Package leaflet: Information for the user

BEKEMV 300 mg concentrate for solution for infusion
eculizumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What BEKEMV is and what it is used for

What is BEKEMV

BEKEMV contains the active substance eculizumab and it belongs to a class of medicines called monoclonal antibodies. Eculizumab binds to and inhibits a specific protein in the body that causes inflammation and so prevents your body's systems from attacking and destroying vulnerable blood cells or kidneys.

What is BEKEMV used for

Paroxysmal Nocturnal Haemoglobinuria

BEKEMV is used to treat adults and children with a certain type of disease affecting the blood system called Paroxysmal Nocturnal Haemoglobinuria (PNH). In patients with PNH, their red blood cells can be destroyed which can lead to low blood counts (anaemia), tiredness, difficulty in functioning, pain, dark urine, shortness of breath, and blood clots. Eculizumab can block the body's inflammatory response, and its ability to attack and destroy its own vulnerable PNH blood cells.

Atypical Haemolytic Uraemic Syndrome

BEKEMV is also used to treat adults and children with a certain type of disease affecting the blood system and kidney called atypical Haemolytic Uraemic Syndrome (aHUS). In patients with aHUS, their kidney and blood cells, including platelets, can be inflamed which can lead to low blood counts (thrombocytopenia and anaemia), reduced or lost kidney function, blood clots, tiredness and difficulty in functioning. Eculizumab can block the body's inflammatory response, and its ability to attack and destroy its own vulnerable blood and kidney cells.

2. What you need to know before you use BEKEMV

Do not use BEKEMV
- If you are allergic to eculizumab or any of the other ingredients of this medicine (listed in section 6).
- In babies and young children below 2 years of age hereditary fructose intolerance (HFI) may not yet be diagnosed and may be fatal, thus, they must not receive this medicine (see "BEKEMV contains sorbitol").
- If you have not been vaccinated against meningococcal infection unless you take antibiotics to reduce the risk of infection until 2 weeks after you have been vaccinated.
- If you have a meningococcal infection.

Warnings and precautions

Meningococcal and other *Neisseria* infections alert

BEKEMV treatment may reduce your natural resistance to infections, especially against certain organisms that cause meningococcal infection (severe infection of the linings of the brain and sepsis) and other *Neisseria* infections including disseminated gonorrhoea.

Consult your doctor before you take BEKEMV to be sure that you receive vaccination against *Neisseria meningitidis*, an organism that causes meningococcal infection, at least 2 weeks before beginning therapy, or that you take antibiotics to reduce the risk of infection until 2 weeks after you have been vaccinated.

Ensure that your current meningococcal vaccination is up to date. You should also be aware that vaccination may not prevent this type of infection. In accordance with national recommendations, your doctor might consider that you need supplementary measures to prevent infection.

If you are at risk of gonorrhoea, ask your doctor or pharmacist for advice before using this medicine.

Meningococcal infection symptoms

Because of the importance of rapidly identifying and treating certain types of infection in patients who receive BEKEMV, you will be provided a card to carry with you, listing specific trigger symptoms. This card is named: "Patient Safety Card".

If you experience any of the following symptoms, you should immediately inform your doctor:
- headache with nausea or vomiting
- headache with a stiff neck or back
- fever
- rash
- confusion
- severe muscle aches combined with flu-like symptoms
- sensitivity to light

Treatment for meningococcal infection while travelling

If you are travelling in a remote region where you are unable to contact your doctor or in which you find yourself temporarily unable to receive medical treatment, your doctor can make arrangements to issue, as a preventive measure, a prescription for an antibiotic to counter *Neisseria meningitidis* that you keep with you. If you experience any of the symptoms amongst those cited above, you should take the antibiotics as prescribed. You should bear in mind that you should see a doctor as soon as possible, even if you feel better after having taken the antibiotics.

Infections

Before starting BEKEMV, inform your doctor if you have any infections.

Allergic reactions

BEKEMV contains a protein and proteins can cause allergic reactions in some people.

Children and adolescents

Patients less than 18 years of age must be vaccinated against *Haemophilus influenzae* and pneumococcal infections.

Older people

There are no special precautions needed for the treatment of patients aged from 65 years and over.

Other medicines and BEKEMV

Tell your doctor or pharmacist if you are using or have recently used or might use any other medicines.

Pregnancy, breast-feeding, and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Women of childbearing potential

The use of effective contraception during treatment and up to 5 months after treatment should be considered in women who are able to get pregnant.

Driving and using machines

BEKEMV has no or negligible influence on the ability to drive and use machines.

BEKEMV contains sorbitol

This medicine contains 50 mg sorbitol in each mL.

