Attachment 1: AusPAR - Adakveo - crizanlizumab - Novartis Pharmaceuticals Australia Pty Ltd - PM-2019-05705-1-6 FINAL 16 July 2021. This is the Product Information that was approved with the submission described in this AusPAR. It may have been superseded. For the most recent PI, please refer to the TGA website at <https://www.tga.gov.au/product-information-pi>

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

Australian Product Information – adakveo® (Crizanlizumab) concentrate for intravenous infusion

1. Name of the medicine

Crizanlizumab.

2. Qualitative and quantitative composition

Each 10 mL vial contains 100 mg of crizanlizumab.

Crizanlizumab is a recombinant humanized IgG2 kappa anti-P-selectin monoclonal antibody produced in Chinese Hamster Ovary (CHO) cells.

Excipients with known effect: contains sugars as sucrose, 753 mg per 10 mL vial.

For the full list of excipients, see Section 6.1 List of excipients.

3. Pharmaceutical form

Concentrate for solution for infusion.

4. Clinical particulars

4.1. Therapeutic indications

ADAKVEO is indicated for the prevention of recurrent vaso-occlusive crises in patients aged 16 years and older with sickle cell disease.

4.2. Dose and method of administration

Patients aged 16 years and over

The recommended dose of ADAKVEO is 5 mg/kg administered over a period of 30 minutes by intravenous (IV) infusion at Week 0, Week 2, and every 4 weeks thereafter.

ADAKVEO can be given alone or with hydroxycarbamide (hydroxyurea) (see section 5.1 Pharmacodynamic Properties, Clinical Trials).

Paediatric use (below 16 years)

The safety and efficacy of ADAKVEO in paediatric patients below the age of 16 years have not been established.

Delayed or missed dose

If a dose is missed, ADAKVEO should be administered as soon as possible.

- If ADAKVEO is administered within 2 weeks after the missed dose, dosing should be continued according to the patient's original schedule.

- If ADAKVEO is administered more than 2 weeks after the missed dose, dosing should be continued every 4 weeks thereafter.

Management recommendations for infusion-related reactions

Table 1 summarises recommendations for the management of infusion-related reactions (IRR) (see section 4.4 Special warnings and precautions, infusion related reactions).

Table 1 Recommendations for the management of infusion-related reactions

Severity of Adverse Drug Reaction	Management recommendation
Mild to Moderate IRR	Temporarily interrupt the infusion or reduce the infusion rate Initiate symptomatic treatment* (e.g. paracetamol/acetaminophen or nonsteroidal anti-inflammatory drug (NSAID) and/or antihistamine) For subsequent infusions consider premedication and/or slower infusion rate
Severe IRR	Discontinue treatment with ADAKVEO Institute appropriate therapy *

**Caution should be exercised with corticosteroids in patients with sickle cell disease unless clinically indicated (e.g. treatment of anaphylaxis)*

Method of Administration

ADAKVEO 10 mg/mL concentrate for solution for infusion vials are for single use in one patient only. Discard any residue.

ADAKVEO should be administered by a healthcare professional. ADAKVEO should be diluted before administration with either sodium chloride 0.9% or dextrose 5%, and must be dosed on the basis of body weight. ADAKVEO diluted solution must be administered through a sterile, non-pyrogenic 0.2 micron in-line filter by intravenous (IV) infusion over a period of 30 minutes. It must not be administered as IV push or bolus.

Preparing the infusion

The diluted solution for infusion should be prepared by a healthcare professional using aseptic techniques. The total dose and required volume of ADAKVEO depends on the patient's body weight; 5 mg of crizanlizumab is administered per kg bodyweight.

The volume of ADAKVEO to be used for the preparation of the infusion is calculated according to the following equation:

Figure 1 Volume of ADAKVEO needed for a single administration

$$\text{Volume (mL)} = \frac{\text{Patient's body weight (kg) x prescribed dose} \quad [5 \text{ mg/kg}]}{\text{Concentration of ADAKVEO} \quad [10 \text{ mg/mL}]}$$

1. Obtain the number of vials of ADAKVEO required to deliver the prescribed dose and bring them to room temperature (for a maximum of 4 hours). One vial is needed for every 10 mL of ADAKVEO (see Table 2).

