apellis Care Educator (ACE)
- EMPAVELI and PNH education

ApellisAssist®

1-866-MY-APL-ASSIST (1-866-692-7527)
FROM 8 AM-8 PM ET, MONDAY-FRIDAY

PNH=paroxysmal nocturnal hemoglobinuria.

Emma is an adult with PNH who's taken EMPAVELI.

"My ACE is amazing. Her training helped give me confidence in self-administering EMPAVELI. She continues to be there for me and is always a phone call away."

Individual experiences may vary.

Your ApellisAssist support partners

With EMPAVELI, you don't have to go it alone.
Learn about your dedicated partners from the ApellisAssist program.

Care Coordinator

Through our specialty pharmacy, PANTHERx Rare, a Care Coordinator will:

- Help schedule your deliveries for medication and supplies
- Explain your insurance benefits or available financial assistance options, if eligible

Apellis Care Educator (ACE)

Your ACE is there for you from the start. They will provide you:

- 1-on-1 training on how to self-administer EMPAVELI—in your home or virtually
- Ongoing support every step of the way
- A wide variety of educational resources
- Answers to questions that may pop up

Care Coordinators and ACEs do not give medical advice. Talk to your doctor for treatment-related questions.

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

EMPAVELI TRIAL OFFER

8 weeks of EMPAVELI treatment at no cost to eligible adults with PNH*

If you haven't tried EMPAVELI yet, you may be eligible for the EMPAVELI Trial Offer regardless of insurance coverage or current treatment.

- Straightforward enrollment for you and your healthcare provider
- The same comprehensive training and support as those currently taking EMPAVELI
- No obligation to continue with EMPAVELI after trial ends

If you and your healthcare provider are ready to try EMPAVELI, you may be eligible to enroll in the **Trial Offer program**.

*Terms, conditions, and eligibility requirements apply. Ask your doctor for more information.

Insurance questions?
In need of financial assistance?

Call an ApellisAssist representative at **1-866-MY-APL-ASSIST (1-866-692-7527)** to connect with your Care Coordinator about insurance questions or financial assistance programs that are available for eligible patients.

ACE=Apellis Care Educator; PNH=paroxysmal nocturnal hemoglobinuria.

EMPAVELI®
(pegcetacoplan) injection
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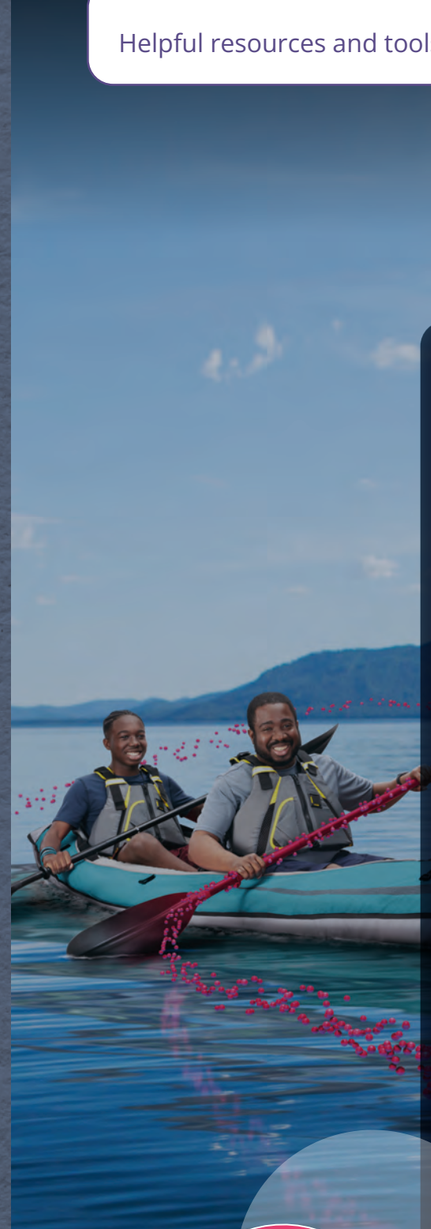


Tools for your journey

Resources, tools, and tips designed for you

No matter where you are in your journey, there are many resources available to help.

- A range of brochures and guides available to download
- Extensive video content including patient stories, ACE support stories, and step-by-step instructions for taking EMPAVELI
- Home Suite Home with tools and videos for traveling with, storing, and organizing your medication
- Social communities to keep in touch on Facebook, Instagram, and YouTube

Angelo is an adult with PNH who's taken EMPAVELI.

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

EMPAVELI®
(pegcetacoplan) injection
1080 mg/20 mL solution

PNH peer 2 peer

Connect 1-on-1 with someone taking EMPAVELI.

The PNH Peer 2 Peer program gives you the chance to connect directly with someone else who is living with PNH.

Hear about their journey living with PNH, ask them questions, and find out about their experiences starting or switching to EMPAVELI.

Your healthcare provider is your best source of information regarding your PNH.

Andrea
A loving grandmother who remained resilient in her path to PNH care

Stacey
A lover of the outdoors who found courage in the face of the unknown

Meet a Peer 2 Peer Connector!
Scan the QR code to schedule time to chat with a Connector.

Stacey is an adult with PNH who's taken EMPAVELI.

Andrea and Stacey are adults with PNH who've taken EMPAVELI.

PNH=paroxysmal nocturnal hemoglobinuria.

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

INDICATION AND IMPORTANT SAFETY INFORMATION

What is EMPAVELI® (pegcetacoplan)?

EMPAVELI is a prescription medicine used to treat adults with a disease called paroxysmal nocturnal hemoglobinuria (PNH).

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

EMPAVELI is a medicine that affects your immune system and may lower the ability of your immune system to fight infections.

EMPAVELI increases your chance of getting serious infections caused by encapsulated bacteria such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B. These serious infections may quickly become life-threatening or cause death if not recognized and treated early.

1. **You must complete or be up to date with the vaccines against *Streptococcus pneumoniae* and *Neisseria meningitidis* at least 2 weeks before your first dose of EMPAVELI.**
2. If you have not completed your vaccines and EMPAVELI must be started right away, you should receive the required vaccines as soon as possible.
3. If you have not been vaccinated and EMPAVELI must be started right away, you should also receive antibiotics to take for as long as your healthcare provider tells you.
4. If you have been vaccinated against these bacteria in the past, you might need additional vaccines before starting EMPAVELI. Your healthcare provider will decide if you need additional vaccines.
5. Vaccines do not prevent all infections caused by encapsulated bacteria. **Call your healthcare provider or get emergency medical care right away if you get any of these signs and symptoms of a serious infection:**

- fever with or without shivers or the chills
- fever with chest pain and cough
- fever with high heart rate
- headache and a fever
- confusion
- clammy skin
- fever and a rash
- fever with breathlessness or fast breathing
- headache with nausea or vomiting
- headache with a stiff neck or stiff back
- body aches with flu-like symptoms
- eyes sensitive to light

Your healthcare provider will give you a Patient Safety Card about the risk of serious infections. Carry it with you at all times during treatment and for 2 months after your last EMPAVELI dose. Your risk of serious infections may continue for several weeks after your last dose of EMPAVELI. It is important to show this card to any healthcare provider who treats you. This will help them diagnose and treat you quickly.

EMPAVELI is only available through a program called the EMPAVELI Risk Evaluation and Mitigation Strategy (REMS). Before you can take EMPAVELI, your healthcare provider must enroll in the EMPAVELI REMS program, counsel you about the risk of serious infections caused by certain bacteria, give you information about the symptoms of serious infections, make sure that you are vaccinated against serious infections caused by encapsulated bacteria and that you receive antibiotics if you need to start EMPAVELI right away and you are not up to date on your vaccines, and give you a Patient Safety Card about your risk of serious infections.

Who should NOT take EMPAVELI?

Do not take EMPAVELI if you:

- are allergic to pegcetacoplan or any of the ingredients in EMPAVELI.
- have a serious infection caused by encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B when you are starting EMPAVELI treatment.

EMPAVELI®
(pegcetacoplan) injection
1080 mg/20 mL solution

Before you take EMPAVELI, tell your healthcare provider about all of your medical conditions, including if you:

- have an infection or fever.
- are pregnant or plan to become pregnant. EMPAVELI may harm your unborn baby. Females who are able to become pregnant should have a pregnancy test before starting treatment with EMPAVELI and use an effective method of birth control during treatment with EMPAVELI and for 40 days after the last dose.
- are breastfeeding or plan to breastfeed. It is not known if EMPAVELI passes into your breast milk. You should not breastfeed during treatment with EMPAVELI and for 40 days after the last dose.

Tell your healthcare provider about all the vaccines you receive and medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements which could affect your treatment.

If you stop taking EMPAVELI, your healthcare provider will need to monitor you closely for at least 8 weeks after stopping EMPAVELI. Stopping treatment with EMPAVELI may cause a breakdown of red blood cells due to PNH.