Sorbitol is a source of fructose. If you (or your child) have hereditary fructose intolerance (HFI), a rare genetic disorder, you (or your child) must not receive this medicine. Patients with HFI cannot break down fructose, which may cause serious side effects.

You must tell your doctor before receiving this medicine if you (or your child) have HFI or if your child can no longer take sweet foods or drinks because they feel sick, vomit or get unpleasant effects such as bloating, stomach cramps or diarrhoea.

BEKEMV contains sodium

This medicine contains less than 1 mmol of sodium (23 mg) per dose, that is to say essentially "sodium free".

BEKEMV contains polysorbate 80

This medicine contains 3.0 mg of polysorbate 80 in each vial (30 mL vial), which is equivalent to 0.3 mg/kg or less at the maximum dose for adult patients and paediatric patients with body weight

more than 10 kg, and is equivalent to 0.6 mg/kg or less at the maximum dose for paediatric patients with body weight 5 to < 10 kg. Polysorbates may cause allergic reactions. Tell your doctor if you/your child has any known allergies.

3. How to use BEKEMV

At least 2 weeks before you start treatment with BEKEMV, your doctor will administer a vaccine against meningococcal infection if it was not previously administered or if your vaccination is outdated. If your child is below the age of vaccination or if you are not vaccinated at least 2 weeks before you start treatment with BEKEMV, your doctor will prescribe antibiotics to reduce the risk of infection until 2 weeks after you have been vaccinated.

Your doctor will administer a vaccine to your child aged less than 18 years against *Haemophilus influenzae* and pneumococcal infections according to the national vaccination recommendations for each age group.

Instructions for proper use

The treatment will be given by your doctor or other health care provider by infusing a dilution of the BEKEMV vial from a drip bag through a tube directly into one of your veins. It is recommended that the beginning of your treatments, called the initial phase, will extend over 4 weeks, followed by a maintenance phase.

<u>If you use this medicine to treat PNH</u>

For adults:

- Initial phase:

Every week for the first four weeks, your doctor will administer an intravenous infusion of diluted BEKEMV. Each infusion will consist of a dose of 600 mg (2 vials of 30 mL) and will take 25 - 45 minutes (35 minutes ± 10 minutes).

- Maintenance phase:

- In the fifth week, your doctor will administer an intravenous infusion of diluted BEKEMV at a dose of 900 mg (3 vials of 30 mL) over a 25 – 45 minute (35 minutes ± 10 minutes) period.
- After the fifth week, your doctor will administer 900 mg of diluted BEKEMV every two weeks as a long-term treatment.

<u>If you use this medicine to treat aHUS</u>

For adults:

- Initial phase:

Every week for the first four weeks, your doctor will administer an intravenous infusion of diluted BEKEMV. Each infusion will consist of a dose of 900 mg (3 vials of 30 mL) and will take 25 – 45 minutes (35 minutes ± 10 minutes).

- Maintenance phase:

- In the fifth week, your doctor will administer an intravenous infusion of diluted BEKEMV at a dose of 1,200 mg (4 vials of 30 mL) over a 25 – 45 minute (35 minutes ± 10 minutes) period.
- After the fifth week, your doctor will administer 1,200 mg of diluted BEKEMV every two weeks as a long-term treatment.

For children and adolescents:

Children and adolescents with PNH or aHUS and who are 40 kg weight and over are treated with the adult dosing.

Children and adolescents with PNH or aHUS and who are under 40 kg weight require a lower dose based on how much they weigh. Your doctor will calculate this.

For children and adolescents with PNH or aHUS above 2 years of age and with body weight below 40 kg:

Patient body weight	**Initial phase**	**Maintenance phase**
30 to < 40 kg	600 mg weekly for the first 2 weeks	900 mg at week 3; then 900 mg every 2 weeks
20 to < 30 kg	600 mg weekly for the first 2 weeks	600 mg at week 3; then 600 mg every 2 weeks
10 to < 20 kg	600 mg single dose at week 1	300 mg at week 2; then 300 mg every 2 weeks
5 to < 10 kg	300 mg single dose at week 1	300 mg at week 2; then 300 mg every 3 weeks

Subjects who undergo plasma exchange may receive additional doses of BEKEMV.

Following each infusion, you will be monitored for about one hour. Your doctor's instructions should be carefully observed.

If you receive more BEKEMV than you should

If you suspect that you have been accidentally administered a higher dose of BEKEMV than prescribed, please contact your doctor for advice.

If you forget an appointment to receive BEKEMV

If you forget an appointment, please contact your doctor immediately for advice and see section below "If you stop using BEKEMV".

