


Biosimilars by Amgen

BEKEMV[®]▼
(eculizumab)

Factsheet -
A guide to
reconstitution,
ordering and
homecare
provision.

A large, decorative graphic on the right side of the page. It features a thick, flowing ribbon that starts as a yellowish-gold color and transitions into a blue color. The ribbon is twisted and loops around itself, creating a sense of movement and depth.

PRODUCT INFORMATION

BEKEMV[®] (eculizumab)^{1,2}

Name of the medicinal product

BEKEMV[®] 300 mg concentrate for solution for infusion

Therapeutic indication of BEKEMV[®]

BEKEMV[®] is indicated in adults and children for the treatment of:

- Paroxysmal nocturnal haemoglobinuria (PNH).
The clinical benefit is demonstrated in patients with haemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history.
- Atypical haemolytic uraemic syndrome (aHUS).

For further details on dosing, special warnings, precautions and adverse events please refer to BEKEMV[®] SmPC at <https://www.medicines.org.uk/emc/product/15378/smpc#about-medicine>

BEKEMV[®] is contraindicated in babies and young children below 2 years of age since they may not yet be diagnosed with hereditary fructose intolerance (HFI). Medicines containing sorbitol/fructose given intravenously may therefore be life-threatening, and are contraindicated in this population (see section 4.4).

Additional Risk Minimisation Materials

Visit <https://www.medicines.org.uk/emc/product/15378/rmms#about-medicine> for additional risk minimisation materials. Here you will find the following : Patient/parent information brochure, Vaccination Certificate, Physician guide, Safety Card.

List of excipients

Acetic acid, Sodium hydroxide, Disodium edetate (EDTA), Sorbitol (E420), Polysorbate 80, Water for injections.

Ingredient sorbitol/Ingredient sorbitol hereditary fructose intolerance (HFI)



This medicine contains 50 mg sorbitol (E420) in each mL. Patients with HFI must not be given this medicine unless strictly necessary.

Babies and young children (below 2 years of age) may not yet be diagnosed with HFI. Medicines (containing sorbitol/fructose) given intravenously may be life-threatening and should be contraindicated in this population (see sections 4.2 and 4.3 of the SmPC).

A detailed history with regard to HFI symptoms has to be taken of each patient prior to being given this medicinal product.



Available single vial pack

DIMENSIONS (mm)

Vial	30.0 x 75.0 (diameter x height)
Box	57.2 x 49.0 x 150.0

Handling Instructions

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 as the medicinal product contains no preservatives.
- Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Method of administration

- Do not administer BEKEMV® as an intravenous push or bolus injection.
- See above for instructions on dilution of the medicinal product before administration.
- 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.

Shelf life and special precautions for storage



Shelf life 36 months.

After dilution, chemical, physical, and microbiological in-use stability has been demonstrated for:

- 96 hours at 2° C to 8° C
- 48 hours at room temperature

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2° C to 8° C, unless dilution has taken place in controlled and validated aseptic conditions.

Special precautions for 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.

If further information is required please contact Amgen Medical Information Department:

Phone: +44 (0)1233 436441

Email: gbinfoline@amgen.com

Vaccination Certificate/proof of antibiotic prophylaxis



The delivery of BEKEMV® is only possible if an Amgen Vaccination Certificate is available showing that the affected patient has been or is being vaccinated against meningococcal infection and/or is receiving antibiotic prophylaxis. The certificate only needs to be submitted once at the time of the first order for all patients.

The supply of BEKEMV® is subject to the requirements of controlled distribution and the completion of a Vaccination and/or antibiotic prophylaxis Certificate is mandatory. Physicians must discuss the benefits and risks of treatment with BEKEMV® with patients and provide them with a patient information brochure and a patient safety card. These are available at:

www.medicines.org.uk/emc/product/15378/rmms#about-medicine.

The Vaccination Certificate should be completed and an existing patient code, for example the patients NHS number OR Blueteq number must be entered.

How to order BEKEMV[®] Direct to Hospital

Vaccination Certificate/proof of antibiotic prophylaxis

First orders of BEKEMV[®] can only be processed if a fully completed signed and dated Vaccination/antibiotic prophylaxis Certificate has been provided by the prescriber. The certificate only needs to be submitted once at the time of the first order for **all** patients.

First order of BEKEMV[®].

A fully completed and signed Amgen Vaccination Certificate should accompany the first order for BEKEMV[®](eculizumab).

Link to Vaccination Certificate - <https://www.medicines.org.uk/emc/rmm/2884/Document>

NB: A patient code – e.g a patient's NHS number or Blueteq number is required for all initial and subsequent orders.

It will not be possible to release BEKEMV[®] until a fully completed Vaccination Certificate is received. Any incomplete Vaccination Certificate will be returned to the customer for completion before an order can be processed.

