



Every vial tells a story

A guide to dosing, administration, and conversion with Aranesp® in the management of anemia due to CKD in patients on dialysis

CKD = chronic kidney disease.

INDICATION

Aranesp® (darbepoetin alfa) is indicated for the treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis.

LIMITATIONS OF USE

- Aranesp® has not been shown to improve quality of life, fatigue, or patient well-being.
- Aranesp® is not indicated for use as a substitute for red blood cell 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 10 and 11.

injection
 **Aranesp®**
darbepoetin alfa

Flexible dosing options

Convenience of less frequent dosing with QW and Q2W intervals vs TIW dosing¹

QW > Dosing helps individualize anemia management in patients with CKD on HD¹

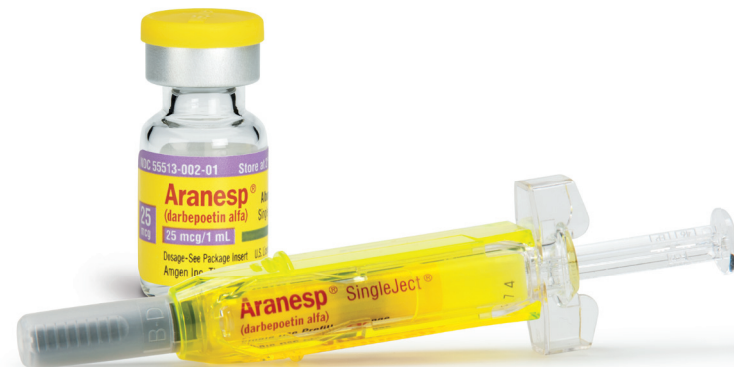
Q2W > Dosing is a convenient option for patients on PD

QW = once weekly; Q2W = once every 2 weeks; TIW = three times weekly; HD = hemodialysis; PD = peritoneal dialysis.

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, Aranesp[®] dose, or dosing strategy that does not increase these risks.
- Use the lowest Aranesp[®] dose sufficient to reduce the need for red blood cell (RBC) transfusions.



Thoughtfully designed administration options

Available in single-dose strength vials and prefilled syringes¹

- Prefilled syringe may reduce the potential for dosing errors²
- UltraSafe[®] Needle Guard is designed to protect from unintentional needlesticks³
- Bar-coded label identifies drug and dose
- No additional wholesale acquisitions cost compared to vials⁴

Please see Important Safety Information, including **Boxed WARNINGS**, on pages 10 and 11.

injection
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Multiple dosing options

Precision dosing with the 10 mcg dose



With the 10 mcg dose strength, doses can be precisely titrated within 5 mcg intervals to individualize treatment^{1,*}

*Except 15 mcg dose.

Aranesp[®] is also available in 150, 200, 300, and 500 mcg dose strengths. The 10, 150, 300, and 500 mcg dose strengths are only available as prefilled syringes.

The IV route of administration is recommended for adult patients on hemodialysis.

IV = intravenous.

IMPORTANT DOSING CONSIDERATIONS

- For patients who do not respond adequately over a 12-week escalation period, increasing the dose further is unlikely to improve response and may increase risks.
- Use the lowest dose that will maintain a hemoglobin (Hb) level sufficient to reduce the need for RBC transfusions.
- For lack or loss of Hb response to Aranesp[®], initiate a search for causative factors. If typical causes of lack or loss of Hb response are excluded, evaluate for pure red cell aplasia (PRCA).

