EMPAVELI- pegcetacoplan injection, solution
Cenexi HSC

HIGHLIGHTS OF PRESCRIBING INFORMATION
EMPAVELI ®(pegcetacoplan) injection, for subcutaneous use

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

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: 2/2024

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

	EMPAVELI (N=46)	**Control Arm * (N=18)**

Adverse Reaction	n (%) Exposure Adjusted Rate (per 100 pt yrs)	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
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

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).

* Control Arm = supportive care (excluding complement inhibitors)
† 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

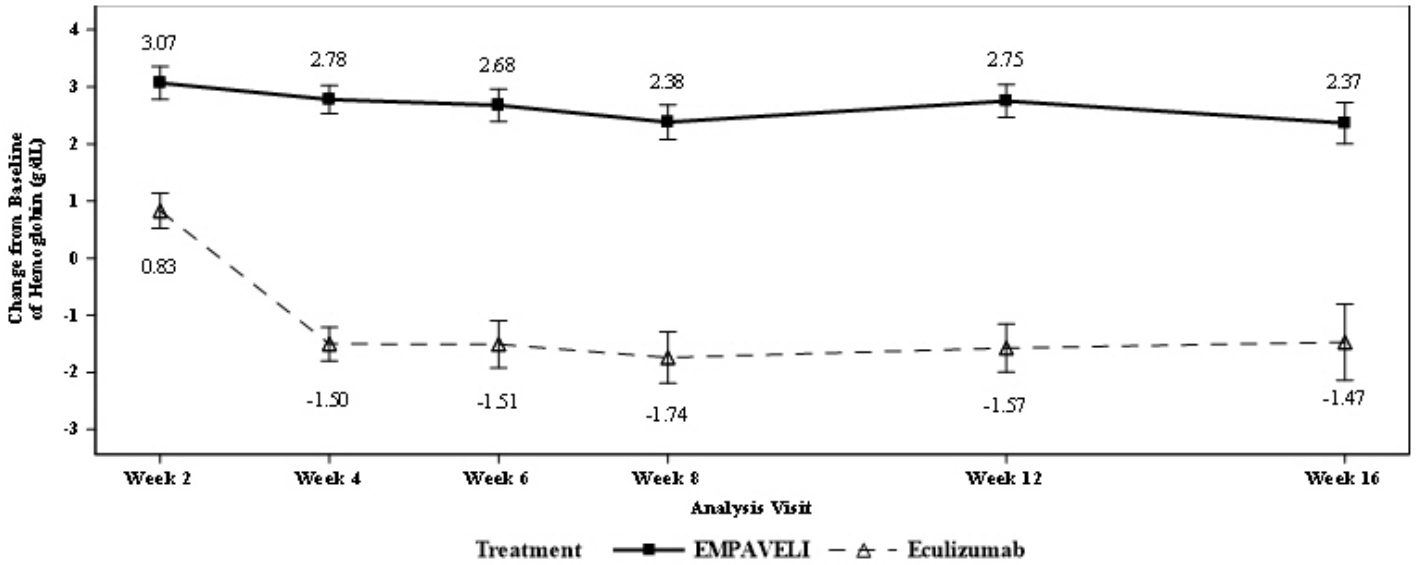
Parameter	**Statistics**	**EMPAVELI (N=41)**	**Eculizumab (N=39)**
Age (years)	Mean (SD)	50.2 (16.3)	47.3 (15.8)

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 (10^9cells/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(10^9cells/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 * (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	n (%)	23 (65.7)	16 (88.9)

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)

* 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 * (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 §(LS ¶Mean CFB, SE #)	-1870 (101.0)	-400 (313.0)	-1470 (-2113.4, -827.3) p<0.0001
Change from baseline in ARC § (LS ¶Mean CFB, SE #)	-123 (9.2)	-19 (25.2)	-103 (-158.9, -48.7) p = 0.0002
Change from baseline in Hb § (LS ¶Mean CFB, SE #)	2.9 (0.38)	0.3 (0.76)	2.7 (0.99, 4.35) p = 0.0019
Transfusion Avoidance †	32 (91%)	1 (6%)	72% (56%, 89%)

(n, %)			p<0.0001 ‡

Data collected after cross-over from the control arm is excluded in analyses.

* Control Arm = supportive care (excluding complement inhibitors)
† 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.
§ The post baseline missing values (including the values after cross-over from the control arm) are imputed using a multiple imputation method.
¶ 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 Usethat 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 Usethat 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
- tiredness
- viral infection

- diarrhea
- pain in the stomach (abdomen)
- respiratory tract infection
- pain in the arms, hands, legs or feet
- low potassium in blood
- 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

EMPAVELI is a registered trademark of Apellis Pharmaceuticals, Inc.
For more information, go to www.EMPAVELI.com or call 1-866-692-7527
EMP-MG-08Feb2024-5.0

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised:02/2024

INSTRUCTIONS FOR USE
EMPAVELI ®(em-puh-vel-ee)
(pegcetacoplan)
injection, for subcutaneous use
infusion pump

Important Information

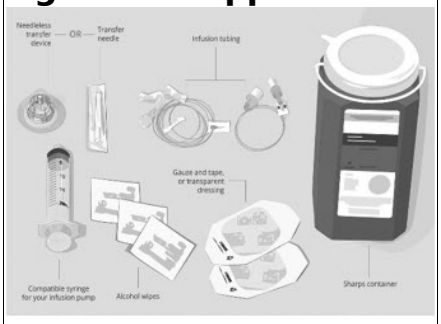
This Instructions for Use is for the infusion pump only. If using EMPAVELI Injector, follow the Instructions for Use that comes with the EMPAVELI Injector.

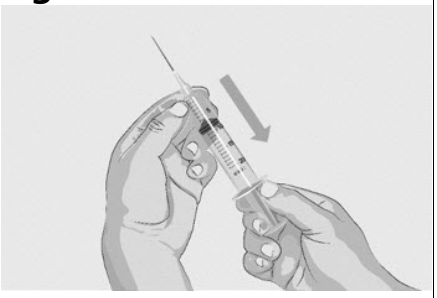
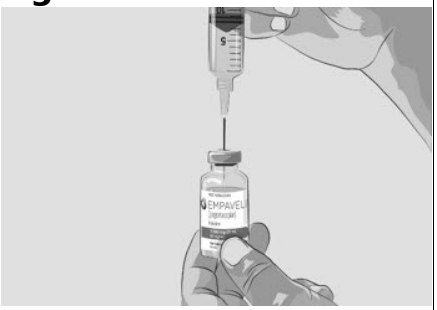
Read **this** Instructions for Use before you start using EMPAVELI with an infusion pump and each time you get a refill as there may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. Your healthcare provider should show you or your caregiver how to infuse EMPAVELI the right way before you use it for the first time. Ask your healthcare provider about any instructions you do not understand.

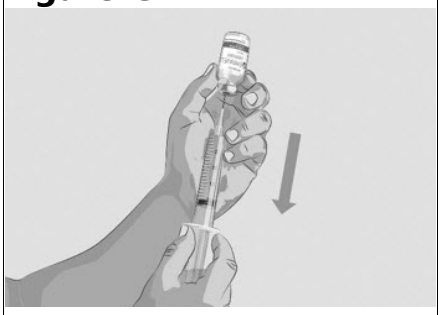
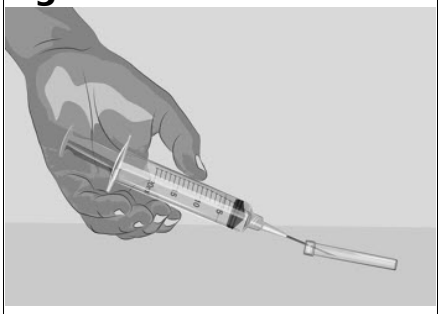
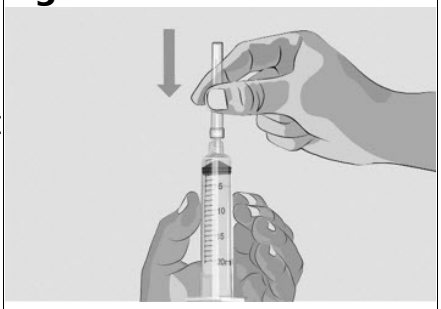
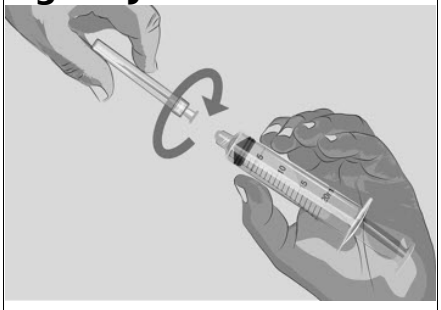
How should I store EMPAVELI?