Table 2 Number of vials needed by body weight (kg)

Body weight (kg)	Dose (mg)	Volume (mL)	Vials (n)
40	200	20	2
60	300	30	3
80	400	40	4
100	500	50	5
120	600	60	6

2. Visually inspect the vials.
   - The solution in the vials should be clear to opalescent. Do not use if particles are present in the solution.
   - The solution should be colourless or may have a slight brownish-yellow tint.
3. Withdraw a volume equal to the required volume of ADAKVEO from a 100 mL infusion bag containing either sodium chloride 0.9% or dextrose 5% and discard.
   - No incompatibilities between the diluted ADAKVEO solution and infusion bags composed of polyvinylchloride (PVC), polyethylene (PE) and polypropylene (PP) have been observed.
4. Withdraw the necessary volume of ADAKVEO from the vials and inject slowly into the previously prepared infusion bag.
   - The solution must not be mixed or co-administered with other drugs through the same intravenous line.
   - Keep the volume of ADAKVEO added to the infusion bag in the range of 10 mL to 96 mL.
5. Mix the diluted solution by gently inverting the infusion bag. DO NOT SHAKE.
6. Discard any unused ADAKVEO.

After administration of ADAKVEO, flush the line with at least 25 mL sodium chloride 0.9% or dextrose 5%.

Storage of the diluted solution

The diluted solution for infusion should be administered as soon as possible.

If not administered immediately, store the prepared solution either:

- At room temperature up to 25°C for no more than 4.5 hours from the start of the preparation to completion of the infusion.

- Under refrigeration at 2°C to 8°C for no more than 24 hours from the start of the preparation to completion of the infusion. This includes the storage of the diluted solution at 2°C to 8°C and the time to warm up at room temperature.

4.3. CONTRAINDICATIONS

ADAKVEO is contraindicated in patients with hypersensitivity to crizanlizumab or to any of the excipients.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Infusion related reactions

In clinical studies, infusion-related reactions (defined as occurring during/within 24 hours) were observed in 3 (2.7%) patients treated with ADAKVEO 5 mg/kg (see section 4.8 Adverse effects (undesirable effects).

In the post-marketing setting, cases of infusion-related reactions including severe pain events were reported, with the majority occurring during the first and second infusions. Some patients also experienced subsequent complications such as acute chest syndrome and fat embolism, particularly those treated with steroids.

Patients should be monitored for and advised of signs and symptoms of infusion-related reactions which may include pain in various locations, headache, fever, chills, nausea, vomiting, diarrhoea, fatigue, dizziness, pruritus, urticaria, sweating, shortness of breath or wheezing.

In the event of severe reactions, ADAKVEO should be discontinued and appropriate therapy should be instituted (see section 4.2 Dose and method of administration).

For management recommendations of a mild or moderate infusion-related reaction (see section 4.2 Dose and method of administration).

Caution should be exercised with corticosteroids in patients with sickle cell disease unless clinically indicated (e.g. treatment of anaphylaxis).

Paediatric use (below 16 years)

The safety and efficacy of ADAKVEO in paediatric patients below the age of 16 years have not been established.

Use in hepatic impairment

No studies have been performed in patients with hepatic impairment (see section 5.2 Pharmacokinetic properties).

Use in renal impairment

No studies have been performed in patients with renal impairment (see section 5.2 Pharmacokinetic properties).

Use in the elderly

No studies have been performed in patients 65 years of age or above.

Effects on laboratory tests

Automated platelet counts: Interference with automated platelet counts (platelet clumping) has been observed in patients treated with ADAKVEO in clinical studies, in particular when tubes containing EDTA (ethylenediaminetetraacetic acid) were used. This may lead to unevaluable or falsely decreased platelet counts. There is no evidence that ADAKVEO causes a reduction in circulating platelets or has a pro-aggregant effect *in vivo.*

To mitigate the potential for laboratory test interference, it is recommended to run the test as soon as possible (within 4 hours of blood collection) or use citrate tubes. When needed, platelet counts can be estimated via a peripheral blood smear.

4.5. Interactions with other medicines and other forms of interactions

Interactions between crizanlizumab and other medicinal products have not been investigated in dedicated studies.

Monoclonal antibodies are not metabolized by cytochrome P450 (CYP450) enzymes. Therefore, medicinal products that are substrates, inhibitors or inducers of CYP450 are not expected to affect the pharmacokinetics of crizanlizumab. In clinical studies, hydroxycarbamide (hydroxyurea) had no effect on crizanlizumab pharmacokinetics in patients.

