RETACRIT is the first and only FDA-approved biosimilar to Epogen®/Procrit® (epoetin alfa) with single- and multiple-dose vials[1-3*†]

INJECTION
Retacrit®
epoetin alfa-epbx
Pfizer

RETACRIT® (epoetin alfa-epbx)

Product Monograph

BUILDING ONTO THE CLINICAL EXPERIENCE OF EPOETIN ALFA

*Biosimilar means that the biological product is approved based on the data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar and the reference product.

†RETACRIT does not have a designation of interchangeability with Epogen/Procrit.

SELECTED SAFETY INFORMATION

WARNINGS: 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

(continued on next page)

Click to view full ISI

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

Indications
Limitations of Use

RETACRIT was granted the same indications as Epogen®/Procrit® (epoetin alfa) by the FDA[1,2]

INDICATIONS

ANEMIA DUE TO CHRONIC KIDNEY DISEASE

RETACRIT is indicated for the treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and not on dialysis, to decrease the need for red blood cell (RBC) transfusion.

ANEMIA DUE TO ZIDOVUDINE IN PATIENTS WITH HIV INFECTION

RETACRIT is indicated for the treatment of anemia due to zidovudine administered at ≤4200 mg/week in patients with HIV infection with endogenous serum erythropoietin levels of ≤500 mUnits/mL.

ANEMIA DUE TO CHEMOTHERAPY IN PATIENTS WITH CANCER

RETACRIT is indicated for the treatment of anemia in patients with nonmyeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of 2 additional months of planned chemotherapy.

REDUCTION OF ALLOGENEIC RED BLOOD CELL TRANSFUSIONS IN PATIENTS UNDERGOING ELECTIVE, NONCARDIAC, NONVASCULAR SURGERY

RETACRIT is indicated to reduce the need for allogeneic RBC transfusions among patients with perioperative hemoglobin >10 to ≤13 g/dL who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery. RETACRIT is not indicated for patients who are willing to donate autologous blood preoperatively.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

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

CHRONIC KIDNEY DISEASE (CONTINUED)

- **Use the lowest RETACRIT® dose sufficient to reduce the need for red blood cell (RBC) transfusions**

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Indications
Limitations of Use

Limitations of use[2]

RETACRIT has not been shown to improve quality of life, fatigue, or patient well-being.

RETACRIT is not indicated for use:

- In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy
- In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure
- In patients with cancer receiving myelosuppressive chemotherapy in whom the anemia can be managed by transfusion
- In patients scheduled for surgery who are willing to donate autologous blood
- In patients undergoing cardiac or vascular surgery
- As a substitute for RBC transfusions in patients who require immediate correction of anemia

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

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

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

(continued on next page)

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RETACRIT is the first and only FDA-approved biosimilar to Epogen®/Procrit® (epoetin alfa) with single- and multiple-dose vials[1-3]

With the largest portfolio of oncology biosimilars—including RETACRIT—Pfizer is committed to expanding options for patient care[3]

Favorable coverage[4]

Potential savings[4]

Support for you and your patients

Pfizer has over 30 years of biologic experience, and more than a decade in the global biosimilars market.[4,5]

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

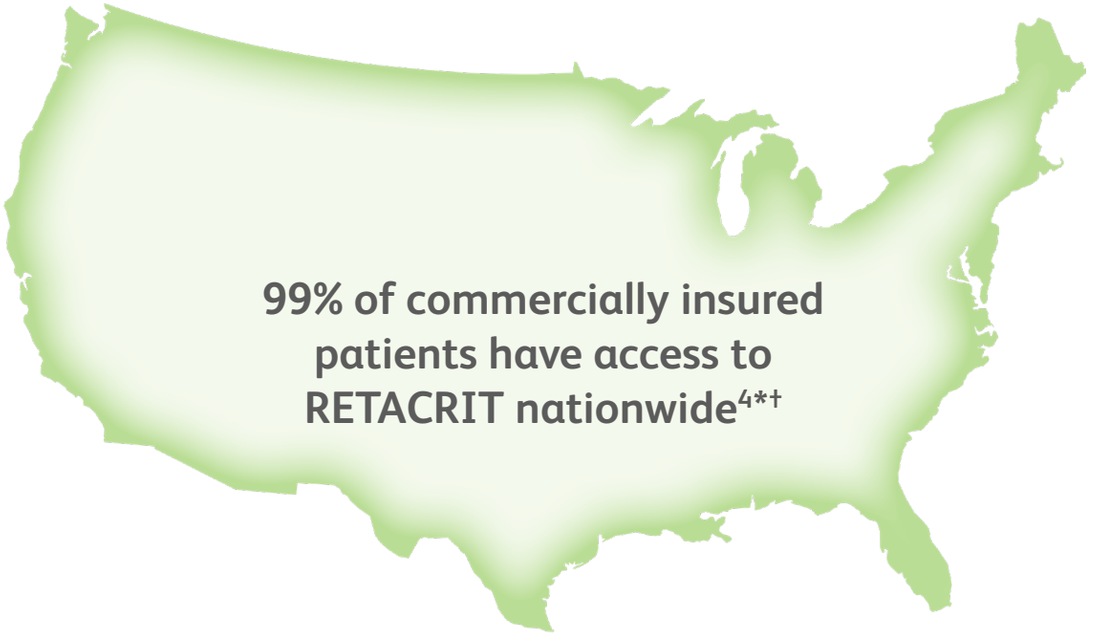
WARNINGS: ESAs INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE (CONTINUED)