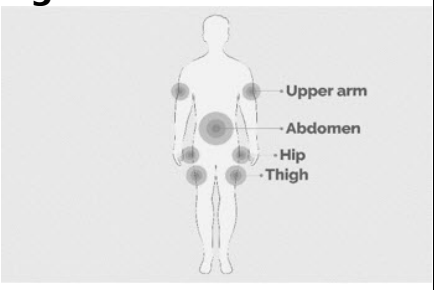
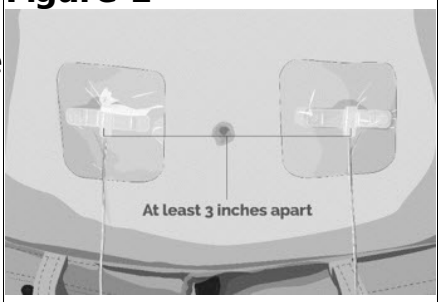
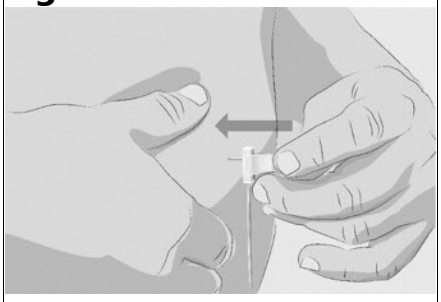
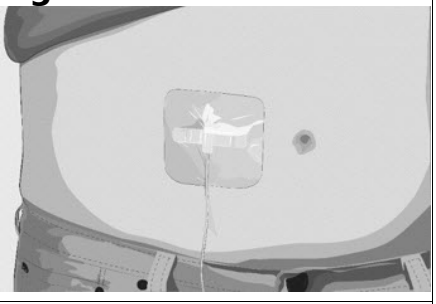
- Store vials of EMPAVELI in the refrigerator between 36°F to 46°F (2°C to 8°C) in the original carton to protect from light.
- Do not use EMPAVELI past the expiration date stamped on the carton.

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

<table>
<tr><td rowspan="4">Step 1</td><td>Prepare for infusion
Before you start:
Find a well-lit, flat work surface area, like a table.
Remove a single vial carton from the refrigerator. Keep the vial in the carton at room temperature and allow it to warm up for about 30 minutes.
Do not try to speed up the warming process.
Gather your supplies (See Figure A):
Infusion pump and manufacturer's instructions (not shown)
Compatible syringe for your infusion pump
Transfer needle OR
Needleless transfer device to draw up the medicine from the vial
Infusion set (not shown; varies according to device manufacturer's instructions)
Infusion tubing
Sharps container
Alcohol wipes
Gauze and tape, or transparent dressing</td><td rowspan="3">Figure A: Supplies
 
</td></tr>
<tr><td>Clean your work surface well using an alcohol wipe.</td></tr>
<tr><td>Wash your hands well with soap and water. Dry your hands.</td></tr>
<tr><td></td><td>Check the vial and liquid
Remove the vial from the carton. Carefully look at the liquid in the vial of</td><td></td></tr>
</table>

	EMPAVELI. ◦ EMPAVELI is a clear, colorless to slightly yellowish liquid. Check for particles or color changes (See **Figure B**).	**Figure B** 
Step 2	**Do not use the vial and call** ApellisAssist at 1-866-MY-APL-ASSIST (1-866-692-7527) **if:** • The liquid looks cloudy, contains particles, or is dark yellow. • The protective flip cap is missing or damaged. • The expiration date on the label has passed.	
Step 3	**Prepare and fill syringe** • Remove the protective flip cap from the top of the vial to show the middle part of the gray rubber stopper of the EMPAVELI vial (See **Figure C**). Throw away the protective flip cap. • Clean the gray rubber stopper with a new alcohol wipe and allow the gray rubber stopper to dry for at least 30 seconds. **Do not** touch the exposed gray rubber stopper after wiping. **Option 1:** If using a needleless transfer device (such as a vial adapter), follow the instructions provided by the device manufacturer. OR **Option 2:** If transfer is done using a transfer needle and a syringe, follow the instructions below: • Attach a sterile transfer needle to a sterile syringe. • Pull back the plunger to the 20-mL mark to fill the syringe with air (See **Figure D**). • Push the air-filled syringe with transfer needle attached down through the center of the vial gray rubber stopper. • The tip of the transfer needle should not be in the solution to avoid creating air bubble(s) (See **Figure E**). • Gently push the air from the syringe into the vial. This will inject the air from	**Figure C**  **Figure D**  **Figure E** 

	the syringe into the vial.	**Figure F**
	• Turn the vial upside down and insert the transfer needle in the EMPAVELI solution (See **Figure F**).	
	• With the transfer needle tip in the EMPAVELI solution, slowly pull the plunger back to fill the syringe with all the EMPAVELI solution (See **Figure G**). • Remove the filled syringe with EMPAVELI and the transfer needle from the vial.	**Figure G** 
	• Remove the transfer needle by **using 1 hand**to slide the needle into the needle cap and **scoop upwards**to cover the needle (See **Figure H**).	**Figure H** 
	• After the needle is covered, push the needle cap down towards the syringe to fully attach it **with 1 hand**to prevent an accidental stick with the needle (See **Figure I**).	**Figure I** 
	• Twist off and remove the transfer needle (See **Figure J**).	**Figure J** 
Step 4	**Prepare infusion pump and tubing** • Gather the infusion pump supplies and follow the device manufacturer's	

Step 4	instructions to prepare the pump and tubing.	
Step 5	**Prepare the infusion site(s)** • Select an area on your stomach (abdomen), thighs, hips, or upper arms for the infusion(s) (See **Figure K**). **Avoid the following infusion areas:** ◦ Do not infuse into areas where the skin is tender, bruised, red, or hard. ◦ Avoid infusing into tattoos, scars, or stretch marks. • Use a different site(s) from the last time you infused EMPAVELI. If there are multiple infusion sites, they should be at least 3 inches apart. Change (rotate) infusion sites in between each infusion (See **Figure L**). • Clean the skin at each infusion site(s) with a new alcohol wipe, starting at the center of each infusion site and working outward in a circular motion (See **Figure M**). • Let the skin dry.	**Figure K**  **Figure L**  **Figure M** 
Step 6	**Insert and secure the infusion needle(s)** • Pinch the skin between your thumb and forefinger around the infusion site (where you plan to insert the needle). • Insert the needle into the skin (See **Figure N**). • Secure the needle(s) using gauze and tape or a transparent dressing placed over the infusion site(s) (See **Figure O**).	**Figure N**  **Figure O** 
	Start infusion • Follow the device manufacturer's	

Step 7	instructions to start the infusion. • Start the infusion right away after drawing EMPAVELI into the syringe. • EMPAVELI infusion takes about 30 minutes (if using 2 infusion sites) or about 60 minutes (if using 1 infusion site) to complete.	
Step 8	**Complete infusion** • Follow the device manufacturer's instructions to complete the infusion.	
Step 9	**Record infusion** • Record your treatment as directed by your healthcare provider.	
Step 10	**Clean up** • After the infusion is complete, remove the dressing and slowly take out the needle(s). Cover the infusion site with a new dressing. • Remove the infusion set from the pump and throw it away into the sharps container (See **Figure P**). • Clean and store the infusion pump according to the device manufacturer's instructions.	
	Dispose of (throw away) used needles and syringes and EMPAVELI infusion tubing. • Put the used needles, syringes, and EMPAVELI infusion tubing in an FDA-cleared sharps disposal container right away after use (See **Figure P**). • **Do not dispose of**(throw away) the used needles, syringes, and EMPAVELI infusion tubing in your household trash. • If you do not have an FDA-cleared sharps disposal container, you may use a household container that is: ◦ made of heavy-duty plastic, ◦ can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out, ◦ upright and stable during use, ◦ leak-resistant, and ◦ properly labeled to warn of	**Figure P** 

Step 11	hazardous waste inside the container. • When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. • For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal. • **Do not**throw away your used sharps disposal container in your household trash unless your community guidelines permit this. • **Do not**recycle your used sharps disposal container.	

Call 1-866-692-7527 to speak with an Apellis representative.
Manufactured for:
Apellis Pharmaceuticals, Inc. 100 Fifth Avenue Waltham, MA 02451

This Instructions for Use has been approved by the U.S. Food and Drug Administration.
Revised 09/2023

EMP-IFU-29Sep2023-4.0

INSTRUCTIONS FOR USE
EMPAVELI ®Injector
(pegcetacoplan)
injection, for subcutaneous use
Single-use on-body injector

Important Information
This Instructions for Use is for the EMPAVELI Injector only.

Read **this**Instructions for Use before you start using the Injector and each time you get a refill as there may be new information. The EMPAVELI Injector is placed on your body to give medicine under the skin. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. Your healthcare provider should show you or your caregiver how to inject EMPAVELI the right way before you use it for the first time. It is important that you do not try to give yourself or someone else the injection unless you have received training from your healthcare provider. Ask your healthcare provider about any instructions you do not understand.

If you have questions, concerns, or need of help, please call ApellisAssist ®at 1-866-MY-APL-ASSIST (1-866-692-7527).