No effect on exposure of co-administered medicinal products is expected based on the metabolic pathways of monoclonal antibodies.

4.6. Fertility, pregnancy and lactation

Effects on fertility

There are no data on the effect of ADAKVEO on human fertility.

In the 26-week repeat-dose toxicity study, cynomolgus monkeys were administered crizanlizumab once every 4 weeks at doses up to 50 mg/kg (at least 13.5 times the human clinical exposure based on AUC in patients with sickle cell disease at 5 mg/kg once every four weeks). There were no adverse effects of crizanlizumab on male and female reproductive organs (organ weights, macroscopic and microscopic evaluations), sperm evaluations (motility, counts, morphology) and female menstrual cycles (number and mean duration) suggesting no effect on fertility under crizanlizumab treatment.

Use in pregnancy – Pregnancy Category B1

There are no adequate and well-controlled studies in pregnant women to inform a product-associated risk. Animal reproduction studies in cynomolgus monkeys have not shown a risk of increased fetal abnormalities. However, an increased incidence in fetal loss (abortions/still births) at doses approximately 2.8 times the exposure at the recommended clinical dose at 5 mg/kg/dose once every 4 weeks likely secondary to anti-drug antibody formation was observed (see Animal data). The potential risk to humans is unknown. As there is no adequate experience in pregnant women, ADAKVEO should only be used during pregnancy if the expected benefit to the patient justifies the potential risk to the fetus.

Clinical considerations - Disease-associated maternal and/or embryo/fetal risk

Women with sickle cell disease have an increased risk of adverse pregnancy outcomes for the mother and the fetus. Increased risks for intrauterine growth restriction, perinatal mortality and

low birthweight have been reported. Women with sickle cell disease are at higher risk for pre-eclampsia, eclampsia, maternal mortality, stillbirth, preterm delivery and small-for-gestational-age infants.

Animal Data

In an enhanced pre- and postnatal development study in cynomolgus monkeys, pregnant animals received intravenous administration of crizanlizumab once every two weeks during the period of organogenesis at doses up to 50 mg/kg (approximately 16 times the human clinical exposure based on AUC in patients with sickle cell disease at 5 mg/kg/dose once every four weeks). No maternal toxicity was observed. There was an increase in fetal loss (abortions or still births) which was higher in the third trimester at crizanlizumab doses resulting in ≥ 2.8 times the exposure (based on AUC) in patients with sickle cell disease at 5 mg/kg/dose once every 4 weeks. These effects may be due to anti-drug antibody formation in affected animals. There were no effects on infant growth and development through 6-months postpartum that were attributable to crizanlizumab.

Measurable crizanlizumab serum concentrations were observed in the infant monkeys at postnatal day 28, confirming that crizanlizumab, like other IgG antibodies, crosses the placental barrier.

Use in lactation.

It is not known if crizanlizumab is transferred into human milk after administration of ADAKVEO. There are no data on the effects of crizanlizumab on the breastfed child or on milk production.

Because many medicinal products, including antibodies, can be transferred into human milk, a risk to the newborns/infants cannot be excluded.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ADAKVEO and any potential adverse effects on the breastfed newborn/infant from ADAKVEO or from the underlying maternal condition.

4.7. Effects on ability to drive and use machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8. Adverse effects (Undesirable effects)

The safety of ADAKVEO has been evaluated in 175 patients with sickle cell disease (any genotype including HbSS, HbSC, Hbbeta0-thalassemia, and Hbbeta+-thalassemia) in two studies: the pivotal study, SUSTAIN, a 52-week, randomized, double-blind, placebo-controlled study (N=66 at 5 mg/kg and N=64 at 2.5 mg/kg), and a single arm, open label pharmacokinetics/pharmacodynamics and safety study (N=45 at 5 mg/kg). Among the 111 patients exposed to the recommended dose (5 mg/kg), the median (min-max) duration of exposure was 54 weeks (4 to 90 weeks). Seventy-five (75) of the 111 patients (68%) were treated in combination with hydroxycarbamide (hydroxyurea). Use of ADAKVEO in combination with hydroxycarbamide (hydroxyurea) did not result in any meaningful differences in safety profile.