Symptoms or problems that can happen due to red blood cell breakdown include:

- decreased hemoglobin level in your blood
- blood in your urine
- shortness of breath
- trouble swallowing
- tiredness
- pain in the stomach (abdomen)
- blood clots
- erectile dysfunction (ED)

What are the possible side effects of EMPAVELI?

EMPAVELI can cause serious side effects including allergic reactions. Allergic reactions can happen during your EMPAVELI infusion. Stop your EMPAVELI infusion and tell your healthcare provider or get emergency medical care right away if you get any of these symptoms during your EMPAVELI infusion:

- chest pain
- trouble breathing or shortness of breath
- swelling of your face, tongue, or throat
- feel faint or pass out

The most common side effects in people with PNH treated with EMPAVELI include injection-site reactions; infections; diarrhea; pain in the stomach (abdomen); respiratory tract infection; pain in the arms, hands, legs, or feet; low potassium in blood; tiredness; viral infection; cough; joint pain; dizziness; headache; and rash.

These are not all of the possible side effects of EMPAVELI. Tell your healthcare provider about any side effect that bothers you or that does not go away.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying full Prescribing Information, including Boxed WARNING regarding risk of serious infections, and Medication Guide for additional information in pocket.

Glossary of terms

Absolute reticulocyte count (ARC)

A test that measures the number of immature red blood cells in your blood. High reticulocyte counts may be a sign of ongoing hemolysis with paroxysmal nocturnal hemoglobinuria (PNH), as the body is making more new red blood cells to replace the ones being destroyed by the immune system.

C3

A protein in the blood that acts as a central point of the complement system, regulating its activation.

C5

Another protein in the blood that is part of the complement system.

Clinical trial

A type of research study that tests how well treatments work in people, as well as possible side effects of treatments.

Complement system

The complement system, also referred to as the complement cascade, is an army of more than 40 different proteins that work together to get rid of dangerous cells and fight infection.

Extravascular hemolysis (EVH)

Destruction of red blood cells that occurs in the liver or spleen.

FACIT-Fatigue scale

This tool consists of a number of questions that are used to assign a score to measure a person's experience with fatigue.

Globin'

Acting in pursuit of higher hemoglobin levels.

Hemoglobin (Hb)

The critical protein found inside red blood cells that enables other cells throughout the body to get the oxygen they need. Hemoglobin acts like drops of glue that can "stick" to oxygen and carry it from the lungs to other tissues. It can also "stick" to waste like carbon dioxide to help remove it from the body.

EMPAVELI®
(pegcetacoplan) injection
1080 mg/20 mL solution

Hemolysis

The breaking apart of red blood cells. It can occur when the immune system attacks these cells as though they were dangerous viruses or bacteria. When red blood cells break open, hemoglobin is released. Hemolysis causes many of the symptoms of PNH.

Immune system

A sophisticated defense network used to protect the body from dangers like disease and infection.

Intravascular hemolysis (IVH)

The destruction of red blood cells inside a blood vessel.

Lactate dehydrogenase (LDH)

An enzyme found in the blood and tissues of the body, including the heart, kidneys, brain, and lungs. Red blood cell destruction results in the release of LDH into the blood. People with PNH often have higher levels of LDH due to ongoing hemolysis.

Normalization

Lab values improving to levels like those of adults who don't have PNH.

Proteins

Molecules that play many important roles in the body and can be thought of as the "workhorses" of cells. Proteins are required for the structure, function, and regulation of the body's organs and tissues.

Red blood cells

A common type of blood cell. Their job is to carry oxygen, using an important molecule, hemoglobin, around the body.

Stabilization

Lab values remaining at a stable level and not getting worse.

U/L

Some test results are reported in U/L, or units per liter. This is a measurement of how many units there are in a liter.

x 10^9 cells/L

A short way to write a number with 9 zeros at the end. This is useful when needing to count the billions of cells in a liter of blood.

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

EMPAVELI®
(pegcetacoplan) injection
1080 mg/20 mL solution

If you're like Monica, an adult with PNH taking EMPAVELI,

Where will you go next?

Scan the QR code to learn more.

Explore the EMPAVELI Injector

Details and resources on using the EMPAVELI Injector are available.

You don't have to go it alone

Your ApellisAssist team, including your ACE, is always at your side.

ACE=Apellis Care Educator; PNH=paroxysmal nocturnal hemoglobinuria.

INDICATION AND IMPORTANT SAFETY INFORMATION

What is EMPAVELI® (pegcetacoplan)?

EMPAVELI is a prescription medicine used to treat adults with a disease called paroxysmal nocturnal hemoglobinuria (PNH).

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

EMPAVELI is a medicine that affects your immune system and may lower the ability of your immune system to fight infections.

EMPAVELI increases your chance of getting serious infections caused by encapsulated bacteria such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B. These serious infections may quickly become life-threatening or cause death if not recognized and treated early.

1. **You must complete or be up to date with the vaccines against *Streptococcus pneumoniae* and *Neisseria meningitidis* at least 2 weeks before your first dose of EMPAVELI.**

Please see full Important Safety Information, including Boxed WARNING regarding risk of serious infections, on pages 44-45, and the accompanying full Prescribing Information and Medication Guide in pocket.

Apellis

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use EMPAVELI safely and effectively. See full prescribing information for EMPAVELI.

EMPAVELI® (pegcetacoplan) injection, for subcutaneous use
Initial U.S. Approval: 2021

WARNING: SERIOUS INFECTIONS CAUSED BY ENCAPSULATED BACTERIA
See full prescribing information for complete boxed warning.

EMPAVELI increases the risk of serious and life-threatening infections caused by encapsulated bacteria including *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenzae* type B.

- **Complete or update vaccination for encapsulated bacteria at least 2 weeks prior to the first dose of EMPAVELI, unless the risks of delaying EMPAVELI outweigh the risks of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria in patients receiving a complement inhibitor. (5.1)**
- **Patients receiving EMPAVELI are at increased risk for invasive disease caused by encapsulated bacteria, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious infections and evaluate immediately if infection is suspected. (5.1)**

EMPAVELI is available only through a restricted program called EMPAVELI REMS.

----------RECENT MAJOR CHANGES----------

Dosage and Administration (2.2, 2.3)	09/2023
Boxed Warning	02/2024
Dosage and Administration (2.1)	02/2024
Contraindications (4)	02/2024
Warnings and Precautions (5.1, 5.2)	02/2024

----------INDICATIONS AND USAGE----------
EMPAVELI is a complement inhibitor indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH). (1)

---------- DOSAGE AND ADMINISTRATION ----------
- Recommended dosage is 1,080 mg administered subcutaneously twice weekly. (2.2)
- EMPAVELI can be administered via a commercially available pump or with EMPAVELI Injector. (2.2,2.3)
- See Full Prescribing Information for instructions on preparation and administration. (2.2, 2.3)

---------- DOSAGE FORMS AND STRENGTHS ----------
- Injection: 1,080 mg/20 mL (54 mg/mL) in a single-dose vial. (3)

----------CONTRAINDICATIONS----------
EMPAVELI is contraindicated:
- in patients with hypersensitivity to pegcetacoplan or any of the excipients. (4)
- for initiation in patients with unresolved serious infection caused by encapsulated bacteria. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Serious infections caused by encapsulated bacteria. (5.1)
- Infusion-Related Reactions: Monitor patients for infusion-related reactions and institute appropriate medical management as needed. (5.3)
- Interference with Laboratory Tests: Use of silica reagents in coagulation panels may result in artificially prolonged activated partial thromboplastin time (aPTT). (5.5)

---------- ADVERSE REACTIONS ----------
Most common adverse reactions in patients with PNH (incidence ≥10%) were injection-site reactions, infections, diarrhea, abdominal pain, respiratory tract infection, pain in extremity, hypokalemia, fatigue, viral infection, cough, arthralgia, dizziness, headache, and rash. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Apellis Pharmaceuticals, Inc. at 1-833-866-3346 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 02/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: SERIOUS INFECTIONS CAUSED BY ENCAPSULATED BACTERIA

EMPAVELI, a complement inhibitor, increases the risk of serious infections, especially those caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B *[see Warnings and Precautions (5.1)]*. Life-threatening and fatal infections with encapsulated bacteria have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.

- **Complete or update vaccination for encapsulated bacteria at least 2 weeks prior to the first dose of EMPAVELI, unless the risks of delaying therapy with EMPAVELI outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria in patients receiving a complement inhibitor. *See Warnings and Precautions (5.1)* for additional guidance on the management of the risk of serious infections caused by encapsulated bacteria.**
- **Patients receiving EMPAVELI are at increased risk for invasive disease caused by encapsulated bacteria, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious infections and evaluate immediately if infection is suspected.**

Because of the risk of serious infections caused by encapsulated bacteria, EMPAVELI is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the EMPAVELI REMS *[see Warnings and Precautions (5.2)]*.