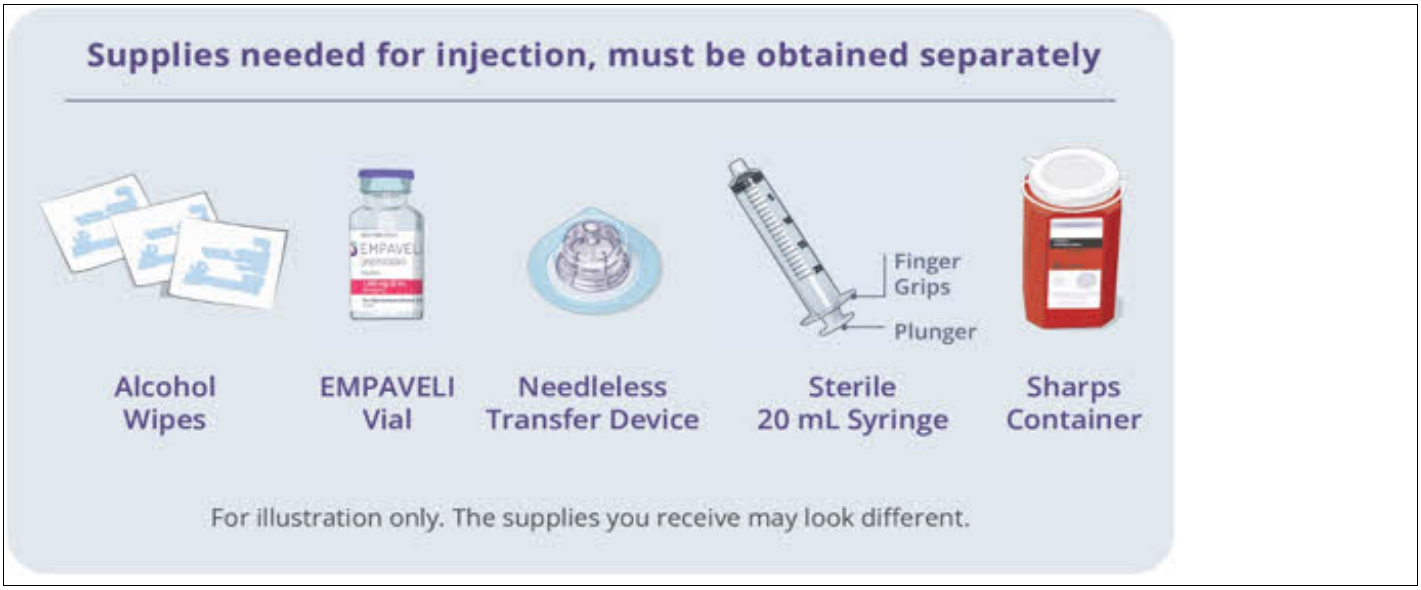
SIDE 1:
Filling the Syringe

Start Here
Complete these instructions on how to prepare EMPAVELI before completing EMPAVELI Injector administration instructions on the back of this page.

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, EMPAVELI Injector, and all medicines out of the reach of children.



Prepare for injection

1

- Find a well-lit, flat work surface area, like a table.
- Remove a single vial carton of EMPAVELI from the refrigerator. Keep the vial in the carton at room temperature and allow it to warm up for about **30 minutes**.

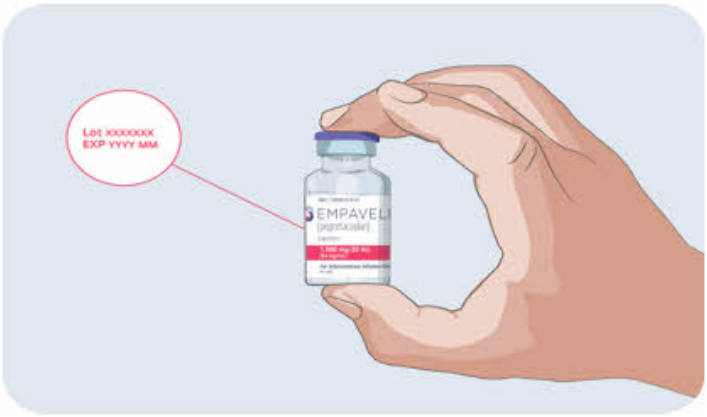
  ⚠ **Do not**try to speed up the warming process.

2

- Wash your hands well with soap and water.
- Dry your hands.

Check the vial and liquid

3



- Remove the vial from the carton. Carefully look at the liquid in the vial of EMPAVELI.
- EMPAVELI is a clear, colorless to slightly yellowish liquid. Check for particles or color changes.

⚠ **Do not** use and call ApellisAssist if:

- The liquid looks cloudy, contains particles, or is dark yellow.
- The protective flip cap is missing from the top of the vial or damaged.
- The expiration date on the label has passed.

4

- Flip up to remove the protective flip cap from the top of the vial to show the exposed middle part of the gray rubber stopper of the EMPAVELI vial.
- Throw away the protective flip cap.

5

- Clean the gray rubber stopper on the top of the EMPAVELI vial with a new alcohol wipe.
- Allow the gray rubber stopper to dry for at least 30 seconds.

⚠ **Do not** touch the exposed gray rubber stopper after wiping.

Prepare and fill the syringe with EMPAVELI using a needleless transfer device (such as a vial adapter)

6

Always follow the Instructions for Use provided by the needleless transfer device's manufacturer (as they may differ from the following steps).

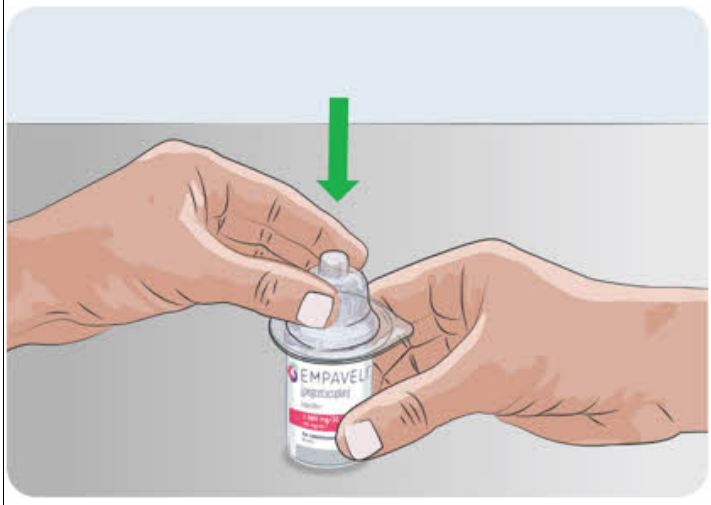
⚠ **Do not**remove the needleless transfer device from the blister package.

⚠ **Do not**touch the spike or the inside of the needleless transfer device.

⚠ **Do not**use the needleless transfer device if it comes out or is dropped out of the package.

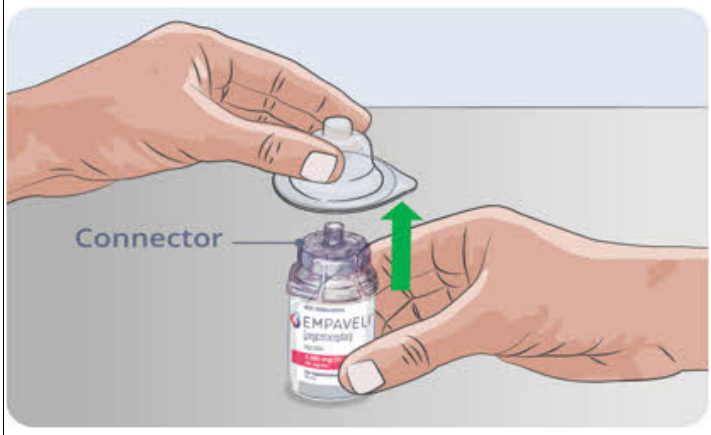
⚠ **Do not**use the needleless transfer device if the package is opened.

7



- Remove the cover of the needleless transfer device package.
- Place the vial on a clean, flat surface and hold the vial by the base with one hand.
- Using the outside of the blister package to firmly hold the needleless transfer device, push needleless transfer device straight down onto the vial top until it snaps securely into place.

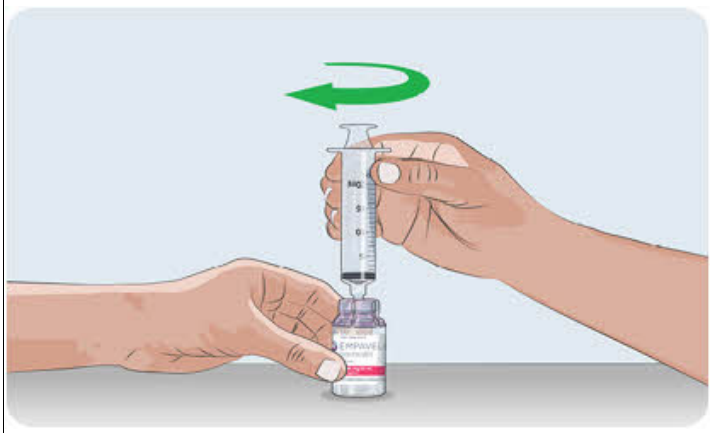
8



- Remove the blister package from the needleless transfer device and throw the blister package away.

⚠ **Do not**touch the connector at the top of the transfer device.