The most frequently reported adverse drug reactions (≥10% of patients) in the ADAKVEO 5 mg/kg group were arthralgia, nausea, back pain, pyrexia and abdominal pain. These adverse drug reactions, along with myalgia, musculoskeletal chest pain, and diarrhoea, may be signs and

symptoms of an infusion related reaction when observed during/within 24 hours of an infusion. The majority of the adverse drug reactions were mild to moderate (grade 1 to 2). Severe adverse reactions were observed for pyrexia and arthralgia (1 case each [0.9%], both grade 3).

No discontinuations due to adverse drug reactions were reported with ADAKVEO 5 mg/kg.

Tabulated summary of adverse drug reactions from clinical studies

Adverse drug reactions from clinical studies (Table 3) are listed by MedDRA system organ class. Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is based on the following convention (CIOMS III): very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000).

Table 3: Percentage of patients with adverse drug reactions in clinical studies

Adverse Drug Reactions	SUSTAIN ADAKVEO 5 mg/kg N=66 n(%)	SUSTAIN Placebo N=62 n(%)	Safety pool ADAKVEO 5 mg/kg N=111 n(%)	Frequency* category
Respiratory, thoracic and mediastinal disorders				
Oropharyngeal pain	4 (6.1)	1 (1.6)	5 (4.5)	common
Gastrointestinal disorders				
Nausea	12 (18.2)	7 (11.3)	18 (16.2)	very common
Abdominal pain**	8 (12.1)	3 (4.8)	12 (10.8)	very common
Diarrhoea	7 (10.6)	2 (3.2)	10 (9.0)	common
Vomiting	5 (7.6)	3 (4.8)	7 (6.3)	common
Skin and subcutaneous tissue disorders				
Pruritus**	5 (7.6)	4 (6.5)	8 (7.2)	common
Musculoskeletal and connective tissue disorders				
Back pain	10 (15.2)	7 (11.3)	16 (14.4)	very common
Arthralgia	12 (18.2)	5 (8.1)	19 (17.1)	very common
Musculoskeletal chest pain	5 (7.6)	0 (0.0)	5 (4.5)	common
Myalgia	5 (7.6)	0 (0.0)	6 (5.4)	common
General disorders and administration site conditions				
Pyrexia	7 (10.6)	4 (6.5)	16 (14.4)	very common
Infusion site reaction**	1 (1.5)	1 (1.6)	3 (2.7)	common
Injury, poisoning and procedural complications				
Infusion-related reaction	2 (3.0)	0 (0.0)	3 (2.7)	common

**Frequency from safety pool (SUSTAIN + A2202) at 5 mg/kg*

***The following groupings (in bold) contain the following MedDRA preferred terms*

***Abdominal pain**: abdominal pain, abdominal pain upper, abdominal pain lower, abdominal discomfort and abdominal tenderness*

***Pruritus**: pruritus and vulvovaginal pruritus*

***Infusion site reaction**: Infusion site extravasation, infusion site pain and infusion site swelling*

Post-marketing experience

The following adverse drug reactions have been derived from post-marketing experience with ADAKVEO via spontaneous case reports and literature cases. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency which is therefore categorized as not known.

General disorders and administration site conditions: Pain (*pain in various locations occurring during/within 24 hours of the infusion (e.g. potential IRR) (see section 4.4 Special warnings and precautions).*

Description of Selected Adverse Reactions

Immunogenicity

In clinical studies, treatment-induced anti-crizanlizumab antibodies were transiently detected in 1 patient among the 111 patients (0.9%) who received ADAKVEO 5mg/kg.

There was no evidence of altered pharmacokinetics or safety profile with anti-crizanlizumab-antibody development.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

Overdose

No cases of overdose have been reported in clinical studies.

General supportive measures and symptomatic treatment should be initiated in cases of suspected overdose.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. Pharmacological properties

5.1 Pharmacodynamic properties

Mechanism of action

Crizanlizumab is a selective IgG2 kappa humanised monoclonal antibody (mAb) that binds to P-selectin with high affinity and blocks the interaction with its ligands including P-selectin glycoprotein ligand 1 (PSGL-1). Crizanlizumab can also dissociate preformed P-selectin/PSGL-1 complex. P-selectin is an adhesion molecule expressed on activated endothelial cells and platelets. It plays an essential role in the initial recruitment of leukocytes and the aggregation of platelets to the site of vascular injury during inflammation.