1 INDICATIONS AND USAGE

EMPAVELI® is indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Vaccination and Prophylaxis

Vaccinate patients against encapsulated bacteria, including *Streptococcus pneumoniae* and *Neisseria meningitidis* (serogroups A, C, W, Y and B), according to current ACIP recommendations at least 2 weeks prior to initiation of EMPAVELI therapy *[see Warnings and Precautions (5.1)]*.

If urgent EMPAVELI therapy is indicated in a patient who is not up to date with vaccines for *Streptococcus pneumoniae* and *Neisseria meningitidis*, according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer these vaccines as soon as possible.

Healthcare professionals who prescribe EMPAVELI must enroll in the REMS for EMPAVELI *[see Warnings and Precautions (5.2)]*.

2.2 Recommended Dosage Regimen

The recommended dose of EMPAVELI is 1,080 mg administered subcutaneously twice weekly. EMPAVELI can be administered via a commercially available infusion pump with a reservoir of at least 20 mL or with EMPAVELI Injector.

Dosage for patients switching to EMPAVELI from C5 inhibitors

To reduce the risk of hemolysis with abrupt treatment discontinuation:

- For patients switching from eculizumab, initiate EMPAVELI while continuing eculizumab at its current dose. After 4 weeks, discontinue eculizumab before continuing on monotherapy with EMPAVELI.
- For patients switching from ravulizumab, initiate EMPAVELI no more than 4 weeks after the last dose of ravulizumab.

Dose Adjustment

- For lactate dehydrogenase (LDH) levels greater than 2 × the upper limit of normal (ULN), adjust the dosing regimen to 1,080 mg every three days.
- In the event of a dose increase, monitor LDH twice weekly for at least 4 weeks.

Missed Dose

- Administer EMPAVELI as soon as possible after a missed dose. Resume the regular dosing schedule following administration of the missed dose.

2.3 Administration

EMPAVELI is for subcutaneous administration using:

- **an infusion pump** OR
- **EMPAVELI Injector, a single-use, disposable on body injector**

EMPAVELI is intended for use under the guidance of a healthcare professional. Train patients and/or caregivers on how to prepare and administer EMPAVELI prior to use. After proper training a patient may self-administer, or the patient's caregiver may administer EMPAVELI, if a healthcare provider determines that it is appropriate.

Follow the steps below and use aseptic technique to prepare and administer EMPAVELI, either by an infusion pump or EMPAVELI Injector:

- Prior to use, allow EMPAVELI to reach room temperature for approximately 30 minutes. Keep the vial in the carton until ready for use to protect from light.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. EMPAVELI is a clear, colorless to slightly yellowish solution. Do not use if the liquid looks cloudy, contains particles, or is dark yellow.
- Discard any unused portion of EMPAVELI.

Preparation with Infusion Pump

- Refer to the EMPAVELI Instructions for Use and the infusion pump manufacturer's instructions for full preparation and administration information.
- Use a needleless transfer device (such as a vial adapter) or a transfer needle to fill the syringe.
- Rotate infusion sites (i.e., abdomen, thighs, hips, upper arms) from one infusion to the next. Do not infuse where the skin is tender, bruised, red, or hard. Avoid infusing into tattoos, scars, or stretch marks.
- If multi-infusion sets are needed, ensure the infusion sites are at least 3 inches apart.
- The typical infusion time is approximately 30 minutes (if using two infusion sites) or approximately 60 minutes (if using one infusion site).

Preparation with EMPAVELI Injector

- Refer to the EMPAVELI Injector Instructions for Use, which comes with the device.
- Use a needleless transfer device (such as a vial adapter).
- EMPAVELI Injector is for abdominal subcutaneous use only. Rotate the site of each subcutaneous administration. Do not inject where the skin is tender, bruised, red, or hard. Avoid injecting into tattoos, scars, or stretch marks.
- Injection time is approximately 30 to 60 minutes.

3 DOSAGE FORMS AND STRENGTHS

Injection: 1,080 mg/20 mL (54 mg/mL) clear, colorless to slightly yellowish solution in a single-dose vial.

4 CONTRAINDICATIONS

EMPAVELI is contraindicated:

- in patients with hypersensitivity to pegcetacoplan or to any of the excipients *[see Warnings and Precautions (5.3)]*.
- for initiation in patients with unresolved serious infection caused by encapsulated bacteria including *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Serious Infections Caused by Encapsulated Bacteria

EMPAVELI, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by encapsulated bacteria including *Streptococcus pneumoniae*, *Neisseria meningitidis* (caused by any serogroup, including non-groupable strains), and *Haemophilus influenzae* type B. Life-threatening and fatal infections with encapsulated bacteria have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors. The initation of EMPAVELI treatment is contraindicated in patients with unresolved serious infection caused by encapsulated bacteria.

Complete or update vaccination against encapsulated bacteria at least 2 weeks prior to administration of the first dose of EMPAVELI, according to the most current ACIP recommendations for patients receiving a complement inhibitor. Revaccinate patients in accordance with ACIP recommendations considering the duration of therapy with EMPAVELI. Note that, ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information. If urgent EMPAVELI therapy is indicated in a patient who is not up to date with vaccines against encapsulated bacteria according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer these vaccines as soon as possible. Various durations and regimens of antibacterial drug prophylaxis have been considered, but the optimal durations and drug regimens for prophylaxis and their efficacy have not been studied in unvaccinated or vaccinated patients receiving complement inhibitors, including EMPAVELI. The benefits and risks of treatment with EMPAVELI, as well as the benefits and risks of antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by encapsulated bacteria.

Vaccination does not eliminate the risk of serious encapsulated bacterial infections, despite development of antibodies following vaccination. Closely monitor patients for early signs and symptoms of serious infection and evaluate patients immediately if an infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if these signs and symptoms occur. Promptly treat known infections. Serious infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of EMPAVELI in patients who are undergoing treatment for serious infections.

EMPAVELI is available only through a restricted program under a REMS *[see Warnings and Precautions (5.2)].*

5.2 EMPAVELI REMS

EMPAVELI is available only through a restricted program under a REMS called EMPAVELI REMS, because of the risk of serious infections caused by encapsulated bacteria *[see Warnings and Precautions (5.1)]*.

Notable requirements of the EMPAVELI REMS include the following:

- Prescribers must enroll in the REMS.
- Prescribers must counsel patients about the risk of serious infections caused by encapsulated bacteria.
- Prescribers must provide the patients with the REMS educational materials.

- Prescribers must assess patient vaccination status for encapsulated bacteria and vaccinate if needed according to current ACIP recommendations two weeks prior to the first dose of EMPAVELI.
- Prescribers must provide a prescription for antibacterial drug prophylaxis if treatment must be started urgently, and the patient is not up to date with vaccinations against encapsulated bacteria according to current ACIP recommendations at least two weeks prior to the first dose of EMPAVELI.
- Pharmacies that dispense EMPAVELI must be certified in the EMPAVELI REMS and must verify prescribers are certified.
- Patients must receive counseling from the prescriber about the need to receive vaccinations against encapsulated bacteria per ACIP recommendations, the need to take antibiotics as directed by the prescriber, and the signs and symptoms of serious infections.
- Patients must be instructed to carry the Patient Safety Card with them at all times during and for 2 months following treatment discontinuation with EMPAVELI.

Further information is available at www.empavelirems.com or 1-888-343-7073

5.3 Infusion-Related Reactions

Systemic hypersensitivity reactions (e.g., facial swelling, rash, urticaria) have occurred in patients treated with EMPAVELI. One patient (less than 1% in clinical studies) experienced a serious allergic reaction which resolved after treatment with antihistamines. If a severe hypersensitivity reaction (including anaphylaxis) occurs, discontinue EMPAVELI infusion immediately, institute appropriate treatment, per standard of care, and monitor until signs and symptoms are resolved.

5.4 Monitoring PNH Manifestations after Discontinuation of EMPAVELI

After discontinuing treatment with EMPAVELI, closely monitor for signs and symptoms of hemolysis, identified by elevated LDH levels along with sudden decrease in PNH clone size or hemoglobin, or reappearance of symptoms such as fatigue, hemoglobinuria, abdominal pain, dyspnea, major adverse vascular events (including thrombosis), dysphagia, or erectile dysfunction. Monitor any patient who discontinues EMPAVELI for at least 8 weeks to detect hemolysis and other reactions. If hemolysis, including elevated LDH, occurs after discontinuation of EMPAVELI, consider restarting treatment with EMPAVELI.