9

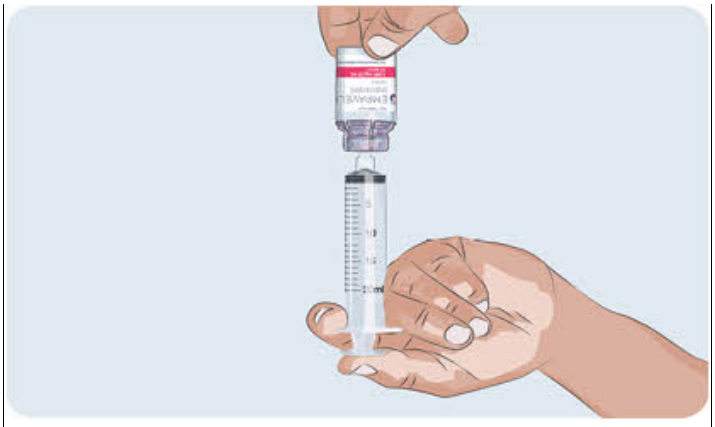
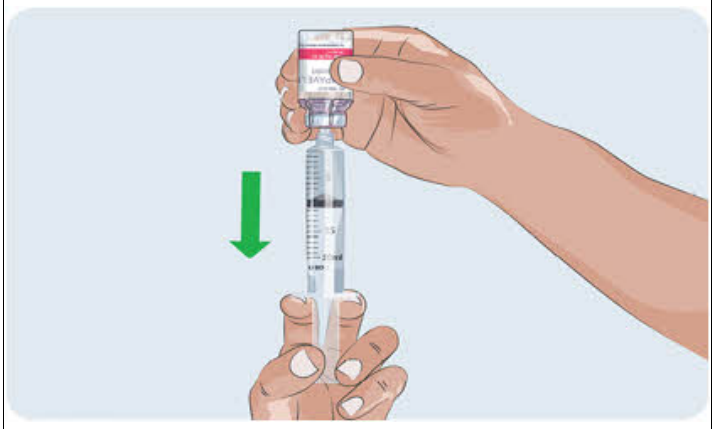
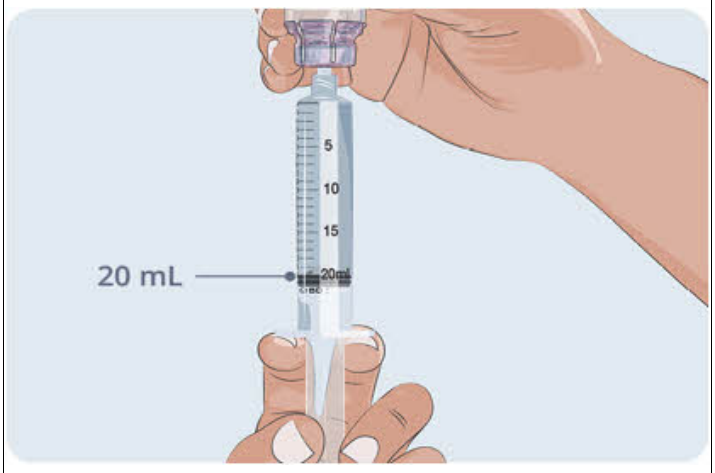
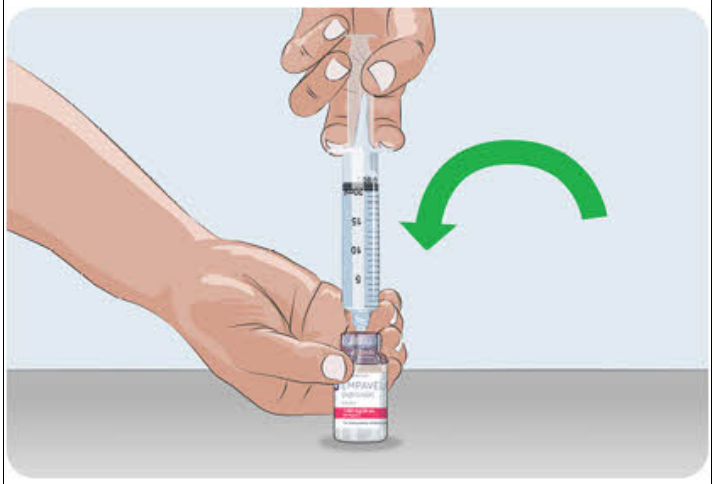


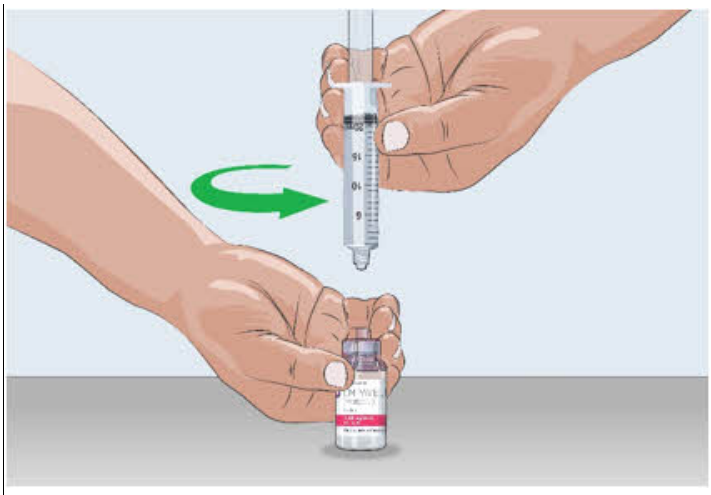
- Remove the syringe from its packaging.

⚠ **Do not**touch the tip of the syringe.

- Attach the syringe to the needleless transfer device by twisting the tip of the syringe to the right (clockwise) onto the top of the needleless transfer device.

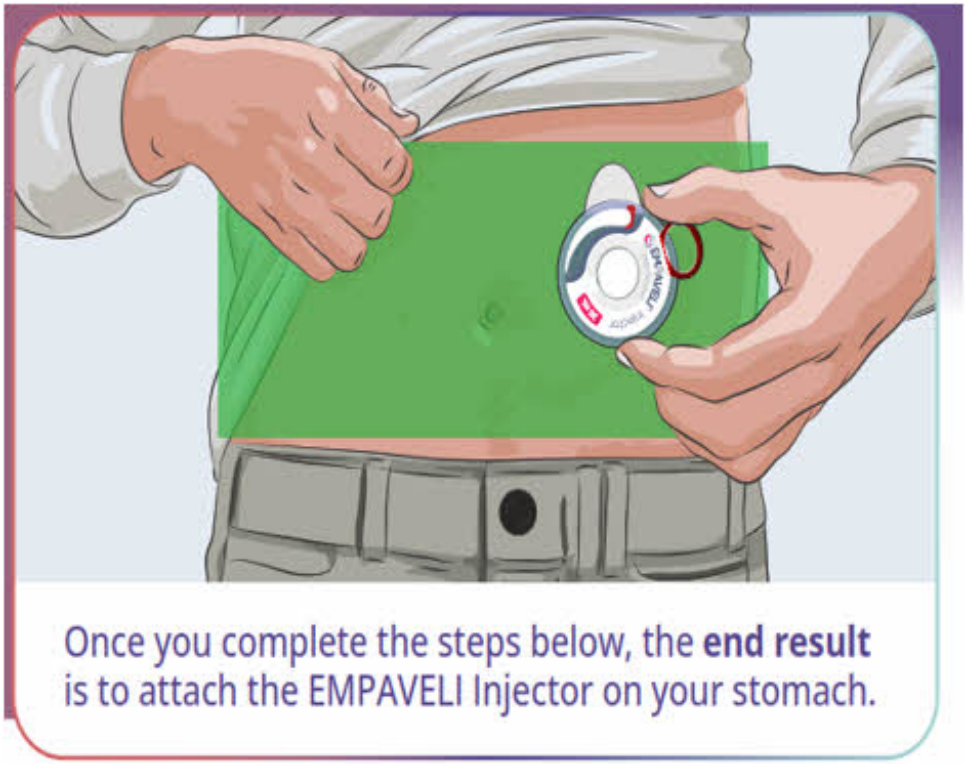
10

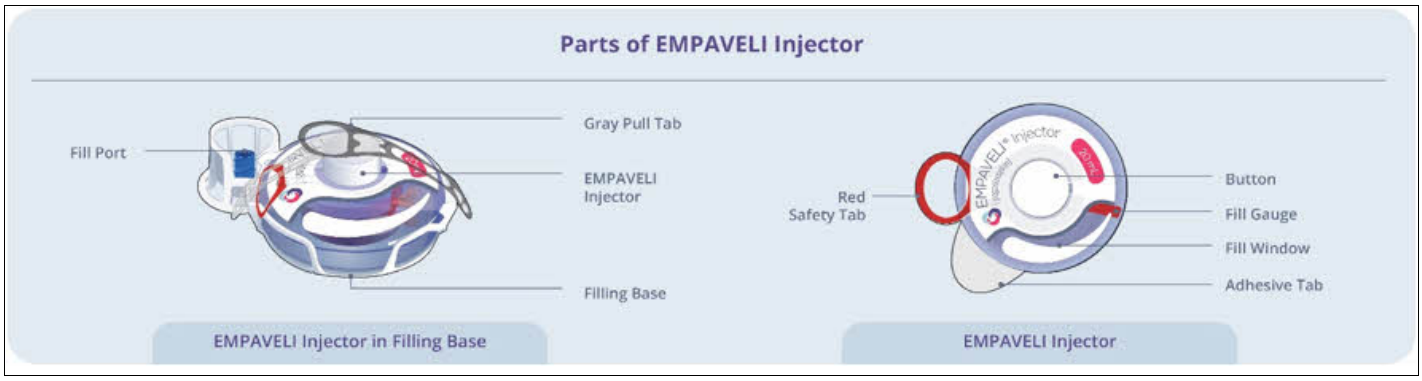
	• Turn the EMPAVELI vial upside down.
11 	• Slowly pull the syringe plunger down to fill the syringe with EMPAVELI.
12 	• Withdraw all EMPAVELI from the vial into the syringe. • Make sure there is 20 mL of EMPAVELI in the syringe. • Remove air from syringe by gently pushing on the plunger.
13 	• While holding the EMPAVELI vial and syringe, turn the EMPAVELI vial and filled syringe upright and place the bottom of the EMPAVELI vial on a flat surface.
14	

	• Remove the filled syringe from the needleless transfer device with one hand while holding the EMPAVELI vial with the other hand and twisting the filled syringe to the left (counterclockwise).
15 	• Place the syringe on a clean, flat surface while you prepare the EMPAVELI Injector. The syringe will not leak when set down. ⚠ **Do not** touch the tip of the filled syringe.
16 	⚠ **Do not** remove the needleless transfer device from the vial. • Throw away the vial with the needleless transfer device attached into the household trash.