CANCER (CONTINUED)

- 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

Click to view full ISI

RETACRIT coverage



- 96% of Medicare lives covered, including managed Medicare[4†]

*Percentage of commercial lives where RETACRIT is covered at parity or at an advantage to Epogen®/Procrit® (epoetin alfa).
†Medical policy data are current as of November 2021. Please verify individual patient benefits to confirm coverage.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

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

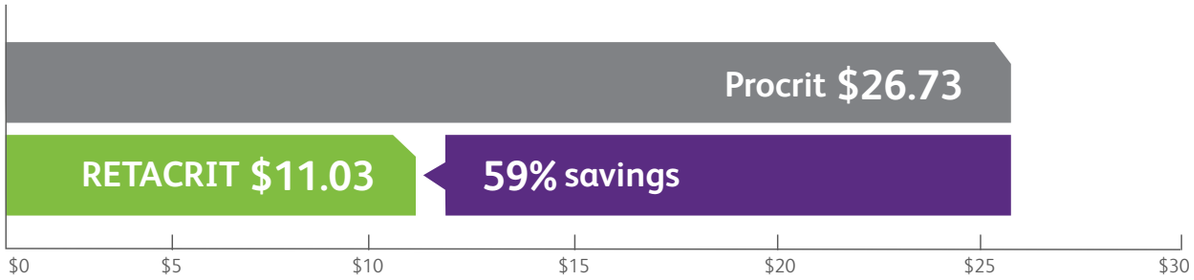
PERISURGERY

- **Due to increased risk of deep venous thrombosis (DVT), DVT prophylaxis is recommended**

Click to view full ISI

Potential cost savings with RETACRIT

Wholesale acquisition cost (WAC) represents a 59% discount per 1000 Units vs Procrit® (epoetin alfa)[4]*



An estimated cumulative maximum potential savings over 10 years from implementation of all available biosimilars could reach as much as $150 billion.[6†]

*WAC is a manufacturer's undiscounted or list price to wholesalers/direct purchasers and, therefore, is not inclusive of discounts to payers, providers, distributors, and other purchasing organizations. Data as of January 2022.

†Estimated reduction in direct spending on biologic drugs between 2017 and 2026 (RAND Corporation). Based on an assumption of a biosimilar market share of 50% and biosimilar prices at 50% of the reference product.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

CONTRAINDICATIONS

RETACRIT® is contraindicated in patients with:

- Uncontrolled hypertension
- Pure red cell aplasia (PRCA) that begins after treatment with RETACRIT® or other erythropoietin protein drugs
- Serious allergic reactions to RETACRIT® or other epoetin alfa products

(continued on next page)

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Navigating access and reimbursement. Together.

Pfizer Oncology together™

Patient Support. Financial Assistance. Together.

If patients need access or reimbursement support, Pfizer Oncology Together is here to help.

Benefits Verification
We can help determine a patient's coverage and out-of-pocket costs.

Prior Authorization (PA) Assistance
We can coordinate with a patient's insurer to determine the PA requirements. After a PA request is submitted, we can follow up with the payer until a final outcome is determined.

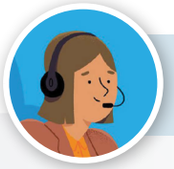
Appeals Assistance
We can review the reasons for a denied claim and provide information on payer requirements. After an appeal is submitted, we can follow up with the payer until a final outcome is determined.