5.5 Interference with Laboratory Tests

There may be interference between silica reagents in coagulation panels and EMPAVELI that results in artificially prolonged activated partial thromboplastin time (aPTT); therefore, avoid the use of silica reagents in coagulation panels.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in greater detail in other sections of the labeling:

- Serious Infections Caused by Encapsulated Bacteria *[see Warnings and Precautions (5.1)]*
- Infusion-Related Reactions *[see Warnings and Precautions (5.3)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Paroxysmal Nocturnal Hemoglobinuria

Study in Complement-Inhibitor Experienced Adult Patients with PNH (Study APL2-302)

The data described below reflect the exposure in 80 adult patients with PNH who received EMPAVELI (n=41) or eculizumab (n=39) at the recommended dosing regimens for 16 weeks. Serious adverse reactions were reported in 7 (17%) patients with PNH receiving EMPAVELI. The most common serious adverse reaction in patients treated with EMPAVELI was infections (5%). The most common adverse reactions (≥10%) with EMPAVELI were injection-site reactions, infections, diarrhea, abdominal pain, respiratory tract infection, viral infection, and fatigue.

Table 1 describes the adverse reactions that occurred in ≥5% of patients treated with EMPAVELI in Study APL2-302.

Table 1: Adverse Reactions Reported in ≥5% of Patients Treated with EMPAVELI in Study APL2-302

Adverse Reaction	**EMPAVELI (N=41) n (%)**	**Eculizumab (N=39) n (%)**
General disorders and administration site conditions		
Injection-site reaction*	16 (39)	2 (5)
Fatigue*	5 (12)	9 (23)
Chest pain*	3 (7)	1 (3)
Infections and infestations		
Infections*	12 (29)	10 (26)
Respiratory tract infection*	6 (15)	5 (13)
Viral Infection*	5 (12)	3 (8)
Gastrointestinal disorders		
Diarrhea	9 (22)	1 (3)
Abdominal pain*	8 (20)	4 (10)
Musculoskeletal disorders		
Back pain*	3 (7)	4 (10)
Nervous system disorders		
Headache	3 (7)	9 (23)
Vascular disorders		
Systemic hypertension*	3 (7)	1 (3)

*The following terms were combined:
Abdominal pain includes: abdominal pain upper, abdominal discomfort, abdominal pain, abdominal pain lower, abdominal tenderness, epigastric discomfort
Back pain includes: back pain, sciatica
Chest pain includes: chest discomfort, non-cardiac chest pain, musculoskeletal chest pain, chest pain
Fatigue includes: asthenia, lethargy, fatigue
Infections include: oral herpes, bacterial infection, fungal infection, gastrointestinal infection, gastrointestinal viral infection, influenza-like illness, nasopharyngitis, pulpitis dental, rhinitis, tonsillitis, tonsillitis bacterial, vulvovaginal mycotic infection, hordeolum, sepsis, furuncle, otitis externa, viral respiratory tract infection, gastroenteritis, upper respiratory tract infection, bronchitis, ear infection, respiratory tract infection, rhinovirus infection, sinusitis, urinary tract infection
Injection-site reaction includes: injection-site erythema, injection-site reaction, injection-site swelling, injection-site induration, injection-site bruising, injection-site pain, injection-site pruritus, vaccination-site reaction, administration-site swelling, injection-site hemorrhage, injection-site edema, injection-site warmth, administration-site pain, application-site pain, injection-site mass, injection-site rash, vaccination-site pain
Respiratory tract infection includes: influenza-like illness, nasopharyngitis, rhinitis, tonsillitis, viral upper respiratory tract infection, upper respiratory tract infection, respiratory tract infection, sinusitis
Systemic hypertension includes: hypertension
Viral infection includes: oral herpes, gastrointestinal viral infection, viral upper respiratory tract infection, rhinovirus infection

Clinically relevant adverse reactions in less than 5% of patients include:

- Intestinal ischemia

- Biliary sepsis
- Hypersensitivity pneumonitis

After the randomized control period, 77 patients continued the study, and all were treated with EMPAVELI monotherapy at the recommended dosing regimen for up to 48 weeks. Serious adverse reactions were reported in 18 patients (23%). Additional adverse reactions reported in >5% of patients treated with EMPAVELI during the open-label part of the study compared to the randomized controlled part in Table 1 were cough (12%), arthralgia (8%), oropharyngeal pain (8%), pyrexia (8%), pain in extremity (7%), thrombocytopenia (7%), abdominal distension (5%), acute kidney injury (5%), anxiety (5%), and myalgia (5%). One patient (1%) died due to COVID-19 infection.

Description of Select Adverse Reactions

Injection-Site Reactions

Injection/infusion-site reactions (e.g., erythema, swelling, induration, pruritis, and pain) have been reported during Study APL2-302. These reactions were mild or moderate in severity.

Diarrhea

Seventeen cases of diarrhea have been reported during the 48 weeks. Fifteen of the cases were mild and two were moderate.

Study in Complement-Inhibitor Naïve Adult Patients with PNH (Study APL2-308)

The data described below reflect the exposure in adult patients with PNH who received EMPAVELI (n=46) or the control arm (supportive care excluding complement inhibitors) (n=18) in Study APL2-308 *[see Clinical Studies (14.1)]*. One patient (2%) who received EMPAVELI died due to septic shock. Serious adverse reactions were reported in 6 (13%) patients with PNH receiving EMPAVELI. The most common adverse reaction (≥10%) in patients treated with EMPAVELI were injection site reactions, infections, viral infection, pain in extremity, hypokalemia, arthralgia, dizziness, abdominal pain, rash, and headache.

Table 2 describes the adverse reactions that occurred in ≥5% of patients treated with EMPAVELI in Study APL2-308.

Table 2: Adverse Reactions Reported in ≥5% of Patients Treated with EMPAVELI in Study APL2-308

Adverse Reaction	**EMPAVELI (N=46) n (%)** **Exposure Adjusted Rate (per 100 pt yrs)**	**Control Arm[a] (N=18) n (%)** **Exposure Adjusted Rate (per 100 pt yrs)**
General disorders and administration site conditions		
Injection-site reaction*	12 (26) 42	0 0
Pyrexia	4(9) 14	0 0
Peripheral edema*	3 (7) 11	0 0
Infections and Infestations		
Infections*	9 (20) 32	4 (22) 74
Viral infection*	6 (13) 21	2 (11) 37

Adverse Reaction	EMPAVELI (N=46) n (%) Exposure Adjusted Rate (per 100 pt yrs)	Control Arm[a] (N=18) n (%) Exposure Adjusted Rate (per 100 pt yrs)
Musculoskeletal and connective tissue disorders		
Pain in extremity	6 (13) 21	0 0
Arthralgia	5 (11) 18	0 0
Musculoskeletal pain	3 (7) 11	0 0
Metabolism and nutrition disorders		
Hypokalemia	6 (13) 21	2 (11) 37
Nervous system disorders		
Dizziness	5 (11) 18	0 0
Headache	5 (11) 18	0 0
Somnolence	3 (7) 11	0 0
Gastrointestinal disorders		
Abdominal pain*	5 (11) 18	1 (6) 18
Skin and subcutaneous tissue disorders		
Rash*	5(11) 18	0 0
Ecchymosis	3 (7) 11	0 0
Erythema	3 (7) 11	0 0
Blood and lymphatic system disorders		
Thrombocytopenia	3 (7) 11	1 (6) 18
Respiratory, thoracic and mediastinal disorders		
Cough*	4 (9) 14	0 0
Epistaxis	3 (7) 11	0 0
Investigations		
Blood creatinine increased	3 (7) 11	0 0

[a]Control Arm = supportive care (excluding complement inhibitors)
EMPAVELI (N=46) group includes patients who received EMPAVELI at any point during the study, including patients randomized to EMPAVELI (N=35) and patients randomized to the control arm and crossed over to EMPAVELI treatment (N=11).
*The following terms were combined:

Infections include**:** acne pustular, anal abscess, cellulitis, gastroenteritis, helicobacter gastritis, hordeolum, nasopharyngitis, esophageal candidiasis, pharyngitis, septic shock, tuberculosis, upper respiratory tract infection, urinary tract infection enterococcal, vaginal infection, pneumocystitis jirovecii pneumonia, pulmonary tuberculosis, urinary tract infection
Abdominal pain includes: abdominal pain, abdominal pain upper.
Injection site reaction includes: injection site bruising, injection site hemorrhage, injection site swelling, application site reaction, infusion site pruritus, injection site erythema, injection site rash, puncture site reaction.
Viral infection includes**:** viral infection, covid-19, covid-19 pneumonia, coronavirus test positive, herpes virus, influenza
Peripheral edema includes**:** peripheral swelling, edema peripheral
Headache includes**:** headache, migraine
Rash includes**:** rash, maculo-papular rash, dermatitis
Cough includes**:** cough, allergic cough

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary
There are insufficient data on EMPAVELI use in pregnant women to inform a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with untreated PNH in pregnancy *(see Clinical Considerations)*. The use of EMPAVELI may be considered following an assessment of the risks and benefits.