SIDE 2:
Injector Administration

Complete these instructions for administering the EMPAVELI Injector after completing syringe filling instructions on the front of this page.





Important information for administration with EMPAVELI Injector

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General use: • **Do not** use EMPAVELI Injector if tamper-proof label has been broken. • **Do not** use EMPAVELI Injector if you have a skin condition on your stomach (injection site). • **Do not** use if you dropped EMPAVELI Injector. • **Do not** use if the sealed plastic tray is open or	**Using EMPAVELI Injector:** • **Do not** apply EMPAVELI Injector along the belt line or on areas where the injector will be affected by folds in the skin. • **Do not** touch the white adhesive on the bottom of EMPAVELI Injector before attaching to stomach. • **Do not** let your clothes touch the clean site. • **Do not** remove the Red	**During injection:** • **Do not** remove EMPAVELI Injector from the skin during injection. • **Do not** bathe, shower, exercise, use hot tubs, whirlpools, or saunas.

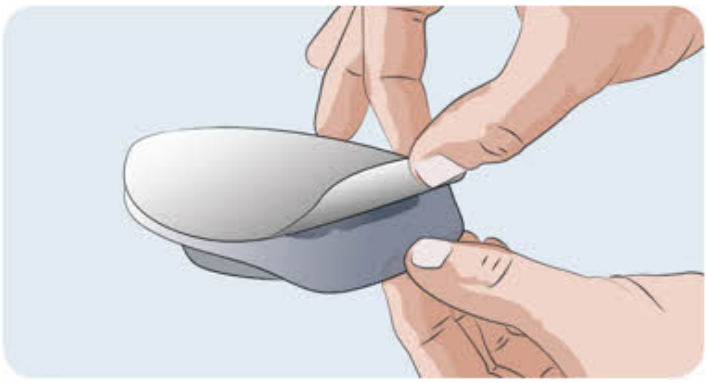
damaged.
- **Do not**use if the expiration date on the box has passed.
- **Do not**use if you have an acrylic allergy. Tell your healthcare provider if you are allergic to acrylic.
- **Do not**reuse EMPAVELI Injector.
- **Do not**store the filled EMPAVELI Injector.
- Wear loose clothes so that they **do not**get in the way of the EMPAVELI Injector.
- **Do not**store the EMPAVELI Injector in direct sunlight. If the EMPAVELI Injector is stored in direct sunlight, **do not**use it and call ApellisAssist at 1-866-MY-APL-ASSIST (1-866-692-7527).

- **Do not**remove the Red Safety Tab until EMPAVELI Injector is attached to body.
- **Do not**remove EMPAVELI Injector from the skin until the button pops out.
- **Do not**throw away (dispose of) the EMPAVELI Injector into household trash. See the section "Remove and Dispose of EMPAVELI Injector" for information on how to dispose of the EMPAVELI Injector.
- Choose an injection site at least 1 inch from the edge of your belly button and the edge of the EMPAVELI Injector, and 1 inch from last injection site.
- Use the EMPAVELI Injector on stomach only.

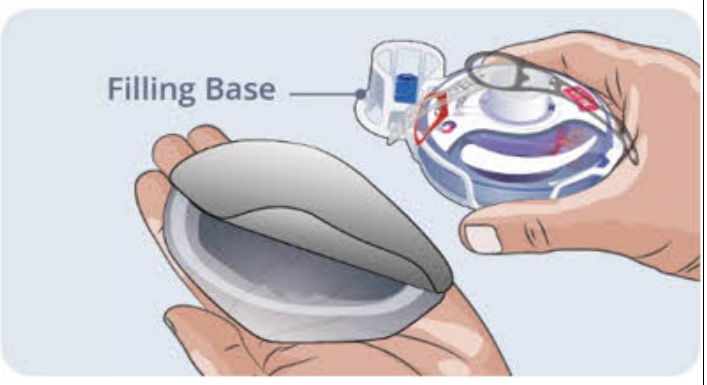
Avoid getting your stomach wet. The EMPAVELI Injector is not waterproof. Water or sweat may loosen EMPAVELI Injector from skin.
- **Do not**sleep or bathe during injection.
- Avoid intense physical activity.
- **Do not**bump or knock the EMPAVELI Injector.
- **Do not**bump the EMPAVELI Injector Button.
- **Do not**use anything to hold the EMPAVELI Injector in place.

Fill injector with EMPAVELI liquid

17

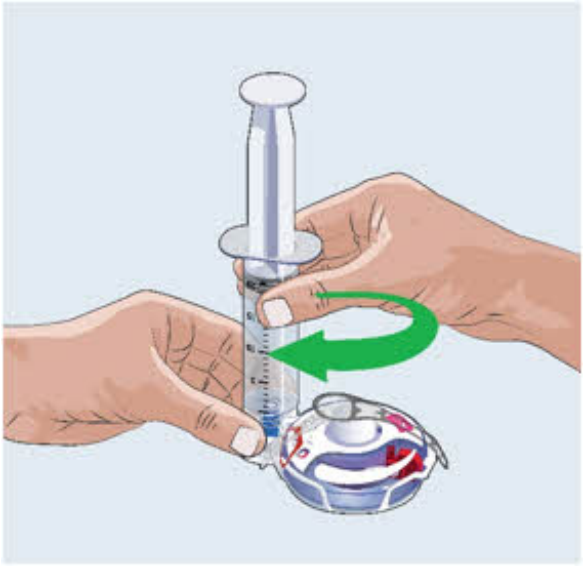


Peel back the cover and remove the clear packaging insert.



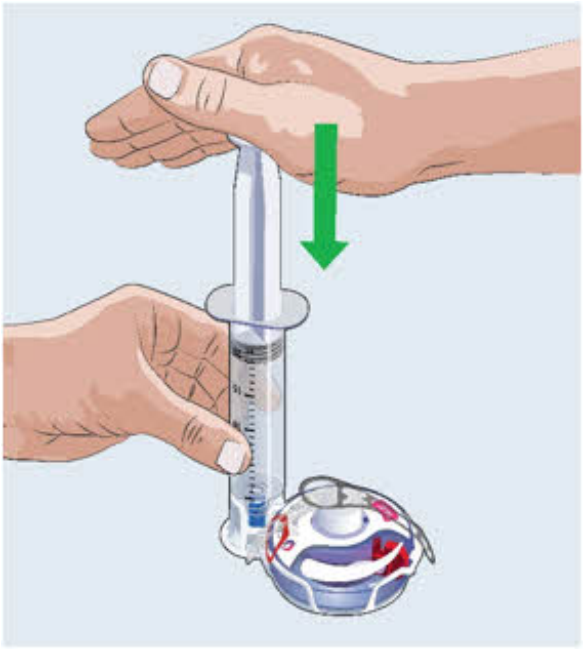
Remove the EMPAVELI Injector and the surrounding Filling Base from the packaging. Place it on a clean, flat surface.

18



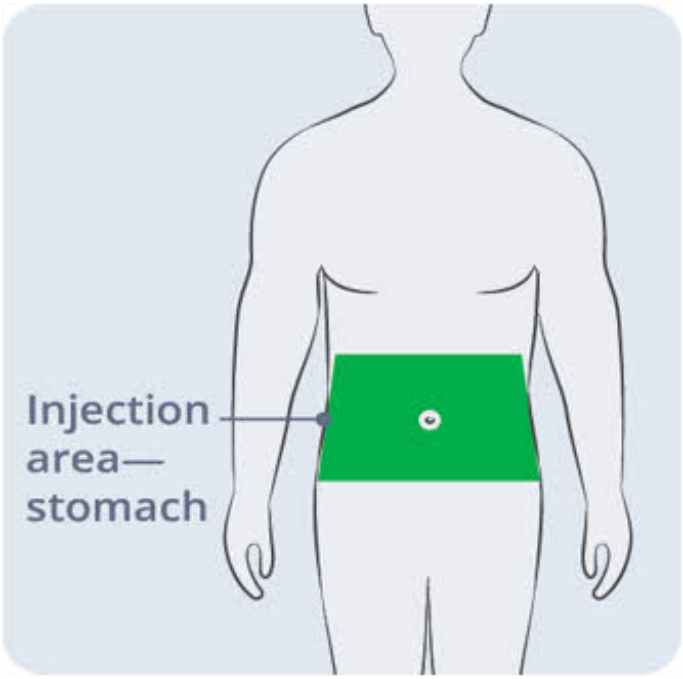
- Pick up the syringe filled with EMPAVELI.
- Twist the filled syringe tip to the right (clockwise) into the Fill Port until it is tight.

19



- Firmly push the syringe plunger down.
- The syringe plunger may be hard to push.
- Watch the Fill Gauge move as EMPAVELI is pushed into the injector.