Product Distribution
RETACRIT is available through most major wholesalers.

Billing and Coding Assistance for IV Products
For your patient claim submissions, we provide easy access to sample forms and template letters, along with billing and coding information for physician's office and hospital outpatient settings of care.

Dedicated Local Support
A Pfizer Oncology Account Specialist can provide detailed information on Pfizer Oncology medications and access resources. In addition, they can help you and your office staff contact a Pfizer Field Reimbursement Manager (FRM) in your area.

FRMs are trained to help address specific access issues—in person or over the phone. They can help educate your staff on our access and reimbursement resources and help address challenging or urgent Pfizer Oncology patient cases you have sent to Pfizer Oncology Together.



FOR LIVE, PERSONALIZED SUPPORT
Call **1-877-744-5675** (Monday–Friday 8 AM–8 PM ET)

VISIT
PfizerOncologyTogether.com

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION
CONTRAINDICATIONS (CONTINUED)

RETACRIT® from multiple-dose vials contains benzyl alcohol and is contraindicated in:

- Neonates, infants, pregnant women, and lactating women. When therapy with RETACRIT® is needed in these patient populations, use single-dose vials; do not admix with bacteriostatic saline containing benzyl alcohol

Click to view full ISI

Introduction
Coverage
Potential Savings
Access and Reimbursement
Tools and Resources

Pfizer is committed to supporting you and your patients

ThisIsLivingWithCancer.com

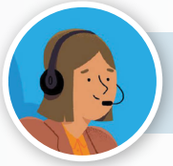
A free app designed to help manage life with cancer

Help your patients and their caregivers stay connected and get organized by telling them about **LivingWith**™.

The **LivingWith** app is available to anyone living with cancer and their loved ones, and is not specific to RETACRIT.

PfizerBiosimilarsResource.com

Pfizer downloadable tools are available to help support you when implementing biosimilars into your practice.



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SELECTED SAFETY INFORMATION

INCREASED MORTALITY, MYOCARDIAL INFARCTION, STROKE, AND THROMBOEMBOLISM

- In controlled clinical trials of patients with chronic kidney disease (CKD) comparing higher hemoglobin targets (13 - 14 g/dL) to lower targets (9 - 11.3 g/dL), epoetin alfa increased the risk of death, myocardial infarction, stroke, congestive heart failure, thrombosis of hemodialysis vascular access, and other thromboembolic events in the higher target groups
- Using ESAs to target a hemoglobin level of greater than 11 g/dL increases the risk of serious adverse cardiovascular reactions and has not been shown to provide additional benefit. 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 greater than 1 g/dL over 2 weeks may contribute to these risks

(continued on next page)

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Introduction
Dosing
Ordering and Product Information

RETACRIT is the first and only FDA-approved biosimilar to Epogen®/Procrit® (epoetin alfa) with single- and multiple-dose vials[1-3]

RETACRIT is a biosimilar to Epogen/Procrit

Same indications as Epogen/Procrit[2]

Same dosing and administration schedule as Epogen/Procrit[2]

Useful ordering and coding information

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

INCREASED MORTALITY, MYOCARDIAL INFARCTION, STROKE, AND THROMBOEMBOLISM (CONTINUED)

- In controlled clinical trials of patients with cancer, epoetin alfa increased the risks for death and serious adverse cardiovascular reactions. These adverse reactions included myocardial infarction and stroke
- 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

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RETACRIT has the same dosing as Epogen®/Procrit® (epoetin alfa)[2]

INDICATIONS	DOSING
Patients with CKD	Recommended starting dose **Adult patients with CKD on dialysis:** • 50 to 100 Units/kg 3 times weekly intravenously or subcutaneously. The IV route is recommended for patients on hemodialysis **Adult patients with CKD not on dialysis:** • 50 to 100 Units/kg 3 times weekly intravenously or subcutaneously **Pediatric patients (1 month and older) with CKD on dialysis:** • 50 Units/kg 3 times weekly intravenously or subcutaneously **Maintenance doses should be individualized. Please see full Prescribing Information.**
Patients with HIV treated with zidovudine	Recommended starting dose **Adult patients:** • 100 Units/kg as an IV or SC injection 3 times per week
Patients on cancer chemotherapy	Recommended starting dose **Adult patients:** • 150 Units/kg subcutaneously 3 times weekly or 40,000 Units subcutaneously weekly until completion of a chemotherapy course **Pediatric patients (5 to 18 years):** • 600 Units/kg intravenously weekly until completion of a chemotherapy course

Do not dilute. Do not mix with other drug solutions.
IV=intravenous; SC=subcutaneous.