If you stop using BEKEMV for PNH

Interrupting or ending treatment with BEKEMV may cause your PNH symptoms to come back more severely soon. Your doctor will discuss the possible side effects with you and explain the risks. Your doctor will want to monitor you closely for at least 8 weeks.

The risks of stopping BEKEMV include an increase in the destruction of your red blood cells, which may cause:
- A significant fall in your red blood cell counts (anaemia),
- Confusion or change in how alert you are,
- Chest pain, or angina,
- An increase in your serum creatinine level (problems with your kidneys), or
- Thrombosis (blood clotting).

If you have any of these symptoms, contact your doctor.

If you stop using BEKEMV for aHUS

Interrupting or ending treatment with BEKEMV may cause your aHUS symptoms to come back. Your doctor will discuss the possible side effects with you and explain the risks. Your doctor will want to monitor you closely.

The risks of stopping BEKEMV include an increase in the inflammation of your platelets, which may cause:

- A significant fall in your platelets (thrombocytopenia),
- A significant rise in destruction of your red blood cells,
- Decreased urination (problems with your kidneys),
- An increase in your serum creatinine level (problems with your kidneys),
- Confusion or change in how alert you are,
- Chest pain, or angina,
- Shortness of breath, or
- Thrombosis (blood clotting).

If you have any of these symptoms, contact your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Your doctor will discuss the possible side effects with you and explain the benefits and risks of BEKEMV with you prior to treatment.

The most serious side effect was meningococcal sepsis. If you experience any of the meningococcal infection symptoms (see section 2 Meningococcal and other *Neisseria* infections alert), you should immediately inform your doctor.

If you are not sure what the side effects below are, ask your doctor to explain them to you.

Very common (may affect more than 1 in 10 people)
- headache

Common (may affect up to 1 in 10 people)
- infection of the lung (pneumonia), common cold (nasopharyngitis), infection of the urinary system (urinary tract infection)
- low white blood cell count (leucopenia), reduction in red blood cells which can make the skin pale and cause weakness or breathlessness
- inability to sleep
- dizziness, high blood pressure
- upper respiratory tract infection, cough, throat pain (oropharyngeal pain), bronchitis, cold sores (herpes simplex)
- diarrhoea, vomiting, nausea, abdominal pain, rash, hair loss (alopecia), itchy skin (pruritus)
- pain in the joints (arms and legs), pain in the limbs (arms and legs)
- fever (pyrexia), feeling tired (fatigue), influenza like illness
- infusion related reaction

Uncommon (may affect up to 1 in 100 people)
- severe infection (meningococcal infection), sepsis, septic shock, viral infection, lower respiratory tract infection, stomach flu (gastrointestinal infection), cystitis
- infection, fungal infection, collection of pus (abscess), type of infection of the skin (cellulitis), influenza, sinusitis, tooth infection (abscess), gum infection
- relatively few platelets in blood (thrombocytopenia), low level of lymphocytes a specific type of white blood cells (lymphopenia), feeling your heartbeat
- serious allergic reaction which causes difficulty in breathing or dizziness (anaphylactic reaction), hypersensitivity
- loss of appetite
- depression, anxiety, mood swings, sleep disorder

- tingling in part of the body (paraesthesia), shaking, taste disorders (dysgeusia), fainting
- vision blurred
- ringing in the ears, vertigo
- sudden and rapid development of extremely high blood pressure, low blood pressure, hot flush, vein disorder
- dyspnoea (difficulty breathing), nose bleed, stuffy nose (nasal congestion), throat irritation, runny nose (rhinorrhoea)
- inflammation of the peritoneum (the tissue that lines most of the organs of the abdomen), constipation, stomach discomfort after meals (dyspepsia), abdominal distension
- hives, redness of the skin, dry skin, red or purple spots under the skin, increased sweating, inflammation of the skin
- muscle cramp, muscle aches, back and neck pain, bone pain
- kidney disorder, difficulties or pain when urinating (dysuria), blood in urine
- spontaneous penile erection
- swelling (oedema), chest discomfort, feeling of weakness (asthenia), chest pain, infusion site pain, chills
- increase of liver enzymes, decrease of the proportion of blood volume that is occupied by red blood cells, decrease in the protein in red blood cells that carries oxygen

Rare (may affect up to 1 in 1,000 people)
- infection by fungi (Aspergillus infection), infection of the joint (arthritis bacterial), *Haemophilus* infection, impetigo, bacterial sexual transmitted disease (gonorrhoea)
- skin tumour (melanoma), bone marrow disorder
- destruction of red blood cells (haemolysis), clumping of cells, abnormal clotting factor, abnormal blood clotting
- disease with thyroid overactivity (Grave's disease)
- abnormal dreams
- irritation of eye
- bruise
- unusual backflow of food from stomach, gum pain
- yellowing of the skin and/or eyes (jaundice)
- skin colour disorder
- spasm of mouth muscle, joint swelling
- menstrual disorder
- abnormal leakage of the infused drug out of the vein, infusion site abnormal sensation, feeling hot

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store BEKEMV

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and vial label after "EXP". The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C). Do not freeze.