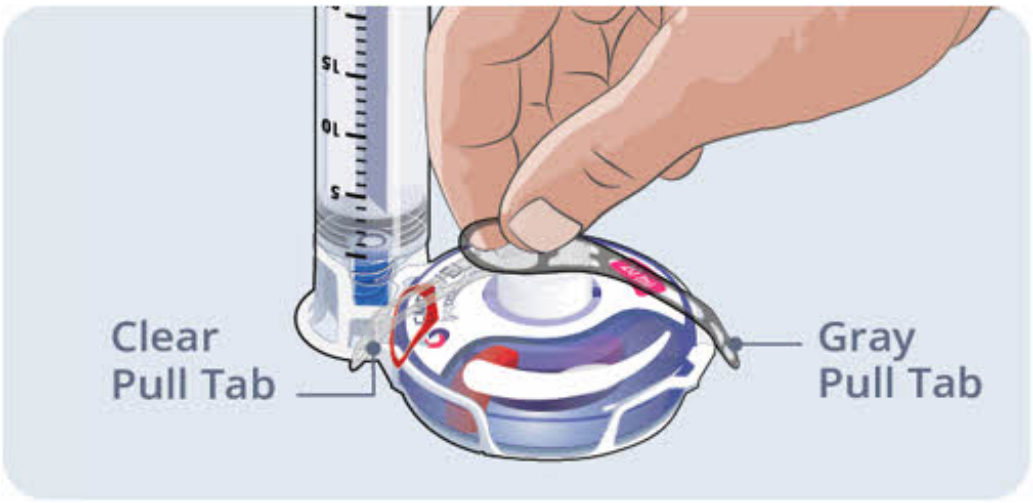
20

	• Make sure the syringe is empty. If needed, press firmly down on the syringe plunger again. ⚠ **Do not**remove syringe from Filling Base. After the EMPAVELI Injector is filled, continue with the preparation and injection. ⚠ **Do not**store filled EMPAVELI Injector.
Attach EMPAVELI Injector to stomach	
21 	• Select an area on your stomach to place the EMPAVELI Injector. ⚠Use the EMPAVELI Injector on your stomach only. • Choose an injection site at least: ◦ 1 inch from the edge of your belly button and the edge of the EMPAVELI Injector. **and** ◦ 1 inch from your last injection site. ⚠ Avoid an injection site that is tender, bruised, red, hard, irritated, scarred, tattooed, or has stretch marks. ⚠ **Do not apply**the EMPAVELI Injector along the belt line or on areas where the EMPAVELI injector will be affected by folds in the skin. ⚠ Wear loose clothes so that they **do not**get in the way of the EMPAVELI Injector.
22	

- Clean the injection site with an alcohol wipe.
- Allow the injection site to dry for at least 30 seconds.

⚠ **Do not** let your clothes touch the clean injection site.

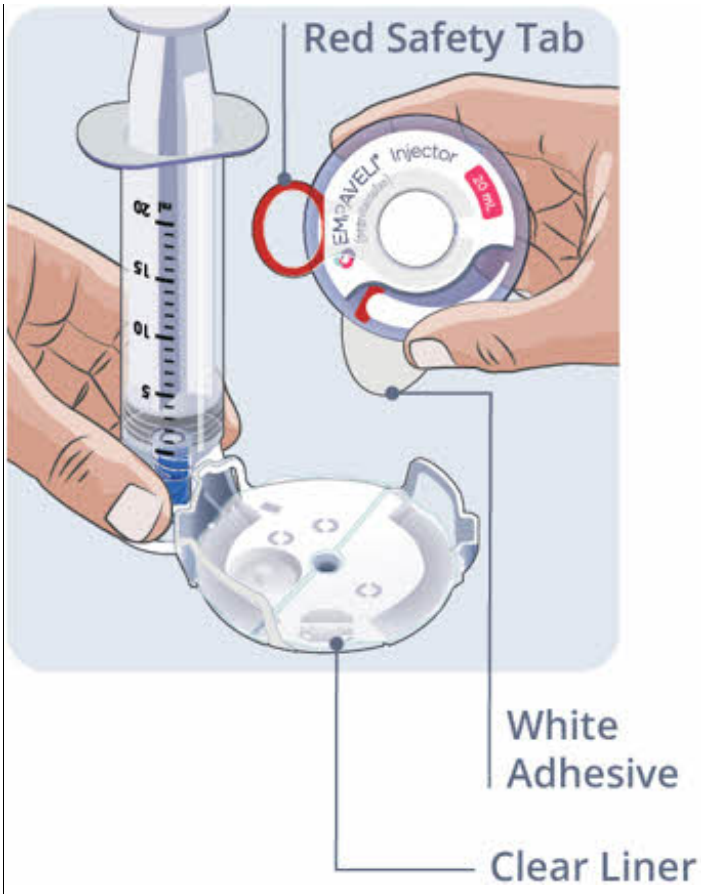
23



- Hold the Gray Pull Tab and pull. Allow both the Gray and Clear Pull Tabs to fall to the side.
- Both tabs may fall to the side or come off completely.

⚠ **Do not** remove the Red Safety Tab until the EMPAVELI Injector is attached to the body.

24



- Hold the sides of the EMPAVELI Injector and pull it straight up to remove it from the Filling Base.

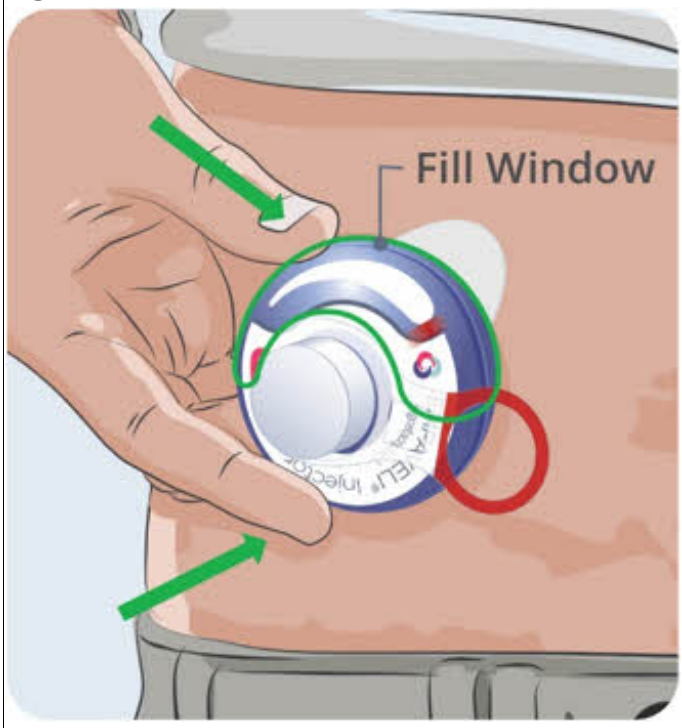
⚠ **Do not**touch the adhesive on the bottom of the EMPAVELI Injector or fold the adhesive onto itself.

- The White Adhesive will stay attached to the EMPAVELI Injector and the Clear Liner will stay attached to the Filling Base.

⚠ **Do not**remove the Red Safety Tab until the EMPAVELI Injector is attached to your body.

⚠Ensure the injection site has been cleaned before attaching EMPAVELI Injector.

25

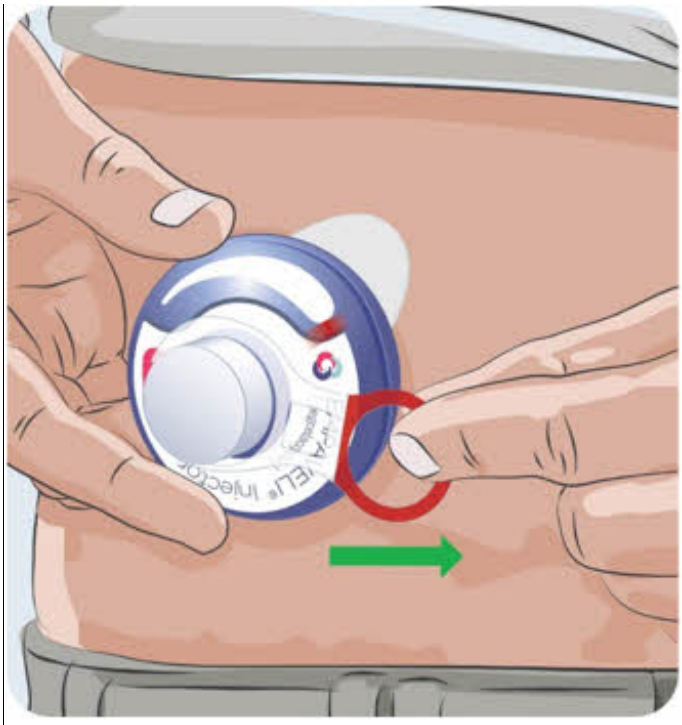


- Position the EMPAVELI Injector so that the Fill Window is pointed up toward your face.
- Press firmly on the clear portion of the EMPAVELI Injector to attach to stomach.

⚠ **Do not**use anything to hold the EMPAVELI Injector in place.