In the chronic pro-inflammatory state associated with sickle cell disease, P-selectin is over-expressed and circulating blood cells and the endothelium are activated and become hyperadhesive. P-selectin mediated multi-cellular adhesion is a key factor in the pathogenesis of vaso-occlusion and vaso-occlusive crises. Elevated levels of P-selectin are found in patients with sickle cell disease.

Binding P-selectin on the surface of the activated endothelium and platelets has been shown to effectively block interactions between endothelial cells, platelets, red blood cells, and leukocytes, thereby preventing vaso-occlusion.

Pharmacodynamics

Throughout clinical studies, treatment with ADAKVEO resulted in a dose-dependent, immediate and sustained P-selectin inhibition (as measured *ex-vivo*) in patients with sickle cell disease.

Clinical trials

The efficacy of ADAKVEO, with or without hydroxycarbamide (hydroxyurea), was evaluated in the pivotal study SUSTAIN, a 52-week, randomized, placebo-controlled, double-blind, multicentre clinical study in sickle cell disease patients with a history of vaso-occlusive crises (VOCs).

In this study, VOCs were defined as those leading to a healthcare visit, which captured all acute episodes of pain with no other cause than a vaso-occlusive event that required a medical facility visit and treatment with oral or parenteral opioids or parenteral non-steroidal anti-inflammatory drugs (NSAIDs). Acute chest syndrome, hepatic sequestration, splenic sequestration, and priapism (requiring a visit to a medical facility) were also considered VOCs.

A total of 198 sickle cell disease patients aged 16 to 63 years (inclusive), with any sickle cell disease genotype (including HbSS, HbSC, HbSbeta0-thalassemia, HbSbeta+-thalassemia, and others) and a history of between 2 and 10 VOCs in the previous 12 months, were randomized 1:1:1 to ADAKVEO 5 mg/kg, ADAKVEO 2.5 mg/kg, or placebo. The majority of patients were Black or African American (91.9%). Patients received ADAKVEO with or without hydroxycarbamide (hydroxyurea). Randomization was stratified by patients already receiving hydroxycarbamide (hydroxyurea) (Y/N) and by number of VOCs in the previous 12 months (2 to 4, 5 to 10). Among the patients that received the recommended dose (5 mg/kg), forty-two (64%) patients were treated with ADAKVEO in combination with hydroxycarbamide (hydroxyurea). Patients were allowed to take pain medications (i.e. paracetamol, NSAIDs and opioids) and to receive occasional transfusions on an as needed basis.

Patients with sickle cell disease who received ADAKVEO 5 mg/kg had a lower median annual rate of VOC compared to patients who received placebo (1.63 vs. 2.98; Hodges-Lehmann, median absolute difference of -1.01 compared with placebo, 95% CI [-2.00, 0.00]) which was statistically significant (p = 0.010). The VOCs occurring during the study were assessed by an independent review committee.

Main efficacy outcomes of the pivotal SUSTAIN study are summarized in Tables 4.

Table 4 Results from SUSTAIN clinical study in sickle cell disease

Event	**Hodges-Lehmann median difference** (95% CI)	**p-value** (Wilcoxon Rank Sum)
Primary endpoint		
Annual rate of VOC	-1.01 (-2.00, 0.00)	0.010
Secondary endpoints		
Annual rate of days hospitalized	0.00 (-4.36, 0.00)	0.450

In the ADAKVEO 5 mg/kg group, clinically significant reductions in the annual rate of VOC were observed in subgroups given hydroxycarbamide (hydroxyurea)/ no hydroxycarbamide (hydroxyurea): HL median difference from -1 VOC compared to placebo per year for both subgroups. Clinically significant reductions were also observed in subgroups by, genotype (HbSS and non- HbSS) and in patients having fewer (2 - 4 events) or more (5 – 10) VOC events in the preceding year.

A greater than two-fold increase in the proportion of patients with no VOC was observed in the ADAKVEO 5 mg/kg group compared to placebo (36% vs 17%; odds ratio (95% CI): 2.85 (1.24, 6.56)). A similar difference was also observed across important subgroups (hydroxycarbamide (hydroxyurea) use, genotype).

Treatment with ADAKVEO 5 mg/kg was also associated with a three-fold longer Kaplan-Meier estimated median time to first VOC compared with placebo (4.07 vs 1.38 months) and a two-fold longer median time from randomization to second VOC compared to placebo (10.32 vs 5.09 months).