BEKEMV vials in the original package may be removed from refrigerated storage **for only one single period of up to 7 days**. At the end of this period the product can be put back in the refrigerator. Store in the original package in order to protect from light. After dilution, the product should be used within 24 hours.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What BEKEMV contains

- The active substance is eculizumab (300 mg/30 mL in a vial corresponding to 10 mg/mL).

- The other ingredients are:
    - acetic acid,
    - sodium hydroxide,
    - disodium edetate (EDTA),
    - sorbitol (E420),
    - polysorbate 80,
    - water for injections.

- BEKEMV contains sorbitol, sodium and polysorbate 80. See section 2.

What BEKEMV looks like and contents of the pack

BEKEMV is presented as a concentrate for solution for infusion (30 mL in a vial – pack size of 1). BEKEMV is a clear to slightly opalescent, colourless to slightly yellow solution.

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Manufacturer
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Instructions for use for healthcare professionals handling BEKEMV

In order to improve the traceability of biological medicinal products, the name and batch number of the administered product should be clearly recorded.

The following information is intended for healthcare professionals only:

1. How is BEKEMV supplied?

Each vial of BEKEMV contains 300 mg of active ingredient in 30 mL of product solution.

2. Before administration

Reconstitution and dilution should be performed in accordance with good practices rules, particularly for the respect of asepsis.

BEKEMV should be prepared for administration by a qualified healthcare professional using aseptic technique.

- Inspect visually BEKEMV solution for particulate matter and discolouration.
- Withdraw the required amount of BEKEMV from the vial(s) using a sterile syringe.
- Transfer the recommended dose to an infusion bag.
- Dilute BEKEMV to a final concentration of 5 mg/mL (initial concentration divided by 2) by adding the appropriate amount of diluent to the infusion bag.
  – For 300 mg doses, use 30 mL of BEKEMV (10 mg/mL) and add 30 mL of diluent.
  – For 600 mg doses, use 60 mL of BEKEMV and add 60 mL of diluent.
  – For 900 mg doses, use 90 mL of BEKEMV and add 90 mL of diluent.
  – For 1,200 mg doses, use 120 mL of BEKEMV and add 120 mL of diluent.
  The final volume of a 5 mg/mL diluted BEKEMV solution is 60 mL for 300 mg doses, 120 mL for 600 mg doses, 180 mL for 900 mg doses or 240 mL for 1,200 mg doses.
- Diluents are sodium chloride 9 mg/mL (0.9%) solution for injection, sodium chloride 4.5 mg/mL (0.45%) solution for injection or 5% dextrose in water.
- Gently agitate the infusion bag containing the diluted BEKEMV solution to ensure thorough mixing of the medicinal product and diluent.
- The diluted solution should be allowed to warm to room temperature [18°C – 25°C] prior to administration by exposure to ambient air.
- The diluted solution must not be heated in a microwave or with any heat source other than the prevailing room temperature.
- Discard any unused portion left in a vial.
- Diluted solution of BEKEMV may be stored at 2°C – 8°C for up to 24 hours prior to administration.

3. Administration

- Do not administer BEKEMV as an intravenous push or bolus injection.
- BEKEMV should only be administered via intravenous infusion.
- The diluted solution of BEKEMV should be administered by intravenous infusion over 25 to 45 minutes (35 minutes ± 10 minutes) in adults and 1 - 4 hours in paediatric patients under 18 years of age via gravity feed, a syringe-type pump, or an infusion pump. It is not necessary to protect the diluted solution of BEKEMV from light during administration to the patient.

The patient should be monitored for one hour following infusion. If an adverse event occurs during the administration of BEKEMV, the infusion may be slowed or stopped at the discretion of the physician. If the infusion is slowed, the total infusion time may not exceed two hours in adults and four hours in paediatric patients under 18 years of age.

4. Special handling and storage

Store in a refrigerator (2°C – 8°C). Do not freeze. Store in the original package in order to protect from light. BEKEMV vials in the original package may be removed from refrigerated storage **for only one single period of up to 7 days**. At the end of this period the product can be put back in the refrigerator.

Do not use this medicine after the expiry date which is stated on the carton and vial label after 'EXP'. The expiry date refers to the last day of that month.