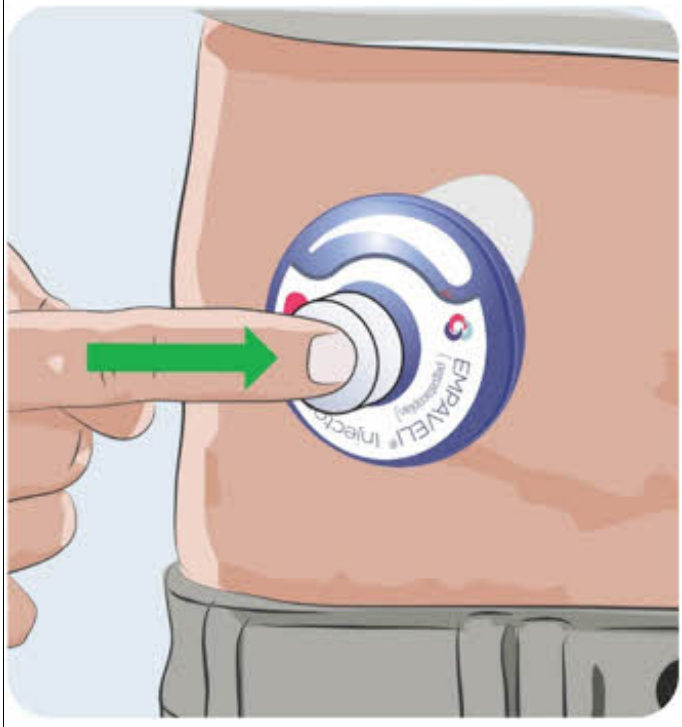
Start Injection

26



- Hold the EMPAVELI Injector with 1 hand. Use the other hand to pull the Red Safety Tab off.
- The EMPAVELI injection will not start until the Red Safety Tab is removed.

27



- Right away, Press the button in firmly until it stays in place to start the EMPAVELI injection.

⚠Pushing the Button in will insert the needle into your skin. You may feel the needle go into your skin.

- Light daily activities can be done during the EMPAVELI injection.

⚠ Be careful not to bump or knock the EMPAVELI Injector or button during the EMPAVELI injection.

⚠ Keep your stomach dry. Avoid intense physical activity. **Do not**sleep or bathe during your EMPAVELI injection.

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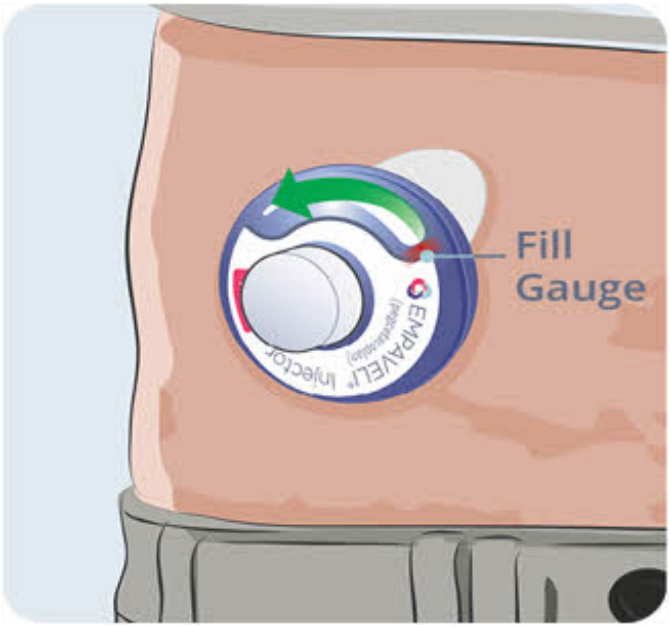
- Your EMPAVELI injection will continue as long as the button is pushed in. It may take approximately 30 to 60 minutes to complete.



- To track progress, watch the Fill Gauge move across Fill Window toward empty. It may take some time to move and may move slowly.

⚠ **Do not**remove the EMPAVELI Injector until the button pops out.

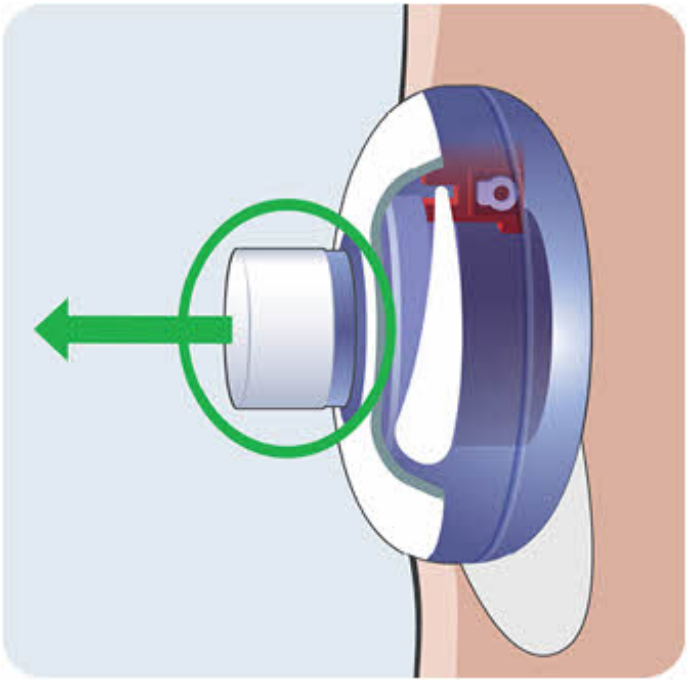
⚠If the button does not pop out after 2 hours (120 minutes), refer to Questions and Answers.

⚠If the EMPAVELI Injector falls off of your body, refer to Questions and Answers.

⚠ **Caution:**Holding down the button will stop the flow of medicine. Injection will begin again when the button is released.

⚠If you have an allergic reaction to the adhesive, call your healthcare provider right away.

29



- When the button pops out, the EMPAVELI injection is done. The needle will be pulled out of the skin and back into the EMPAVELI Injector.

⚠The button popping out is the only way to know if the EMPAVELI injection is complete. **Do not**remove the EMPAVELI Injector until the Button pops out.

Remove and dispose of EMPAVELI Injector

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- Use your thumb to lift the Adhesive Tab. Hold the Adhesive Tab against the EMPAVELI Injector.
- Slowly peel the EMPAVELI Injector away from your skin.

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- Put your used EMPAVELI Injector in an FDA-cleared sharps disposal container right away after use.

⚠ **Do not**throw away the EMPAVELI Injector in the household trash.

⚠The Filling Base with the syringe attached, alcohol wipe, and packaging may be placed in your household trash.

- If you **do not**have an FDA-cleared sharps disposal container, you may use a household container that is:
  - made of heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles

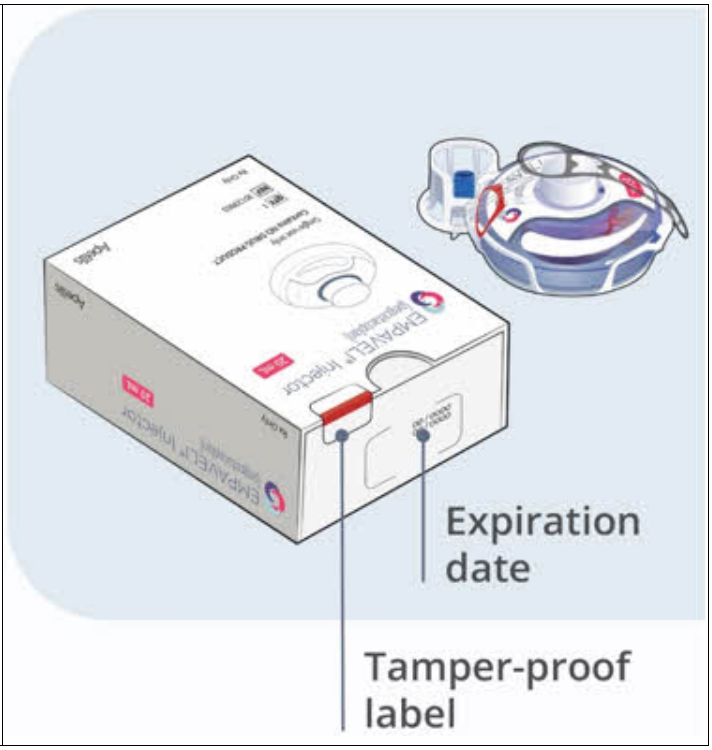
and syringes.

- For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: **http:/www.fda.gov/safesharpsdisposal**.
- **Do not**throw away (dispose of) your used sharps disposal container in your household trash unless your community guidelines permit this.
- **Do not**recycle your used sharps disposal container.
- Keep the used EMPAVELI Injector and sharps disposal container out of the reach of children.