Orders should be placed via Amgen UK & Ireland Customer Service:

E-mail: cs-uk@amgen.com

Tel: 020 3024 0072

Hours: 8:30am - 16:30pm (Mon - Fri)

Please place all BEKEMV[®] orders as a separate order. Do not include any other products in this order to avoid any potential delays to those other products.

Please ensure orders are received by Amgen by 14:00pm, This will allow the Customer Service team to verify that all documentation requirements have been completed. (A fully completed Purchase Order containing the patient code and a fully completed Vaccination Certificate).

We endeavour to deliver all validated BEKEMV[®] orders placed by 14:00pm on the next working day, please however allow 2 working days when ordering.

Subsequent orders of BEKEMV[®] direct to hospital

Any subsequent orders of BEKEMV[®] must always contain the patient code.

This patient code must always match the code that was included on the original vaccination certificate.

Orders should be placed via Amgen UK & Ireland Customer Service:

E-mail: cs-uk@amgen.com

Tel: 020 3024 0072

Hours: 8:30am - 16:30pm (Mon - Fri)

Please ensure orders are received by Amgen by 14:00pm, This will allow the Customer Service team to verify that all documentation requirements have been completed. (A fully completed Purchase Order containing the patient code and a fully completed Vaccination Certificate).

We endeavour to deliver all validated BEKEMV[®] orders placed by 14:00pm on the next working day, please however allow 2 working days when ordering.

It is not possible to place routine orders for BEKEMV[®] via Electronic Data Interchange (EDI).

The first order of BEKEMV[®] has to have Amgen approved Vaccination Certificate.



How to transition a BEKEMV[®] (eculizumab) patient into Homecare

BEKEMV[®] may also be delivered and administered to the patients via Homecare companies. Home infusion may be considered for patients who have tolerated infusions well in the hospital. The decision of a patient to receive home infusions should be made after evaluation and recommendation from the treating physician.

Please refer to section 4.2 of the SmPC for more information on BEKEMV[®].
<https://www.medicines.org.uk/emc/product/15378/smpc#about-medicine>

To refer patients into Homecare here are the requirements for enrollment.

- 1 Homecare registration form
- 2 The BEKEMV[®] prescription form
- 3 A **copy** of the original Amgen Vaccination Certificate that was sent to AMGEN at point of first order.

Contact details

For questions or additional information regarding the use of BEKEMV[®], please contact Amgen Medical Information Department:

+44 (0)1223 436441 or E-mail : gbinfoline@amgen.com

BEKEMV® (eculizumab) Brief Prescribing Information

Please refer to the Summary of Product Characteristics (SPC) before prescribing BEKEMV. **Pharmaceutical Form:** One vial of 30 mL containing 300 mg eculizumab (10 mg/mL). **Indication:** BEKEMV is indicated in adults and children for the treatment of: Paroxysmal nocturnal haemoglobinuria (PNH). Evidence of clinical benefit is demonstrated in patients with haemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history; Atypical haemolytic uraemic syndrome (aHUS). **Dosage:** In Paroxysmal nocturnal haemoglobinuria: Adult patients (≥ 18 years of age) Initial phase: 600 mg weekly for the first 4 weeks; maintenance phase: 900 mg week 5, followed by 900 mg every 14 (± 2) days In Atypical haemolytic uraemic syndrome: Adult patients (≥ 18 years of age) Initial phase: 900 mg weekly for the first 4 weeks; maintenance phase: 1,200 mg week 5, followed by 1,200 mg every 14 (± 2) days Paediatric patients (above 2 years of age) with PNH or aHUS ≥ 40 kg initial and maintenance phases: treated with the adult dosing recommendations. **30 to <40 kg initial phase:** 600 mg weekly for the first 2 weeks; maintenance phase: 900 mg at week 3; then 900 mg every 2 weeks. **20 to <30 kg initial phase:** 600 mg weekly for the first 2 weeks; maintenance phase: 600 mg at week 3; then 600 mg every 2 weeks. **10 to <20 kg initial phase:** 600 mg weekly x 1; maintenance phase: 300 mg at week 2; then 300 mg every 2 weeks. **5 to <10 kg initial phase:** 300 mg weekly x 1; maintenance phase: 300 mg at week 2; then 300 mg every 3 weeks. For adult and paediatric aHUS patients above 2 years of age supplemental dosing of BEKEMV is required in the setting of concomitant PE/PI (plasmapheresis or plasma exchange, or fresh frozen plasma infusion) - please see SPC for dosing details. **Administration:** Dilute to a concentration of 5 mg/mL, see SPC for further information on administration and diluents. Administer via an intravenous infusion over 25 – 45 minutes (35 minutes \pm 10 minutes) in adults and 1-4 hours in paediatric patients via gravity feed, a syringe-type pump, or an infusion pump. Patients should be monitored for 1 hour post infusion. **Elderly:** No evidence to suggest that special precautions are required, although experience is limited. **Renal impairment:** No dose adjustment. **Hepatic impairment:** The safety and efficacy have not been studied in patients with hepatic impairment. **Contraindications:** Hypersensitivity to eculizumab or to any of the excipients listed in the SPC. BEKEMV is contraindicated in babies and young children below 2 years of age since they may not yet be diagnosed with hereditary fructose intolerance (HFI). Medicines containing sorbitol/fructose given intravenously may therefore be life-threatening, and are contraindicated in this population. Must not initiate therapy in patients with unresolved *Neisseria meningitidis* infection or patients who are not currently vaccinated against *Neisseria meningitidis* (unless they receive prophylactic treatment with appropriate antibiotics until 2 weeks after vaccination). **Special warnings and precautions:** BEKEMV is not expected to affect the aplastic component of anaemia in patients with PNH. **Meningococcal infection:** Increased risk of