Treatment of pregnant cynomolgus monkeys with pegcetacoplan at a subcutaneous dose of 28 mg/kg/day (2.9 times human exposure based on AUC) from the gestation period through parturition resulted in a statistically significant increase in abortions or stillbirths compared to controls *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of major birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriages in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations
Disease-associated maternal and/or fetal/neonatal risk
PNH in pregnancy is associated with adverse maternal outcomes, including worsening cytopenias, thrombotic events, infections, bleeding, miscarriages and increased maternal mortality, and adverse fetal outcomes, including fetal death and premature delivery.

Data
Animal Data
Animal reproduction studies with pegcetacoplan were conducted in cynomolgus monkeys. Pegcetacoplan treatment of pregnant cynomolgus monkeys at a subcutaneous dose of 28 mg/kg/day (2.9 times human exposure based on AUC) from the gestation period through parturition resulted in a statistically significant increase in abortions and stillbirths compared to controls. No increase in abortions or stillbirths occurred at a dose of 7 mg/kg/day (1.3 times human exposure based on AUC). No maternal toxicity or teratogenic effects were observed in offspring delivered at term. No developmental effects were observed in infants up to 6 months postpartum. Systemic exposure to pegcetacoplan of less than 1% of maternal levels was detected in fetuses from monkeys treated with 28 mg/kg/day from the period of organogenesis through the second trimester.

8.2 Lactation

Risk Summary
It is not known whether pegcetacoplan is secreted in human milk or whether there is potential for absorption and harm to the infant. There are no data on the effects of pegcetacoplan on milk production. Pegcetacoplan is present in milk of lactating monkeys *(see Animal Data)*. Since many medicinal products are secreted into human milk, and because of the potential for serious adverse reaction in a breastfeeding child, breastfeeding should be discontinued during treatment and for 40 days after the last dose.

Data

Animal Data

Pegcetacoplan was detectable in milk of lactating monkeys at less than 1% concentration of serum levels but was not detectable in the serum of nursing infants.

8.3 Females and Males of Reproductive Potential

Contraception

Females

EMPAVELI may cause embryo-fetal harm when administered to pregnant women *[see Use in Specific Populations (8.1)]*. Pregnancy testing is recommended for females of reproductive potential prior to treatment with EMPAVELI. Advise female patients of reproductive potential to use effective contraception during treatment with EMPAVELI and for 40 days after the last dose.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

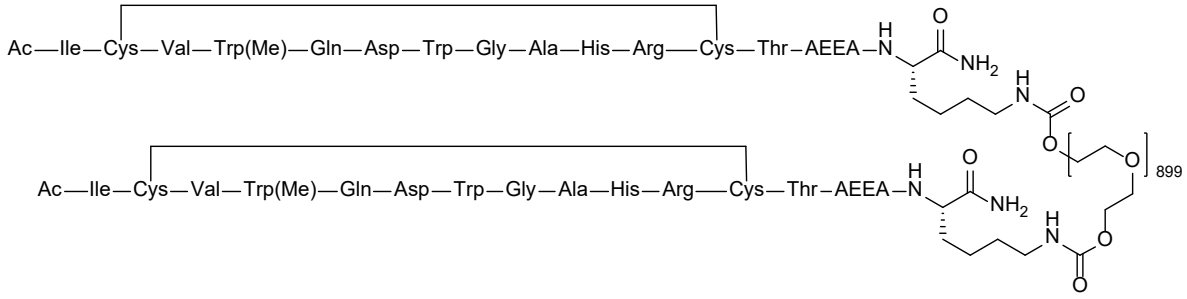
8.5 Geriatric Use

Clinical studies of EMPAVELI did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between geriatric and younger patients.

11 DESCRIPTION

EMPAVELI contains pegcetacoplan, a complement inhibitor. Pegcetacoplan is a symmetrical molecule comprised of two identical pentadecapeptides covalently bound to the ends of a linear 40-kiloDalton (kDa) PEG molecule. The peptide portions of pegcetacoplan contain 1-methyl-L-tryptophan (Trp(Me)) in position 4 and amino(ethoxyethoxy)acetic acid (AEEA) in position 14.

The molecular weight of pegcetacoplan is approximately 43.5 kDa. The molecular formula is $C_{1970}H_{3848}N_{50}O_{947}S_4$. The structure of pegcetacoplan is shown below.



EMPAVELI injection is a sterile, clear, colorless to slightly yellowish aqueous solution for subcutaneous use and is supplied in a 20-mL single-dose vial. Each 1 mL of solution contains 54 mg of pegcetacoplan, 41 mg of sorbitol, 0.384 mg of glacial acetic acid, 0.490 mg of sodium acetate trihydrate, and Water for Injection USP. EMPAVELI may also contain sodium hydroxide and/or additional glacial acetic acid for adjustment to a target pH of 5.0.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Pegcetacoplan binds to complement protein C3 and its activation fragment C3b, thereby regulating the cleavage of C3 and the generation of downstream effectors of complement activation. In PNH, extravascular hemolysis (EVH) is facilitated by C3b opsonization while intravascular hemolysis (IVH) is

mediated by the downstream membrane attack complex (MAC). Pegcetacoplan acts proximally in the complement cascade controlling both C3b-mediated EVH and terminal complement-mediated IVH.

12.2 Pharmacodynamics

In patients with PNH administered multiple doses of pegcetacoplan, the mean C3 concentration increased from 0.94 g/L at baseline to 3.80 g/L at Week 16 and sustained through Week 48 (Study APL2-302). In study APL2-308, the mean C3 concentration increased from 0.95 g/L at baseline to 3.56 g/L at Week 26 *[see Clinical Studies (14.1)]*.

The percentage of PNH Type II + III RBCs increased from 66.2% at baseline to 93.9% at Week 16 and sustained through Week 48 (Study APL2-302). In Study APL2-308, the mean percentage of PNH Type II + III RBCs increased from 42.4% at baseline to 90.0% at Week 26.

The mean percentage of PNH Type II + III RBCs with C3 deposition decreased from 17.8% at baseline to 0.20% at Week 16 and sustained through Week 48 (Study APL2-302). In Study APL2-308, the mean percentage of PNH Type II + III RBCs with C3 deposition decreased from 2.85% at baseline to 0.09% at Week 26.

Cardiac Electrophysiology
At the recommended dose of EMPAVELI, no large mean increases in QTc interval (i.e., greater than 20 msec) were observed.

12.3 Pharmacokinetics

In patients with PNH, the serum pegcetacoplan concentrations achieved steady-state approximately 4 to 6 weeks following the first dose. The exposure of pegcetacoplan increased proportionally over a dose range from 45 to 1,440 mg (0.04 to 1.33 times the approved recommended dose). The mean (CV%) trough serum concentration observed at Week 16 was 706 (15.1%) mcg/mL and sustained through Week 48 (Study APL2-302). In Study APL2-308, mean (CV%) trough serum concentration was 744 (25.5%) mcg/mL at Week 26.

Absorption
The median T_{max} of pegcetacoplan is between 108 and 144 hours (4.5 to 6.0 days) after a single dose.

Distribution
The mean (CV%) volume of distribution of pegcetacoplan is approximately 3.98 L (32%) in patients with PNH.

Elimination
The estimated mean (CV%) of clearance (CL) is 0.36 L/day (30%) and median effective half-life of elimination ($t_{1/2}$) is 8.6 days in patients with PNH.

Metabolism
Pegcetacoplan is expected to be metabolized into small peptides and amino acids by catabolic pathways.

Specific Populations
There were no clinically significant differences on the pharmacokinetics of pegcetacoplan based on age (19 to 81 years old), sex, race (Asian vs. non-Asian), renal impairment, and hepatic function as evaluated by total bilirubin (0.06-8.8 mg/dL), albumin (3.0-5.5 g/dL), aspartate aminotransferase (6.0-302 IU/L), or alanine aminotransferase (4.0-209 IU/L).

12.6 Immunogenicity
There is insufficient information to characterize the anti-drug antibody response to EMPAVELI and the effects of anti-drug antibodies on pharmacokinetics, pharmacodynamics, safety, or effectiveness of pegcetacoplan products.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal carcinogenicity studies of pegcetacoplan have not been conducted.

Pegcetacoplan was not mutagenic when tested in an *in vitro* bacterial reverse mutation (Ames) and was not genotoxic in an *in vitro* assay in human TK6 cells or in an *in vivo* micronucleus assay in mice.

Effects of pegcetacoplan on fertility have not been studied in animals. There were no microscopic abnormalities in male or female reproductive organs in toxicity studies in rabbits and monkeys.