Doses designed for individualized treatment

Multiple dosing options can be combined to individualize treatment of patients¹

	10	20	25	30	35	40	45	50	55
DOSE STRENGTHS (mcg)	10 mcg	10 mcg	25 mcg	10 mcg	10 mcg	40 mcg	10 mcg	25 mcg	10 mcg
		10 mcg		10 mcg	25 mcg		10 mcg	25 mcg	10 mcg
				10 mcg			25 mcg		10 mcg
									25 mcg
DOSE STRENGTHS (mcg)	60	65	70	75	80	85	90	95	100
	60 mcg	25 mcg	10 mcg	25 mcg	40 mcg	25 mcg	25 mcg	10 mcg	100 mcg
		40 mcg	60 mcg	25 mcg	40 mcg	60 mcg	25 mcg	25 mcg	
				25 mcg			40 mcg	60 mcg	

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Conversion from epoetin alfa

Converting your patients with CKD on dialysis from epoetin alfa to QW Aranesp®¹

Use the FDA-approved ESA conversion table in the Aranesp® PI¹

PREVIOUS EPOETIN ALFA DOSE (units/week)	QW ARANESP® STARTING DOSE	
	Adult (mcg/week)	Child (mcg/week)
< 1,500	6.25	*
1,500 to 2,499	6.25	6.25
2,500 to 4,999	12.5	10
5,000 to 10,999	25	20
11,000 to 17,999	40	40
18,000 to 33,999	60	60
34,000 to 89,999	100	100
≥ 90,000	200	200

- The dose conversions depicted above do not accurately estimate the once-monthly dose of Aranesp® in patients with CKD not on dialysis
- Pediatric patients with CKD: Aranesp® safety and efficacy were similar between adults and pediatric patients with CKD when Aranesp® was used for initial treatment of anemia or patients were transitioned from treatment with epoetin alfa to Aranesp®

*For pediatric patients receiving a weekly epoetin alfa dose of < 1,500 units/week, the available data are insufficient to determine an Aranesp® conversion dose.

ESA = erythropoiesis-stimulating agent; PI = prescribing information.

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Conversion examples for adult patients on dialysis¹

PREVIOUS EPOETIN ALFA DOSE		ARANESP® STARTING DOSE
Per administration	Per week	QW
3,000 units/administration	× 3 = 9,000 units/week	25 mcg
4,000 units/administration	× 3 = 12,000 units/week	40 mcg

Aranesp® is administered QW or Q2W¹

- Administer Aranesp® once weekly in patients who were receiving epoetin alfa 2 to 3 times weekly
- Administer Aranesp® once every 2 weeks in patients who were receiving epoetin alfa once weekly
- Maintain the route of administration (intravenous or subcutaneous injection)

IMPORTANT SAFETY INFORMATION

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



Dosing information: Aranesp® for anemia due to CKD

- 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 (Hb) level of greater than 11 g/dL.
- No trial has identified a Hb target level, Aranesp® dose, or dosing strategy that does not increase these risks.
- Individualize dosing and use the lowest dose of Aranesp® sufficient to reduce the need for red blood cell (RBC) transfusions.
- Physicians and patients should weigh the possible benefits of decreasing transfusions against the increased risks of death and other serious cardiovascular adverse events.

CONSIDERATIONS

- Correct or exclude other causes of anemia before initiating Aranesp®.
- Evaluate the iron status in all patients before and during treatment.
- 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 therapy.
- Appropriately control hypertension prior to initiation of and during treatment with Aranesp®.
 - Reduce or withhold Aranesp® if blood pressure becomes difficult to control.

INITIATING ARANESP® FOR ADULT PATIENTS WITH CKD ON DIALYSIS	
<ul style="list-style-type: none"> • Initiate Aranesp® treatment when the Hb level is < 10 g/dL. • QW recommended starting dose: 0.45 mcg/kg as an IV or SC injection once weekly, as appropriate. <ul style="list-style-type: none"> – The IV route of administration is recommended for patients on hemodialysis. 	<ul style="list-style-type: none"> • Q2W recommended starting dose: 0.75 mcg/kg as an IV or SC injection once every 2 weeks, as appropriate.
INITIATING ARANESP® FOR PEDIATRIC PATIENTS (LESS THAN 18 YEARS) WITH CKD	
<ul style="list-style-type: none"> • Initiate Aranesp® treatment when the Hb level is < 10 g/dL. <p>On dialysis and not on dialysis:</p> <ul style="list-style-type: none"> • QW recommended starting dose: 0.45 mcg/kg as an IV or SC injection once weekly, as appropriate. 	