Please see the full RETACRIT Prescribing Information for additional details.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

INCREASED MORTALITY AND/OR INCREASED RISK OF TUMOR PROGRESSION OR RECURRENCE IN PATIENTS WITH CANCER

- ESAs resulted in decreased locoregional control/progression-free survival (PFS) and/or overall survival (OS). Adverse effects on PFS and/or OS were observed in studies of patients receiving chemotherapy for breast cancer, lymphoid malignancy, and cervical cancer; in patients with advanced head and neck cancer receiving radiation therapy; and in patients with non-small cell lung cancer or various malignancies who were not receiving chemotherapy or radiotherapy

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Introduction
Dosing
Ordering and Product Information

RETACRIT has the same dosing as Epogen®/Procrit® (epoetin alfa)[2]

INDICATIONS	DOSING
Surgery patients	**Recommended regimens for patients undergoing elective, noncardiac, nonvascular surgery** • 300 Units/kg per day subcutaneously for 15 days total: administered daily for 10 days before surgery, on the day of surgery, and for 4 days after surgery • 600 Units/kg subcutaneously in 4 doses, administered 21, 14, and 7 days before surgery and on the day of surgery Deep venous thrombosis prophylaxis is recommended during RETACRIT therapy.

Do not dilute. Do not mix with other drug solutions.

RETACRIT from multiple-dose vials contains benzyl alcohol and is contraindicated in[2]:

- Neonates, infants, pregnant women, and lactating women. When therapy with RETACRIT is needed in these patient populations, use single-dose vials; do not admix with bacteriostatic saline containing benzyl alcohol

Please see accompanying full Prescribing Information (Section 2: Dosage and Administration) for additional dosage and administration information for each indication.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION
HYPERTENSION

- RETACRIT® is contraindicated in patients with uncontrolled hypertension. Following initiation and titration of epoetin alfa, approximately 25% of patients on dialysis required initiation of or increases in antihypertensive therapy; hypertensive encephalopathy and seizures have been reported in patients with CKD receiving RETACRIT®
- Appropriately control hypertension prior to initiation of and during treatment with RETACRIT®. Reduce or withhold RETACRIT® if blood pressure becomes difficult to control. Advise patients of the importance of compliance with antihypertensive therapy and dietary restrictions

Click to view full ISI

RETACRIT has the same dosing as Epogen®/Procrit® (epoetin alfa)[2]

Important dosing information[2]

Evaluation of iron stores and nutritional factors
Evaluate the iron status in all patients before and during treatment. Administer supplemental iron therapy when serum ferritin is less than 100 mcg/L or when serum transferrin saturation is less than 20 %. The majority of patients with CKD will require supplemental iron during the course of ESA therapy.

Monitoring of response to therapy
Correct or exclude other causes of anemia (eg, vitamin deficiency, metabolic or chronic inflammatory conditions, bleeding, etc) before initiating RETACRIT. Following initiation of therapy and after each dose adjustment, monitor hemoglobin weekly until the hemoglobin level is stable and sufficient to minimize the need for RBC transfusion.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

SEIZURES

- Epoetin alfa products, including RETACRIT®, increase the risk of seizures in patients with CKD. During the first several months following initiation of RETACRIT®, monitor patients closely for premonitory neurologic symptoms. Advise patients to contact their healthcare practitioner for new-onset seizures, premonitory symptoms or change in seizure frequency

LACK OR LOSS OF HEMOGLOBIN RESPONSE TO RETACRIT®

- For lack or loss of hemoglobin response to RETACRIT®, initiate a search for causative factors (eg, iron deficiency, infection, inflammation, bleeding). If typical causes of lack or loss of hemoglobin response are excluded, evaluate for PRCA. In the absence of PRCA, follow dosing recommendations for management of patients with an insufficient hemoglobin response to RETACRIT® therapy

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Introduction

Dosing

Ordering and Product Information

RETACRIT injection, solution for IV or SC use

Ordering RETACRIT—What you need to know[2,4,7]