13.2 Animal Toxicology and/or Pharmacology

In toxicology studies in rabbits and cynomolgus monkeys, epithelial vacuolation and infiltrates of vacuolated macrophages were observed in multiple tissues, including the renal tubules, following daily subcutaneous doses of pegcetacoplan up to 7 times the human dose. These findings are attributable to uptake of the PEG moieties of pegcetacoplan. Renal degeneration was observed microscopically in rabbits at exposures (C_{max} and AUC) less than those for the human dose, and in monkeys at exposures approximately 2.7-fold those for the human dose. The clinical significance of these findings is uncertain.

14 CLINICAL STUDIES

14.1 Paroxysmal Nocturnal Hemoglobinuria

The efficacy and safety of EMPAVELI in patients with PNH were assessed in two open-label, randomized-controlled Phase 3 studies: Study APL2-302 (NCT03500549) and Study APL2-308 (NCT04085601). All patients who completed the studies were eligible to enroll in a separate long-term extension study.

In both studies, patients were vaccinated against *Streptococcus pneumoniae*, *Neisseria meningitidis* types A, C, W, Y, and B, and *Haemophilus influenzae* type B (Hib), either within 2 years prior to Day 1 or within 2 weeks after starting treatment with EMPAVELI. Patients vaccinated after initiation of treatment with EMPAVELI received prophylactic treatment with appropriate antibiotics until 2 weeks after vaccination. In addition, prophylactic antibiotic therapy was administered at the discretion of the investigator in accordance with local treatment guidelines for patients with PNH receiving treatment with a complement inhibitor.

A dose of 1,080 mg twice weekly was used for patients randomized to the EMPAVELI group of each study. If required, the dose of EMPAVELI could be adjusted to 1,080 mg every 3 days. EMPAVELI was administered as a subcutaneous infusion; the infusion time was approximately 20 to 40 minutes.

Study in Complement-Inhibitor Experienced Adult Patients with PNH (Study APL2-302)

The study enrolled patients with PNH who had been treated with a stable dose of eculizumab for at least the previous 3 months and with Hb levels less than 10.5 g/dL.

Eligible patients entered a 4-week run-in period during which they received EMPAVELI 1,080 mg subcutaneously twice weekly in addition to their current dose of eculizumab. Patients were then randomized in a 1:1 ratio to receive either 1,080 mg of EMPAVELI twice weekly or their current dose of eculizumab through the duration of the 16-week randomized controlled period (RCP).

Randomization was stratified based on the number of packed red blood cell (PRBC) transfusions within the 12 months prior to Day -28 (<4; ≥4) and platelet count at screening (<100,000/mm^3; ≥100,000/mm^3). Following completion of the RCP, all patients entered a 32-week open-label period (OLP) and received monotherapy with EMPAVELI. Patients initially randomized to eculizumab entered a second 4-week run-in period during which they received EMPAVELI in addition to eculizumab before continuing on to receive EMPAVELI monotherapy. All patients who completed the 48-week period were eligible to enroll in a separate long-term extension study.

A total of 80 patients were randomized to receive treatment, 41 to EMPAVELI and 39 to eculizumab. Demographics and baseline disease characteristics were generally well balanced between treatment groups (see Table 2). The median times from PNH diagnosis to Day -28 were 6.0 and 9.7 years, respectively, for EMPAVELI and eculizumab. The baseline mean total PNH RBC clone sizes (Type III) were 47% for EMPAVELI and 50% for eculizumab. Twenty-nine percent and 23% of patients had a history of major adverse vascular events, and 37% and 26% had a history of thrombosis for patients receiving EMPAVELI or eculizumab, respectively. Within 28 days prior to the first dose of EMPAVELI or eculizumab, respectively, 34% and 31% of patients used anti-thrombotic agents (anti-platelet and/or anticoagulants). During Study APL2-302, 37% and 36% of patients on EMPAVELI and eculizumab, respectively, used antithrombotic agents. A total of 38 patients in the group treated with EMPAVELI and 39 patients in the eculizumab group completed the 16-week RCP and continued into the 32-week OLP. Because of adverse reactions of hemolysis, 3 patients were discontinued from the EMPAVELI group during the RCP. Two out of 41 patients in the EMPAVELI group needed the dose adjustment to 1,080 mg every 3 days.

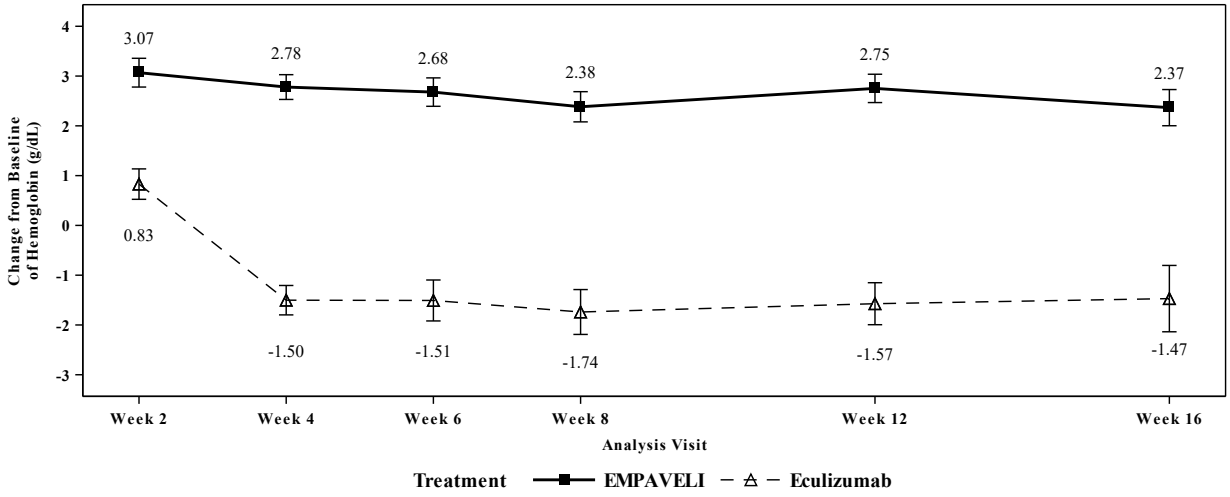
Table 3: Patient Baseline Demographics and Characteristics in Study APL2-302

Parameter	**Statistics**	**EMPAVELI (N=41)**	**Eculizumab (N=39)**
Age (years)	Mean (SD)	50.2 (16.3)	47.3 (15.8)
Sex			
Female	n (%)	27 (65.9)	22 (56.4)
Race			
Asian	n (%)	5 (12.2)	7 (17.9)
Black or African American	n (%)	2 (4.9)	0
White	n (%)	24 (58.5)	25 (64.1)
Other	n (%)	0	1 (2.6)
Not reported	n (%)	10 (24.4)	6 (15.4)
Ethnicity			
Hispanic or Latino	n (%)	2 (4.9)	1 (2.6)
Not Hispanic or Latino	n (%)	29 (70.7)	32 (82.1)
Not reported	n (%)	10 (24.4)	6 (15.4)
Hemoglobin level (g/dL)	Mean (SD)	8.7 (1.1)	8.7 (0.9)
Absolute reticulocyte count (10^9 cells/L)	Mean (SD)	218 (75.0)	216 (69.1)
LDH level (U/L)	Mean (SD)	257.5 (97.7)	308.6 (284.8)
Number of transfusions in last 12 months prior to Day -28	Mean (SD)	6.1 (7.3)	6.9 (7.7)
<4	n (%)	20 (48.8)	16 (41.0)
≥4	n (%)	21 (51.2)	23 (59.0)

The efficacy of EMPAVELI was based on change from baseline to Week 16 (during RCP) in hemoglobin level. Baseline was defined as the average of measurements recorded prior to taking the first dose of EMPAVELI. Supportive efficacy data included transfusion avoidance, defined as the proportion of patients who did not require a transfusion during the RCP, and change from baseline to Week 16 in absolute reticulocyte count (ARC).

EMPAVELI was superior to eculizumab for the change from baseline in hemoglobin level at Week 16 (p<0.0001). The adjusted mean change from baseline in hemoglobin level was 2.37 g/dL in the group treated with EMPAVELI versus -1.47 g/dL in the eculizumab group (Figure 1), demonstrating an adjusted mean increase of 3.84 g/dL with EMPAVELI compared to eculizumab at Week 16 (95% CI, 2.33-5.34).

Figure 1: Adjusted Mean (± SE) Change from Baseline to Week 16 in Hemoglobin (g/dL) in Study APL2-302*



*Treatment effect estimates from a mixed model are shown. The mixed model contained the categorical effects of treatment, visit, treatment by visit interaction, and stratification factors (transfusion history and platelet count at screening), and the continuous covariate of baseline value.

Non-inferiority was demonstrated in the endpoints of transfusion avoidance and change from baseline in ARC at Week 16.

