

Every vial tells a story

A guide to dosing and administering EPOGEN®



Not actual size.

Indication

EPOGEN® (epoetin alfa) is indicated for the treatment of anemia due to chronic kidney disease (CKD) in patients on dialysis to decrease the need for red blood cell (RBC) transfusion.

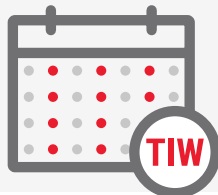
Limitations of Use:

- EPOGEN® has not been shown to improve quality of life, fatigue, or patient well-being.
- EPOGEN® is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia.

Please see Important Safety Information, including **Boxed WARNINGS** about INCREASED RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE, on pages 6 and 7.

INJECTION
EPOGEN[®]
(EPOETIN ALFA)
RECOMBINANT

EPOGEN® is designed with flexible TIW dosing options and IV administration that you control



TIW Administration

Dose and corresponding rise in Hb in 2 weeks with EPOGEN® TIW dosing¹

STARTING DOSE (3 times weekly intravenously)	HEMOGLOBIN INCREASE IN 2 WEEKS
50 Units/kg	0.5 g/dL
100 Units/kg	0.8 g/dL

Data from 13 clinical studies involving IV administration of EPOGEN® to 1010 anemic adult patients on dialysis. Starting doses were 50 to 150 Units/kg TIW. In the 3 largest studies, the median maintenance dose necessary to maintain the Hb between 10 and 12 g/dL was approximately 75 Units/kg TIW.¹

TIW = three times a week

Hb = hemoglobin

Important Safety Information, including Boxed WARNINGS

WARNING: ESAs INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE

Chronic Kidney Disease:

- In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL.
- No trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks.
- Use the lowest EPOGEN® dose sufficient to reduce the need for red blood cell (RBC) transfusions.



EPOGEN® is available in single-dose and multidose vials¹



Multiple dosing options (single-dose vials and multidose vials)¹

- 2,000 Units/mL, 3,000 Units/mL, 4,000 Units/mL, 10,000 Units/mL, 20,000 Units/mL and 20,000 Units/2mL
- Innovative dosing options for precise titration

Dosing information: EPOGEN® (epoetin alfa) for anemia due to CKD

In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered ESAs to target a Hb level of greater than 11 g/dL. No trial has identified a Hb target level, ESA dose, or dosing strategy that does not increase these risks.

Individualize dosing and use the lowest dose of EPOGEN® sufficient to reduce the need for RBC transfusions.

Physicians and patients should weigh the possible benefits of decreasing transfusions against the increased risks of death and other serious cardiovascular adverse reactions.

Considerations

- Correct or exclude other causes of anemia before initiating EPOGEN®¹
- Evaluate the iron status of all patients before and during treatment¹
- Administer supplemental iron therapy if serum ferritin is < 100 mcg/L or serum transferrin saturation is < 20%. The majority of patients with CKD will require supplemental iron during the course of ESA therapy¹
- In pregnant women, lactating women, neonates, and infants, use only single-dose vials (the benzyl alcohol-free formulation). Do not mix EPOGEN® with bacteriostatic saline (which contains benzyl alcohol) when administering to these patients¹
- Appropriately control hypertension prior to initiation of and during treatment with EPOGEN®¹
- Reduce or withhold EPOGEN® if blood pressure becomes difficult to control¹

Please see Important Safety Information, including **Boxed WARNINGS**, on pages 6 and 7.



Initiating and monitoring doses of EPOGEN®

Initiating EPOGEN® for adult patients¹

- Initiate EPOGEN® treatment when the Hb level is < 10 g/dL
- The recommended starting dose for adult patients is 50 to 100 Units/kg TIW intravenously or subcutaneously. The IV route of administration is recommended for patients on hemodialysis

Initiating EPOGEN® for pediatric patients (ages 1 month or older)¹

- Initiate EPOGEN® treatment when the Hb level is < 10 g/dL
- The recommended starting dose for pediatric patients is 50 Units/kg TIW intravenously or subcutaneously. The IV route of administration is recommended for patients on hemodialysis

Monitor and Assess Hb regularly

Following initiation of therapy and after each dose adjustment, monitor Hb at least weekly until the Hb level is stable and sufficient to minimize the need for RBC transfusion. Thereafter, Hb should be monitored at least monthly, provided that Hb levels remain stable.

Important Safety Information (cont'd)

- EPOGEN® is contraindicated in patients with:
 - Uncontrolled hypertension
 - Pure red cell aplasia (PRCA) that begins after treatment with EPOGEN® or other erythropoietin protein drugs
 - Serious allergic reactions to EPOGEN®

Dose adjustments



Dosage adjustments¹

When adjusting therapy, consider Hb rate of rise, rate of decline, ESA responsiveness, and Hb variability.

- A single Hb excursion may not require a dosing change
- Do not increase the dose more frequently than once every 4 weeks
- Decreases in dose can occur more frequently
- Avoid frequent dose adjustments



Reduce or interrupt dose¹

If Hb rises rapidly (eg, more than 1 g/dL in any 2-week period), reduce the dose by 25% or more, as needed, to reduce rapid responses.