SC = subcutaneous.

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MONITORING	
Following initiation of therapy and after each dose adjustment, monitor Hb at least weekly until the Hb is stable and sufficient to minimize the need for RBC transfusion. <ul style="list-style-type: none"> • Thereafter, Hb should be monitored at least monthly, provided that Hb levels remain stable. 	
DOSE ADJUSTMENTS	
When adjusting therapy, consider Hb rate of rise, rate of decline, ESA responsiveness, and Hb variability. <ul style="list-style-type: none"> – 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 DOSE	INCREASE DOSE
<ul style="list-style-type: none"> • 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. <p>FOR ADULT PATIENTS WITH CKD</p> <ul style="list-style-type: none"> • On dialysis: reduce or interrupt dose if the Hb level approaches or exceeds 11 g/dL. <p>FOR PEDIATRIC PATIENTS (LESS THAN 18 YEARS) WITH CKD</p> <ul style="list-style-type: none"> • If the hemoglobin level approaches or exceeds 12 g/dL, reduce or interrupt the dose of Aranesp®. 	<ul style="list-style-type: none"> • If the Hb has not increased by more than 1 g/dL after 4 weeks of therapy, increase the dose by 25% when appropriate.

Patients who do not respond adequately to Aranesp®

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

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



Important Safety Information including **Boxed WARNINGS**

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Chronic Kidney Disease:

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- No trial has identified a hemoglobin target level, Aranesp® dose, or dosing strategy that does not increase these risks.
- Use the lowest Aranesp® 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.

- Aranesp® is contraindicated in patients with:
 - Uncontrolled hypertension
 - Pure red cell aplasia (PRCA) that begins after treatment with Aranesp® or other erythropoietin protein drugs
 - Serious allergic reactions to Aranesp®
- 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 Aranesp®.
- Aranesp® increases the risk of seizures in patients with CKD. Monitor patients closely for new-onset seizures, premonitory symptoms, or change in seizure frequency.
- For lack or loss of hemoglobin response to Aranesp®, 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 Aranesp®.
 - 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 Aranesp® is not approved).
 - If severe anemia and low reticulocyte count develop during treatment with Aranesp®, withhold Aranesp® and evaluate patients for neutralizing antibodies to erythropoietin.
 - Permanently discontinue Aranesp® in patients who develop PRCA following treatment with Aranesp® 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 Aranesp®. Immediately and permanently discontinue Aranesp® 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 Aranesp®) in the postmarketing setting. Discontinue Aranesp® therapy immediately if a severe cutaneous reaction, such as SJS/TEN, is suspected.
- Adverse reactions (≥ 10%) in Aranesp® clinical studies in patients with CKD were hypertension, dyspnea, peripheral edema, cough, and procedural hypotension.

Please see accompanying Aranesp® full Prescribing Information, including **Boxed WARNINGS** and Medication Guide, in pocket.

injection

 darbepoetin alfa

Aranesp[®] provides multiple dosing options



- Convenience of less frequent dosing with QW and Q2W intervals vs TIW dosing¹
- Prefilled syringes and vials¹
- Ability to titrate doses precisely within 5 mcg intervals^{1,*}

*Except 15 mcg dose.



Visit anemiahub.com for more anemia management tools and resources

Please see Important Safety Information, including **Boxed WARNINGS**, on pages 10 and 11.

Please see accompanying Aranesp[®] full Prescribing Information, including **Boxed WARNINGS** and Medication Guide, in pocket.

References: 1. Aranesp[®] (darbepoetin alfa) prescribing information, Amgen. 2. Adapa RM, Mani V, Murray LJ, et al. Errors during the preparation of drug infusions: a randomized controlled trial. *Br J Anaesth.* 2012;109(5):729-734. 3. UltraSafe[®] Needle Guards [brochure]. Carlsbad, CA: Safety Syringes, Inc.; 2007. 4. Data on file, Amgen; [WAC Pricing; 2020].

AMGEN[®]

Nephrology

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