The adjusted means, treatment differences, and confidence intervals (CIs) for additional efficacy results are shown in Table 4.

Table 4: Additional Efficacy Results at Week 16 in Study APL2-302

	EMPAVELI (N=41)	**Eculizumab (N=39)**	**Difference (95% CI)**
Transfusion avoidance, n (%)	35 (85%)	6 (15%)	63%* (48%, 77%)
Change from baseline in ARC (10^9 cells/L), LS† mean (SE)‡	-136 (6.5)	28 (11.9)	-164 (-189.9, -137.3)

*Difference in percentages and 95% CI were based on the stratified Miettinen–Nurminen method.
†LS = Least square
‡SE = Standard error

Efficacy was generally similar across subgroups based on sex, race, and age.

All 77 patients who completed the RCP entered the 32- week OLP, during which all patients received EMPAVELI, resulting in a total exposure of up to 48 weeks. Between Week 16 and Week 48, 10 patients discontinued the study, all due to adverse reactions, and thirteen patients had a dose adjustment to 1,080 mg every three days. The efficacy results at Week 48 were generally consistent with those at Week 16.

Study in Complement-Inhibitor Naïve Adult Patients with PNH (Study APL2-308)

Study APL2-308 enrolled patients with PNH who had not been treated with any complement inhibitor within 3 months prior to enrollment and with Hb levels less than the lower limit of normal (LLN). Eligible patients were randomized in a 2:1 ratio to receive EMPAVELI or supportive care [excluding complement inhibitors (e.g., transfusions, corticosteroids, supplements such as iron, folate, and vitamin B_{12}), hereafter referred to as the control arm] through the duration of the 26-week treatment period. Randomization was stratified based on the number of packed red blood cell (PRBC) transfusions within the 12 months prior to Day -28

(<4; ≥4). At any point during the study, a patient assigned to the control arm treatment group who had Hb levels ≥2 g/dL below baseline or presented with a PNH associated thromboembolic event was offered cross-over to EMPAVELI for the remainder of the study.

A total of 53 patients were randomized, 35 to EMPAVELI and 18 to the control arm. Demographics and baseline disease characteristics were generally well balanced between treatment groups (see Table 4). The mean times from PNH diagnosis to Day 1 were 5.7 and 5.5 years, respectively, for EMPAVELI and the control arm. The baseline mean total PNH RBC clone sizes (Type III) were 31% for EMPAVELI and 28% for the control arm. In the EMPAVELI group, 2.9% of patients had a history of major adverse vascular events. Two patients (5.7%) in the EMPAVELI group and 3 patients (16.7%) in the control arm group had a history of at least 1 type of thrombosis. Within 28 days prior to the first dose of EMPAVELI or the control arm, respectively, 17.1% and 27.8% of patients used anti-thrombotic agents (anti-platelet and/or anticoagulants). During Study APL2-308, 8.6% and 0% of patients on EMPAVELI and the control arm, respectively, used antithrombotic agents. Eleven of 18 patients randomized to the control transitioned to cross-over therapy with EMPAVELI due to a decreased Hb level ≥2 g/dL below baseline. Three patients treated with EMPAVELI required dose adjustment to 1,080 mg every 3 days. Three patients (5.7%; two patients in the EMPAVELI group and one patient in the control arm group) discontinued the study, none due to an adverse reaction.

Table 5: Patient Baseline Demographics and Characteristics in Study APL2-308

Parameter	**Statistics**	**EMPAVELI (N=35)**	**Control Arm[a] (N=18)**
Age (years)	Mean (SD)	42.2 (12.7)	49.1 (15.6)
Sex Female	n (%)	16 (45.7)	8 (44.4)
Race American Indian or Alaska Native	n (%)	9 (25.7)	2 (11.1)
Asian	n (%)	23 (65.7)	16 (88.9)
Black or African American	n (%)	2 (5.7)	0
Other	n (%)	1 (2.9)	0
Ethnicity Hispanic or Latino	n (%)	12 (34.3)	2 (11.1)
Not Hispanic or Latino	n (%)	23 (65.7)	16 (88.9)
Hemoglobin level (g/dL)	Mean (SD)	9.4 (1.4)	8.7 (0.8)
Absolute reticulocyte count (10^9 cells/L)	Mean (SD)	230.2 (81.0)	180.3 (109.1)
LDH level (U/L)	Mean (SD)	2151.0 (909.4)	1945.9 (1003.7)
Number of transfusions in last 12 months prior to Day -28	Mean (SD)	3.9 (4.4)	5.1 (5.0)
<4	n (%)	21 (60.0)	8 (44.4)
≥4	n (%)	14 (40.0)	10 (55.6)

[a]Control Arm = supportive care (excluding complement inhibitors)

The efficacy of EMPAVELI was based on the percentage of patients achieving hemoglobin stabilization, defined as avoidance of a >1 g/dL decrease in hemoglobin levels from baseline in the absence of transfusion, and the change from baseline in LDH level. Supportive efficacy data included change from baseline in absolute reticulocyte count (ARC), change from baseline in hemoglobin, and transfusion avoidance, defined as the proportion of patients who did not require a transfusion through Week 26. Baseline was defined as the average of measurements recorded prior to taking the first dose of EMPAVELI or prior to randomization to the control arm treatment group.

Efficacy results are shown in Table 6 below.

Table 6: Efficacy Results During the 26-Week Study in Study APL2-308

	EMPAVELI (N=35)	**Control Arm[a] (N=18)**	**Difference (95% CI) p-value**
Hemoglobin Stabilization[§] (n, %)	30 (85.7%)	0 (0%)	73% (57%, 89%) p<0.0001*
Change from Baseline in LDH[b] (LS[†] Mean CFB, SE[‡])	-1870 (101.0)	-400 (313.0)	-1470 (-2113.4, -827.3) p<0.0001
Change from baseline in ARC[b] (LS[†] Mean CFB, SE[‡])	-123 (9.2)	-19 (25.2)	-103 (-158.9, -48.7) p = 0.0002
Change from baseline in Hb[b] (LS[†] Mean CFB, SE[‡])	2.9 (0.38)	0.3 (0.76)	2.7 (0.99, 4.35) p = 0.0019
Transfusion Avoidance[§] (n, %)	32 (91%)	1 (6%)	72% (56%, 89%) p<0.0001*

[a]Control Arm = supportive care (excluding complement inhibitors)
[b]The post baseline missing values (including the values after cross-over from the control arm) are imputed using a multiple imputation method.
Data collected after cross-over from the control arm is excluded in analyses.
[§]Patients who crossed over from the control arm group to the EMPAVELI group, withdrew from the study, or were lost to follow up are considered as failing to achieve the criteria.
*p-value is obtained by stratified Cochran-Mantel-Haenszel test.
[†]LS = Least square
[‡]SE = Standard error

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied
EMPAVELI injection is a clear, colorless to slightly yellowish aqueous solution for subcutaneous infusion supplied as 1,080 mg/20 mL (54 mg/mL) solution in 20-mL single-dose vials.

EMPAVELI is available in 20-mL single-dose vials individually packaged in cartons that are supplied in 8-count convenience cartons. NDC 73606-010-01.

Storage and Handling
Store vials of EMPAVELI refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not use beyond the expiration date stamped on the carton.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Serious Infections Caused by Encapsulated Bacteria
Advise patients of the risk of serious infection. Inform patients of the need to complete or update their vaccinations against encapsulated bacteria at least 2 weeks prior to receiving the first dose of EMPAVELI or receive antibacterial drug prophylaxis if EMPAVELI treatment must be initiated immediately and they have not been previously vaccinated. Inform the patient that they are required to be revaccinated according to current ACIP recommendations for encapsulated bacteria while on EMPAVELI therapy *[see Warnings and Precautions (5.1)]*.

Inform patients that vaccination may not prevent serious infection and strongly advise patients to seek immediate medical attention if these signs or symptoms occur. These signs and symptoms include the following:

- fever with or without shivers or the chills
- fever with chest pain and cough
- fever with breathlessness/fast breathing
- fever with high heart rate
- headache and a fever
- headache with a stiff neck or stiff back
- fever and a rash
- confusion
- headache with nausea or vomiting
- body aches with flu-like symptoms
- clammy skin
- eyes sensitive to light

Inform patients that they will be given a Patient Safety Card for EMPAVELI that they should carry with them at all times. This card describes symptoms which, if experienced, should prompt the patient to seek immediate medical evaluation.

EMPAVELI REMS

EMPAVELI is available only through a restricted program called EMPAVELI REMS *[see Warnings and Precautions (5.2)]*.