meningococcal infection. All patients must be vaccinated against meningococcal infections at least 2 weeks prior to receiving BEKEMV unless the risk of delaying BEKEMV therapy outweighs the risks of developing a meningococcal infection. Patients initiated with BEKEMV less than 2 weeks after receiving a meningococcal vaccine must receive treatment with appropriate prophylactic antibiotics until 2 weeks after vaccination. Vaccines against serogroups A, C, Y, W135 and B where available are recommended in preventing the commonly pathogenic meningococcal serogroups. Patients must receive vaccination according to current national vaccination guidelines. Vaccination may further activate complement. As a result, patients with complement-mediated diseases, including PNH and aHUS may experience increased signs and symptoms of their underlying disease, such as haemolysis (PNH) or thrombotic microangiopathy (TMA) (aHUS). Therefore, patients should be closely monitored for disease symptoms after recommended vaccination. Vaccination may not be sufficient to prevent meningococcal infection. Consideration should be given to official guidance on the appropriate use of antibacterial agents. Cases of serious or fatal meningococcal infections have been reported. All patients should be monitored for early signs of meningococcal infections and evaluated immediately if infection is suspected and treated with appropriate antibiotics if necessary. Patients should be informed of signs and symptoms of infection and steps taken to seek medical care immediately. Physicians must discuss the benefits and risks of BEKEMV therapy with patients and provide them with a patient information brochure and a patient safety card. **Other systemic infections:** Use with caution in patients with active systemic infections. Patients may have increased susceptibility to infections, especially with *Neisseria* and encapsulated bacteria. Serious infections with *Neisseria species* (other than *Neisseria meningitidis*), including disseminated gonococcal infections, have been reported. Patients should be provided with information from the package leaflet to increase their awareness of potential serious infections and the signs and symptoms of them. Physicians should advise patients about gonorrhoea prevention. **Infusion reactions:** Administration may result in infusion reactions or immunogenicity that could cause allergic or hypersensitivity reactions, including anaphylaxis. Anaphylactic reaction has been reported as an uncommon side effect ($\geq 1/1000$ to $< 1/100$). BEKEMV treatment should be interrupted in all patients who experience severe infusion reactions and appropriate medical therapy administered. **Immunogenicity:** Infrequent antibody responses have been detected in eculizumab-treated patients across all clinical studies. **Immunisation:** Prior to initiating BEKEMV therapy, it is recommended that PNH and aHUS patients initiate immunisations according to current immunisation guidelines. Patients less than 18 years of age must be vaccinated against *Haemophilus influenzae* and pneumococcal infections, and strictly need to adhere to the national vaccination recommendations for each age

group. **Anticoagulant therapy:** Treatment with BEKEMV should not alter anticoagulant treatment. **PNH laboratory monitoring:** Patients should be monitored for signs and symptoms of intravascular haemolysis, including serum lactate dehydrogenase (LDH) levels. PNH patients receiving BEKEMV therapy should be similarly monitored for intravascular haemolysis by measuring LDH levels and may require dose adjustment within the recommended 14 ± 2 day dosing schedule during the maintenance phase (up to every 12 days). **aHUS laboratory monitoring:** Patients should be monitored for signs and symptoms of TMA by measuring platelet counts, serum LDH and serum creatinine, and may require dose adjustment within the recommended 14 ± 2 day dosing schedule during the maintenance phase (up to every 12 days). **Discontinuation for PNH:** Patients who discontinue should be monitored for serious intravascular haemolysis or other reactions for at least 8 weeks. If serious haemolysis occurs, consider: blood transfusion (packed RBCs), or exchange transfusion if the PNH RBCs are $>50\%$ of the total RBCs by flow cytometry; anticoagulation; corticosteroids or reinstatement of BEKEMV. **Discontinuation for aHUS:** Patients who discontinue should be monitored closely for signs and symptoms of severe TMA complications. Monitoring may be insufficient to predict or prevent severe TMA complications after discontinuation of BEKEMV. Severe TMA complications post discontinuation can be identified by (i) any two, or repeated measurement of anyone, of the following: a decrease in platelet count of 25% or more as compared to either baseline or to peak platelet count during BEKEMV treatment; an increase in serum creatinine of 25% or more as compared to baseline or to nadir during BEKEMV treatment; or, an increase in serum LDH of 25% or more as compared to baseline or to nadir during BEKEMV treatment; or (ii) any one of the following: a change in mental status or seizures; angina or dyspnoea; or thrombosis. If severe TMA complications occur after BEKEMV discontinuation, consider reinstatement of BEKEMV treatment, supportive care with PE/PI, or appropriate organ-specific supportive measures including renal support with dialysis, respiratory support with mechanical ventilation or anticoagulation. **Educational materials:** All physicians who intend to prescribe BEKEMV must ensure they are familiar with the physician's guide to prescribing. Physicians must discuss the benefits and risks of BEKEMV therapy with patients and provide them with a patient information brochure and a patient safety card. **Excipients:** This medicine contains 50 mg sorbitol (E420) in each mL. Patients with HFI must not be given this medicine unless strictly necessary. Babies and young children