Symbol	Symbol Title	Symbol Definition
	Manufacturer	Indicates the medical device manufacturer
	Date of manufacture	Indicates the date when the medical device was manufactured
	Catalogue number	Indicates the manufacturer's catalogue number so that the medical device can be identified
	Batch code	Indicates the manufacturer's batch code so that the batch or lot can be identified
	Use by date	Indicates the date after which the medical device is not to be used
	Consult instructions for use	Indicates the need for the user to consult the instructions for use
	Caution	Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself
	Storage temperature range	Indicates the temperature limits to which the medical device can be safely exposed
	Keep dry	Indicates a medical device that needs to be protected from moisture
	Unique device identifier	Indicates the manufacturer's device identifier so that a specific medical device can be identified
	Do not re-use	Indicates a medical device that is intended for one use, or for use on a single patient during a single procedure
	Do not resterilize	Indicates a medical device that is not to be resterilized
	Sterilized using irradiation	Indicates a medical device that has been sterilized using irradiation
	Non-pyrogenic	Indicates a medical device that is non-pyrogenic
	Do not use if package is damaged	Indicates a medical device that should not be used if the package has been damaged or opened
Rx Only	Prescription only	Requires prescription in the United States

How to store the EMPAVELI Injector

- Keep the EMPAVELI Injector in unopened tray inside the original box.
- **Do not**open the tray until ready for EMPAVELI injection.
- **Store**the EMPAVELI Injector unit in clean, dry area away from heat and sunlight, at a temperature between 36°F to 86°F (2°C to 30°C).
- **Use**the EMPAVELI Injector where the temperature is between 41°F to 104°F (5°C to 40°C).



Questions and answers

Can I use more than 1 syringe to fill the EMPAVELI Injector?

No, use only 1 syringe per EMPAVELI Injector.

What should I do if the syringe plunger will not push down to fill the EMPAVELI Injector?

You must firmly press down on the plunger to fill the EMPAVELI Injector. It will feel like there is resistance.

Can I remove the EMPAVELI Injector from my stomach and put it on later to finish injection?

No. The EMPAVELI Injector cannot be reattached. If you take it off, you may not get your full dose.

How long should the injection take?

The injection time is approximately 30 to 60 minutes.

If the button has not popped out after 2 hours (120 minutes), press and hold the button while you remove the EMPAVELI Injector from your skin.

⚠ **Do not**touch the bottom of the EMPAVELI Injector as the needle will be exposed. Set the EMPAVELI Injector aside and call ApellisAssist at 1-866-MY-APL-ASSIST (1-866-692-7527).

What if the Button will not push in and lock?

Make sure that you have taken off the Red Safety Tab. If the Red Safety Tab is removed, make sure you have tried to push the Button in all the way. If you still cannot push the button all the way in, then the EMPAVELI Injector is damaged. Remove your EMPAVELI Injector and set aside. Open a new EMPAVELI Injector and start over. Call ApellisAssist at 1-866-MY-APL-ASSIST (1-866-692-7527).

What if the EMPAVELI Injector falls off of my body?

If the EMPAVELI Injector falls off of your body, pick it up carefully. Do not touch the needle or any medicine that may be on the EMPAVELI Injector. Set the EMPAVELI Injector aside and out of the reach of children. Call ApellisAssist at 1-866-MY-APLASSIST

(1-866-692-7527) right away.

Is it normal for skin to be bumpy or irritated during an injection?

No. Your body may be sensitive to the adhesive on the EMPAVELI Injector or to the medicine. Call your healthcare provider right away.

Is it normal for skin to be red after an injection?

Your skin may be slightly red after adhesive removal. If the redness does not go away after 1-2 days, call your healthcare provider.

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

Manufactured by:
Enable Injections, Inc. 2863 E. Sharon Road Cincinnati, OH 45421, USA
10130600 Rev 04

Patent: EnableInjections.com/patent

This Instructions for Use has been approved by the U.S. Food and Drug Administration.
Issued: 09/2023

EMP INJ-IFU-29Sep2023-1.0

PRINCIPAL DISPLAY PANEL - 1,080 mg/20 mL Vial Carton

NDC 73606-010-01

EMPAVELI ®
(pegcetacoplan)
Injection

1,080 mg/20 mL
(54 mg/mL)

For Subcutaneous Infusion Only

Dispense the enclosed
Medication Guide to each patient.

One 20 mL Single-Dose Vial.
Discard unused portion.

Rx only
Apellis

PRINCIPAL DISPLAY PANEL - 20 mL Injector Carton

EMPAVELI ®Injector
(pegcetacoplan)

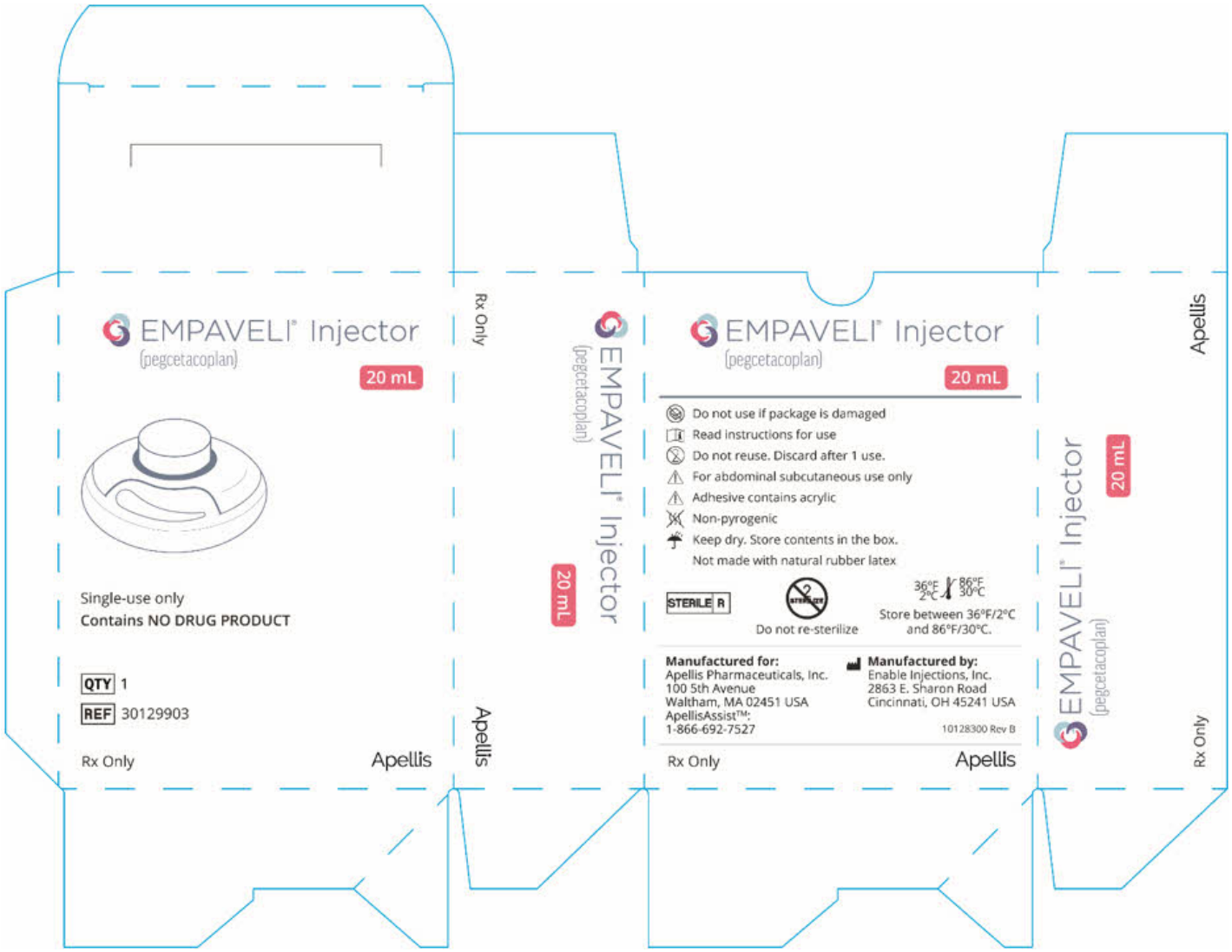
20 mL

Single-use only
Contains NO DRUG PRODUCT

QTY 1

REF 30129903

Rx Only
Apellis



EMPAVELI

pegcetacoplan injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:82454-0010
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
PEGCETACOPLAN (UNII: TO3JYR3BOU) (PEGCETACOPLAN - UNII:TO3JYR3BOU)	PEGCETACOPLAN	1080 mg in 20 mL

Inactive Ingredients	
Ingredient Name	**Strength**
SORBITOL (UNII: 506T60A25R)	820 mg in 20 mL
ACETIC ACID (UNII: Q40Q9N063P)	

SODIUM ACETATE (UNII: 4550K0SC9B)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics			
Color	white	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:82454-0010-1	1 in 1 CARTON	05/14/2021	
1		20 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA215014	05/14/2021	

Labeler - Cenexi HSC (268155718)

Establishment

Name	Address	ID/FEI	Business Operations
Juzen Chemical Corporation		691036974	api manufacture(82454-0010)

Establishment

Name	Address	ID/FEI	Business Operations
Bachem AG		482220311	api manufacture(82454-0010)

Establishment

Name	Address	ID/FEI	Business Operations
Eurofins Lancaster Laboratories, Inc.		069777290	analysis(82454-0010)

Establishment

Name	Address	ID/FEI	Business Operations
Eurofins Advantar Laboratories, Inc.		849636258	analysis(82454-0010)

Establishment

Name	Address	ID/FEI	Business Operations

Cangene BioPharma, LLC		050783398	manufacture(82454-0010)

Establishment

Name	Address	ID/FEI	Business Operations
Nelson Laboratories, LLC		151663234	analysis(82454-0010)

Establishment

Name	Address	ID/FEI	Business Operations
AndersonBrecon Inc		053217022	pack(82454-0010)

Establishment

Name	Address	ID/FEI	Business Operations
Cenexi HSC		268155718	manufacture(82454-0010)