Behind Aranesp®
are multiple dosing options

A guide to dosing, administration, and conversion with Aranesp® in the management of anemia due to CKD in patients on dialysis¹

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 RECURRENT, on pages 10 and 11.
Convenient dose intervals

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

<table>
<thead>
<tr>
<th>Interval</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>QW</td>
<td>Dosing helps individualize anemia management in patients with CKD on HD</td>
</tr>
<tr>
<td>Q2W</td>
<td>Dosing is a convenient option for patients on PD</td>
</tr>
</tbody>
</table>

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 syringes

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

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

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.*

*Except 15 mcg dose.

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

IV = intravenous.

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Conversion from *epoetin alfa*

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

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

<table>
<thead>
<tr>
<th>PREVIOUS EPOETIN ALFA DOSE (units/week)</th>
<th>QW ARANESP® STARTING DOSE (mcg/week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1,500</td>
<td>6.25</td>
</tr>
<tr>
<td>1,500 to 2,499</td>
<td>6.25</td>
</tr>
<tr>
<td>2,500 to 4,999</td>
<td>12.5</td>
</tr>
<tr>
<td>5,000 to 10,999</td>
<td>25</td>
</tr>
<tr>
<td>11,000 to 17,999</td>
<td>40</td>
</tr>
<tr>
<td>18,000 to 33,999</td>
<td>60</td>
</tr>
<tr>
<td>34,000 to 89,999</td>
<td>100</td>
</tr>
<tr>
<td>≥ 90,000</td>
<td>200</td>
</tr>
</tbody>
</table>

• 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 dialysis

<table>
<thead>
<tr>
<th>PREVIOUS EPOETIN ALFA DOSE</th>
<th>ARANESP® STARTING DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per administration</td>
<td>Per week</td>
</tr>
<tr>
<td>3,000 units/administration</td>
<td>× 3 = 9,000 units/week</td>
</tr>
<tr>
<td>4,000 units/administration</td>
<td>× 3 = 12,000 units/week</td>
</tr>
</tbody>
</table>

Aranesp® is administered QW or Q2W

• 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.

**DOSE ADJUSTMENTS**

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

- **For adult patients with CKD**
  - If the Hb level approaches or exceeds 11 g/dL, reduce or interrupt the dose of Aranesp®.
- **For pediatric patients (less than 18 years) with CKD**
  - If the hemoglobin level approaches or exceeds 12 g/dL, reduce or interrupt the dose of Aranesp®.

**INCREASE DOSE**

- **For adult patients with CKD**
  - If the Hb level approaches or exceeds 11 g/dL, 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 weeks may be at even greater risk for cardiovascular reactions and mortality than other patients.
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 RECURRENTCE

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- 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 D 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 click on the link for the Aranesp® full Prescribing Information including Boxed WARNINGS and Medication Guide.

Links to https://www.pi.amgen.com/-/media/amgen/repositorysites/pi-amgen-com/aranesp/ckd/aranesp_mg_hcp_english.pdf
Aranesp® Provides
Convenient Dosing Intervals

- Convenience of less frequent dosing with QW and Q2W intervals vs TIW dosing
- Prefilled syringes and vials
- Ability to titrate doses precisely within 5 mcg intervals

*Except 15 mcg dose.

Visit anemiahub.com for more anemia management tools and resources

References:
1. Aranesp® (darbepoetin alfa) prescribing information, Amgen.
4. Data on file, Amgen; [WAC Pricing; 2012].

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