(below 2 years of age) may not yet be diagnosed with HFI. Medicines containing sorbitol/fructose given intravenously may be life-threatening and should be contraindicated in this population. A detailed history with regard to HFI symptoms has to be taken of each patient prior to being given BEKEMV. BEKEMV contains less than 1 mmol of sodium (23 mg) per dose, that is to say essentially "sodium free". **Traceability:** In order to improve traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. **Interaction with other medicinal products:** No interaction studies have been performed. **Fertility:** The use adequate contraception to prevent pregnancy and for at least 5 months after the last dose should be considered for women of childbearing potential. **Pregnancy:** There are no well controlled studies in pregnant women treated with eculizumab, please refer to the SPC for further information. **Breast-feeding:** Limited data available please refer to the SPC for further information. **Undesirable effects:** In all clinical studies, the most serious adverse reaction was meningococcal sepsis which is a common presentation of meningococcal infections in patients treated with eculizumab. **Very common adverse reactions ($\geq 1/10$):** Headache. **Common adverse reactions ($\geq 1/100$ to $< 1/10$):** pneumonia, upper respiratory tract infection, bronchitis, nasopharyngitis, urinary tract infection, oral herpes, leucopenia, anaemia, insomnia, dizziness, dysgeusia, hypertension, cough, oropharyngeal pain, diarrhoea, vomiting, nausea, abdominal pain, rash, pruritus, alopecia, arthralgia, myalgia, pyrexia, fatigue, influenza like illness. Please refer to the SPC for a full list of adverse reactions. Other cases of *Neisseria species* have been reported including sepsis with *Neisseria gonorrhoeae*, *Neisseria sicca/subflava*, *Neisseria spp* unspecified. Cases of haemolysis have been reported with missed or delayed eculizumab dose in PNH clinical trials. Cases of TMA complication have been reported in the setting of missed or delayed eculizumab dose in aHUS clinical trials. The most common adverse reaction reported in paediatric PNH patients was headache. **Legal Category:** POM. **Presentation, Basic Cost and Marketing Authorisation Number Great Britain (GB):** BEKEMV 300 mg concentrate for solution for infusion: PLGB 13832/0077– 1 pack of 30mL vial; £3,150. **Marketing Authorisation Holder GB:** Amgen Limited, 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK. Further information is available from Amgen Limited, 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK. BEKEMV is a trademark owned by Amgen Inc. **Date of PI preparation:** January 2024 (Ref: GB-959-1223-80003)

This medicinal product is subject to additional monitoring. Adverse events should be reported. Reporting forms and information can be found at <https://yellowcard.mhra.gov.uk> or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Amgen Limited on +44 (0) 1223 436441.



Electronic Certificate

Version: 0 . 9

Document Number: GB-959-0124-80003

Document Name: Bekemv Fact Sheet UK

Country: Great Britain

Product: BEKEMV

Branding: Branded

Type: GRP Material

Sub Type: Leave Behind

Classification:

Material Intent: Promotional

Expiration Date:

Certification Statement

We certify that the final electronic form of this material is in accordance with the regulations set forth by the health authority (where applicable) for the country of this document, and is a fair and truthful presentation of the facts about the product.

Role	Signature
Latha Krishnamoorthy - Medical Signatory Certification (lkrish01@amgen.com)	Meaning: As the Medical Signatory, I approve this document for use. Date: 25-Apr-2024 16:09:25 GMT+0000
Elaine Forster - Second Signatory Certification (elainef@amgen.com)	Meaning: As the Second Signatory, I approve this document for use. Date: 26-Apr-2024 09:11:53 GMT+0000