5.2 Pharmacokinetic properties

Absorption

Crizanlizumab is administered intravenously. The median time to reach maximum serum concentration of crizanlizumab (Tmax) was 1.63 hours at steady state following an intravenous administration of 5 mg/kg over a period of 30 minutes in sickle cell disease patients.

Distribution

Since crizanlizumab is a humanized monoclonal antibody, its distribution is typical of endogenous human antibodies within the vascular and extracellular spaces. The volume of distribution (Vz) was 4.26 L after a single 5 mg/kg intravenous infusion of crizanlizumab in healthy volunteers.

Biotransformation/Metabolism

Antibodies are primarily eliminated via proteolysis by lysosomal enzymes in the liver to small peptides and amino acids.

Excretion

In healthy volunteers, the mean terminal elimination half-life (T1/2) was 10.6 days and the mean clearance was 11.7 mL/hr at crizanlizumab dose level 5 mg/kg. In patients with sickle cell disease, the mean elimination T1/2 during dosing interval was 7.6 days. There was no indication of accelerated clearance or time-dependent change in the pharmacokinetic properties of crizanlizumab following repeated administration.

Linearity/non-linearity

The exposure to crizanlizumab (mean Cmax, AUClast, or AUCinf) increased in non-linear manner over the dose range of 0.2 to 8 mg/kg in healthy volunteers.

Special populations

Renal/hepatic impairment

No dedicated studies have been performed to investigate the pharmacokinetics of crizanlizumab in patients with renal or hepatic impairment, since the kidneys and the liver are not a major organ for monoclonal antibody metabolism or excretion.

Paediatric patients below 16 years

Pharmacokinetics in paediatric patients below the age of 16 years have not been investigated.

5.3 Preclinical safety data

Non-clinical data revealed no hazard for humans based on tissue cross-reactivity testing, safety pharmacology and repeated dose studies.

Genotoxicity

Formal genotoxicity studies have not been conducted with crizanlizumab. As a large protein molecule, crizanlizumab is not expected to interact directly with DNA or other chromosomal material.

Carcinogenicity

Formal carcinogenicity studies have not been conducted with crizanlizumab.

Animal toxicology and/or pharmacology

In the 26-week repeat-dose toxicity study, administration of crizanlizumab in cynomolgus monkeys at dose levels up to 50 mg/kg/dose once every 4 weeks (at least 13.5 times the human clinical exposure based on AUC in patients with sickle cell disease at 5 mg/kg once every four weeks) resulted in minimal to moderate inflammation of the vessels in multiple tissues in 2 of 10 animals.

6. Pharmaceutical particulars

6.1 List of excipients

Sucrose, sodium citrate, citric acid, polysorbate 80, water for injection.

6.2 Incompatibilities

ADAKVEO must not be mixed with other medicinal products.

No incompatibilities have been observed between ADAKVEO and infusion sets composed of polyvinylchloride (PVC), polyethylene (PE-lined PVC), polyurethane, and in-line filter membranes composed of polyethersulfone (PES), polyamide (PA), polysulphone (PSU).

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage

- Store refrigerated at 2°C to 8°C in the original carton to protect from light until time of use.
- Do not freeze.

6.5 Nature and contents of container

Colourless 10 mL glass vial with a chlorobutyl rubber stopper and an aluminium cap with a plastic flip-off disk.

6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical properties

Chemical structure

Crizanlizumab is a high-affinity humanized anti-human-P-selectin monoclonal antibody that belongs to the IgG2a/ κ isotype subclass. It is expressed in a Chinese hamster ovary (CHO) cell line (CHO-C8TD) and consists of two heavy chains and two light chains. Both heavy chains of crizanlizumab contain oligosaccharide chains linked to the protein backbone at Asn298.

CAS number

1690318-25-2

7. Medicine schedule (Poisons Standard)

Prescriptions Only Medicine (S4)

8. Sponsor

Novartis Pharmaceuticals Australia Pty Limited

ABN 18 004 244 160

54 Waterloo Road

Macquarie Park NSW 2113

Telephone 1 800 671 203

Web site: www.novartis.com.au

® = Registered Trademark

9. Date of first approval

8 April 2021

10. Date of revision

NA

Internal document code: ada060421i based on CDS 8 January 2021