- **For adult patients with CKD:** Reduce or interrupt dose if the Hb level approaches or exceeds 11 g/dL
- **For pediatric patients (ages 1 month or older):** Reduce or interrupt dose if the Hb level approaches or exceeds 12 g/dL



Increase dose¹

If the Hb has not increased by more than 1 g/dL after 4 weeks of therapy, increase the dose by 25% when appropriate.

Dosing information (cont'd): Patients who do not respond adequately to EPOGEN®

- For patients who do not respond adequately over a 12-week escalation period, increasing the EPOGEN® dose further is unlikely to improve response and may increase risks¹
- Use the lowest dose that will maintain a Hb level sufficient to reduce the need for RBC transfusions¹
- Evaluate other causes of anemia¹
- If typical causes of lack or loss of Hb response are excluded, evaluate for pure red cell aplasia (PRCA)¹
- Discontinue EPOGEN® if responsiveness does not improve¹

Patients with CKD and an insufficient Hb response to ESA therapy or a rate of Hb rise >1 g/dL over 2 weeks may be at an even greater risk for cardiovascular reactions and mortality than other patients.

Please see Important Safety Information, including **Boxed WARNINGS**, on pages 6 and 7.

Important Safety Information, including BOXED WARNINGS

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Chronic Kidney Disease:

- In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL.
- No trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks.
- Use the lowest EPOGEN® dose sufficient to reduce the need for red blood cell (RBC) transfusions.

Cancer:

- ESAs shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies of patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers.
- To decrease these risks, as well as the risk of serious cardiovascular and thromboembolic reactions, use the lowest dose needed to avoid RBC transfusions.
- Use ESAs only for anemia from myelosuppressive chemotherapy.
- ESAs are not indicated for patients receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
- Discontinue following the completion of a chemotherapy course.

Perisurgery:

- Due to increased risk of Deep Venous Thrombosis (DVT), DVT prophylaxis is recommended.

- EPOGEN® is contraindicated in patients with:
 - Uncontrolled hypertension
 - Pure red cell aplasia (PRCA) that begins after treatment with EPOGEN® or other erythropoietin protein drugs
 - Serious allergic reactions to EPOGEN®
- EPOGEN® from multidose vials contains benzyl alcohol and is contraindicated in neonates, infants, pregnant women, and lactating women.
- Use caution in patients with coexistent cardiovascular disease and stroke.
- Patients with CKD and an insufficient hemoglobin response to ESA therapy may be at even greater risk for cardiovascular reactions and mortality than other patients. A rate of hemoglobin rise of > 1 g/dL over 2 weeks may contribute to these risks.
- In controlled clinical trials, ESAs increased the risk of death in patients undergoing coronary artery bypass graft surgery (CABG) and the risk of deep venous thrombosis (DVT) in patients undergoing orthopedic procedures.
- Control hypertension prior to initiating and during treatment with EPOGEN®.
- EPOGEN® increases the risk of seizures in patients with CKD. Monitor patients closely for new-onset seizures, premonitory symptoms, or change in seizure frequency.

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Important Safety Information (cont'd)

- For lack or loss of hemoglobin response to EPOGEN®, initiate a search for causative factors. If typical causes of lack or loss of hemoglobin response are excluded, evaluate for PRCA.
- Cases of PRCA and of severe anemia, with or without other cytopenias that arise following the development of neutralizing antibodies to erythropoietin have been reported in patients treated with EPOGEN®.
 - This has been reported predominantly in patients with CKD receiving ESAs by subcutaneous administration.
 - PRCA has also been reported in patients receiving ESAs for anemia related to hepatitis C treatment (an indication for which EPOGEN® is not approved).
 - If severe anemia and low reticulocyte count develop during treatment with EPOGEN®, withhold EPOGEN® and evaluate patients for neutralizing antibodies to erythropoietin.
 - Permanently discontinue EPOGEN® in patients who develop PRCA following treatment with EPOGEN® or other erythropoietin protein drugs. Do not switch patients to other ESAs.
- Serious allergic reactions, including anaphylactic reactions, angioedema, bronchospasm, skin rash, and urticaria may occur with EPOGEN®. Immediately and permanently discontinue EPOGEN® if a serious allergic reaction occurs.
- Blistering and skin exfoliation reactions including Erythema multiforme and Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN), have been reported in patients treated with ESAs (including EPOGEN®) in the postmarketing setting. Discontinue EPOGEN® therapy immediately if a severe cutaneous reaction, such as SJS/TEN, is suspected.
- Serious and fatal reactions including “gaspings syndrome” can occur in neonates and infants treated with benzyl alcohol-preserved drugs, including EPOGEN® multiple-dose vials. There is a potential for similar risks to fetuses and infants exposed to benzyl alcohol in utero or in breast-fed milk, respectively.
- Adverse reactions (≥ 5%) in EPOGEN® clinical studies in patients with CKD were hypertension, arthralgia, muscle spasm, pyrexia, dizziness, medical device malfunction, vascular occlusion, and upper respiratory tract infection.

Please see EPOGEN® full [Prescribing Information](#), including **Boxed WARNINGS**, and [Medication Guide](#).

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EPOGEN® vials not shown at actual size. Not all vial sizes shown.



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Please see EPOGEN® full [Prescribing Information](#), including **Boxed WARNINGS**, and [Medication Guide](#).

REFERENCE

1. EPOGEN® (epoetin alfa) Prescribing Information, Amgen.

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