Inform the patient of the following notable requirements:

- Patients must receive counseling about the risk of serious infections caused by encapsulated bacteria.
- Patients must receive written educational materials about this risk.
- Patients must be instructed to carry the Patient Safety Card with them at all times during and for 2 months following treatment with EMPAVELI.
- Patients must be instructed to complete or update vaccinations against encapsulated bacteria per ACIP recommendations as directed by the prescriber prior to treatment with EMPAVELI.
- Patients must receive antibiotics as directed by the prescriber if they are not up to date with vaccinations against encapsulated bacteria and have to start EMPAVELI right away.

Anaphylaxis and infusion-related reactions

Advise patients of the risk of anaphylaxis and infusion-related reactions. Inform patients that anaphylaxis is life-threatening and strongly advise patients to seek immediate medical attention if these signs or symptoms occur. These signs and symptoms include the following:

- difficulty breathing including shortness of breath and wheezing
- swollen tongue or throat
- feeling faint
- rapid heart rate
- skin reactions, including hives and itching
- nausea or vomiting
- confusion and anxiety
- dizziness or fainting

Discontinuation

Inform patients with PNH that they may develop hemolysis due to PNH when EMPAVELI is discontinued and that they will be monitored by their healthcare professional for at least 8 weeks following discontinuation of EMPAVELI.

Inform patients who discontinue EMPAVELI to keep the Patient Safety Card with them for 2 months after the last dose of EMPAVELI, because the increased risk of serious infection persists for several weeks following discontinuation of EMPAVELI.

Manufactured for:
Apellis Pharmaceuticals, Inc.
100 Fifth Avenue
Waltham, MA 02451

For patent information: www.apellis.com/productpatent

EMP-PI-08Feb2024-5.0

MEDICATION GUIDE
EMPAVELI® (em-puh-vel-ee)
(pegcetacoplan)
injection, for subcutaneous use

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

EMPAVELI is a medicine that affects your immune system. EMPAVELI may lower the ability of your immune system to fight infections.

- **EMPAVELI increases your chance of getting serious infections caused by encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B. These serious infections may quickly become life-threatening or cause death if not recognized and treated early.**
  - You must complete or be up to date with the vaccines against *Streptococcus pneumoniae* and *Neisseria meningitidis* at least 2 weeks before your first dose of EMPAVELI.
  - If you have not completed your vaccines and EMPAVELI must be started right away, you should receive the required vaccines as soon as possible.
  - If you have not been vaccinated and EMPAVELI must be started right away, you should also receive antibiotics to take for as long as your healthcare provider tells you.
  - If you have been vaccinated against these bacteria in the past, you might need additional vaccines before starting EMPAVELI. Your healthcare provider will decide if you need additional vaccines.
  - Vaccines do not prevent all infections caused by encapsulated bacteria. **Call your healthcare provider or get emergency medical care right away if you get any of these signs and symptoms of a serious infection:**
    - fever with or without shivers or the chills
    - fever with chest pain and cough
    - fever with high heart rate
    - headache and fever
    - confusion
    - clammy skin
    - fever and a rash
    - fever with breathlessness or fast breathing
    - headache with nausea or vomiting
    - headache with a stiff neck or stiff back
    - body aches with flu-like symptoms
    - eyes sensitive to light

Your healthcare provider will give you a Patient Safety Card about the risk of serious infections. Carry it with you at all times during treatment and for 2 months after your last dose of EMPAVELI. Your risk of serious infections may continue for several weeks after your last dose of EMPAVELI. It is important to show this card to any healthcare provider who treats you. This will help them diagnose and treat you quickly.

EMPAVELI is only available through a program called the EMPAVELI Risk Evaluation and Mitigation Strategy (REMS). Before you can take EMPAVELI, your healthcare provider must:

- enroll in the EMPAVELI REMS program
- counsel you about the risk of serious infections caused by certain bacteria
- give you information about the symptoms of serious infections
- make sure that you are vaccinated against serious infections caused by encapsulated bacteria and that you receive antibiotics if you need to start EMPAVELI right away and you are not up to date on your vaccines
- give you a **Patient Safety Card** about your risk of serious infections, as discussed above

For more information about side effects, see **"What are the possible side effects of EMPAVELI?"**

What is EMPAVELI?

EMPAVELI is a prescription medicine used to treat adults with a disease called paroxysmal nocturnal hemoglobinuria (PNH).

It is not known if EMPAVELI is safe and effective in children.

Do not take EMPAVELI if you:

- are allergic to pegcetacoplan or any of the ingredients in EMPAVELI. See the end of this Medication Guide for a complete list of ingredients in EMPAVELI.
- have a serious infection caused by encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, or *Haemophilus influenzae* type B when you are starting EMPAVELI treatment.

Before you take EMPAVELI, tell your healthcare provider about all of your medical conditions, including if you:

- have an infection or fever.
- are pregnant or plan to become pregnant. EMPAVELI may harm your unborn baby. Females who are able to become pregnant should have a pregnancy test before starting treatment with EMPAVELI.

- Females who are able to become pregnant should use an effective method of birth control (contraception) during treatment with EMPAVELI and for 40 days after the last dose.

- are breastfeeding or plan to breastfeed. It is not known if EMPAVELI passes into your breast milk. You should not breastfeed during treatment with EMPAVELI and for 40 days after the last dose.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. EMPAVELI and other medicines can affect each other, causing side effects.

Know the medicines you take and the vaccines you receive. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take EMPAVELI?

- **See the detailed Instructions for Use that comes with your EMPAVELI for information about how to prepare and infuse your dose of EMPAVELI with your infusion pump.**
- **See the detailed Instructions for Use that comes with your EMPAVELI Injector for information about how to prepare and inject your dose of EMPAVELI with your EMPAVELI Injector.**
- Your healthcare provider should show you how to prepare and administer EMPAVELI before you use it for the first time.
- Use EMPAVELI exactly as your healthcare provider tells you. Do not use more or less than your healthcare provider tells you to.
- EMPAVELI is given under the skin (subcutaneously) 2 times each week. If there is an increase in your LDH, an enzyme in your blood, your healthcare provider may tell you to take EMPAVELI every 3 days.
- **If you are changing treatment from eculizumab to EMPAVELI, you should continue eculizumab for 4 weeks after your first dose of EMPAVELI. After 4 weeks, you should stop treatment with eculizumab.**
- **If you are changing treatment from ravulizumab to EMPAVELI, you should take your starting dose of EMPAVELI no more than 4 weeks after your last dose of ravulizumab.**
- **If you have PNH and you stop taking EMPAVELI, your healthcare provider will need to monitor you closely for at least 8 weeks after stopping EMPAVELI. Stopping treatment with EMPAVELI may cause a breakdown of red blood cells due to PNH.**

  Symptoms or problems that can happen due to red blood cell breakdown include:

  - decreased hemoglobin level in your blood
  - blood in your urine
  - shortness of breath
  - trouble swallowing
  - tiredness
  - pain in the stomach (abdomen)
  - blood clots
  - erectile dysfunction (ED)

If you miss a dose of EMPAVELI, take the missed dose as soon as possible. Take your next dose at your regularly scheduled time.

What are the possible side effects of EMPAVELI?

EMPAVELI can cause serious side effects including:

- See **"What is the most important information I should know about EMPAVELI?"**
- **Allergic reactions.** Allergic reactions can happen during your EMPAVELI infusion. Stop your EMPAVELI infusion and tell your healthcare provider or get emergency medical care right away if you get any of these symptoms during your EMPAVELI infusion:
  - chest pain
  - trouble breathing or shortness of breath
  - swelling of your face, tongue, or throat
  - feel faint or pass out

The most common side effects in people with PNH treated with EMPAVELI include:

- injection-site reactions
- infections
- diarrhea
- pain in the stomach (abdomen)
- respiratory tract infection
- pain in the arms, hands, legs or feet
- low potassium in blood
- tiredness
- viral infection
- cough
- joint pain
- dizziness
- headache
- rash

Tell your healthcare provider about any side effect that bothers you or that does not go away. These are not all of the possible side effects of EMPAVELI. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store EMPAVELI?

- Store vials of EMPAVELI in the refrigerator between 36°F to 46°F (2°C to 8°C) in the original carton to protect from light.
- Do not use EMPAVELI past the expiration date stamped on the carton.

Keep EMPAVELI and all medicines out of the reach of children.

General information about the safe and effective use of EMPAVELI.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use EMPAVELI for a condition for which it was not prescribed. Do not give EMPAVELI to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about EMPAVELI that is written for health professionals.

What are the ingredients in EMPAVELI?

Active ingredient: pegcetacoplan

Inactive ingredients: sorbitol, glacial acetic acid, sodium acetate trihydrate, Water for Injection USP. EMPAVELI may also contain sodium hydroxide and/or additional glacial acetic acid for pH adjustment.

Manufactured for:

Apellis Pharmaceuticals, Inc. 100 Fifth Avenue Waltham, MA 02451
For patent information: www.apellis.com/productpatent

For more information, go to www.EMPAVELI.com or call 1-866-692-7527
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