Strength	2,000 Units/mL	3,000 Units/mL	4,000 Units/mL	10,000 Units/mL	40,000 Units/mL	20,000 Units/mL	20,000 Units/2 mL
Unit of Sale NDC	0069-1305-10	0069-1306-10	0069-1307-10	0069-1308-10	0069-1309-04	0069-1311-10	0069-1318-10
Unit of Sale Quantity	1 carton (10 SDVs)	1 carton (10 SDVs)	1 carton (10 SDVs)	1 carton (10 SDVs)	1 carton (4 SDVs)	1 carton (10 MDVs)	1 carton (10 MDVs)
Unit of Sale List Price*	$220.60	$330.90	$441.20	$1,103.00	$1,764.80	$2,206.00	$2,206.00

HCPCS Code	Descriptor
Q5105	Injection, epoetin alfa-epbx, biosimilar, (RETACRIT) (for ESRD on dialysis), 100 units
Q5106	Injection, epoetin alfa-epbx, biosimilar, (RETACRIT) (for non-ESRD use), 1,000 units

MDV=multiple-dose vial; SDV=single-dose vial.
*As of May 2021.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

PURE RED CELL APLASIA

- 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 epoetin alfa. 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 RETACRIT® is not approved)
- If severe anemia and low reticulocyte count develop during treatment with RETACRIT®, withhold RETACRIT® and evaluate patients for neutralizing antibodies to erythropoietin. **Contact Pfizer Inc. at 1-800-438-1985 to perform assays for binding and neutralizing antibodies.** Permanently discontinue RETACRIT® in patients who develop PRCA following treatment with RETACRIT® or other erythropoietin protein drugs. Do not switch patients to other ESAs

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Introduction

Dosing

Ordering and Product Information

RETACRIT injection, solution for IV or SC use

Storage and handling[2]

Store refrigerated between 36 °F to 46 °F (2 °C to 8 °C)

Protect RETACRIT from light by storing in its original carton until ready for use

Do not use RETACRIT that has been shaken or frozen or if the green area of the freeze strip indicator is cloudy or white

Please see full Prescribing Information for additional details.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

SERIOUS ALLERGIC REACTIONS

- Serious allergic reactions, including anaphylactic reactions, angioedema, bronchospasm, skin rash, and urticaria may occur with epoetin alfa products. Immediately and permanently discontinue RETACRIT® and administer appropriate therapy if a serious allergic or anaphylactic reaction occurs

SEVERE CUTANEOUS REACTIONS

- 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 epoetin alfa) in the postmarketing setting. Discontinue RETACRIT® therapy immediately if a severe cutaneous reaction, such as SJS/TEN, is suspected

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RETACRIT is the first and only FDA-approved biosimilar to Epogen®/Procrit® (epoetin alfa) with single- and multiple-dose vials[1-3]

A totality of evidence supports biosimilarity to Epogen/Procrit[2,8]

Biosimilarity established based on a totality of evidence[2,8]

Extrapolation allows potential approval for nonstudied indications[8]

No clinically meaningful differences in terms of efficacy or safety[4,9]

Using the totality of evidence, including extrapolation, RETACRIT was granted the same indications as Epogen/Procrit by the FDA.[1,8]

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

RISK OF SERIOUS ADVERSE REACTIONS DUE TO BENZYL ALCOHOL PRESERVATIVE

- RETACRIT® from multiple-dose vials contains benzyl alcohol and is contraindicated for use in neonates, infants, pregnant women, and lactating women. In addition, do not mix RETACRIT® with bacteriostatic saline (which also contains benzyl alcohol) when administering RETACRIT® to these patient populations
- Serious and fatal reactions including "gasping syndrome" can occur in neonates and infants treated with benzyl alcohol-preserved drugs, including RETACRIT® multiple-dose vials. The "gasping syndrome" is characterized by central nervous system depression, metabolic acidosis, and gasping respirations. There is a potential for similar risks to fetuses and infants exposed to benzyl alcohol in utero or in breastfed milk, respectively. RETACRIT® multiple-dose vials contain 8.5 mg of benzyl alcohol per mL. The minimum amount of benzyl alcohol at which serious adverse reactions may occur is not known

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RETACRIT is the first and only FDA-approved biosimilar to Epogen®/Procrit® (epoetin alfa) with single- and multiple-dose vials[1-3]

RETACRIT was approved by the FDA based on the totality of evidence demonstrating it is highly similar to Epogen/Procrit[2,8]

CLINICAL STUDIES	RETACRIT demonstrated no clinically meaningful differences in efficacy compared to Epogen/Procrit at a similar dose[9]
CLINICAL PHARMACOLOGY (PK/PD)	RETACRIT met all PK/PD equivalence requirements in 2 studies[9]
NONCLINICAL	RETACRIT is similar to Epogen/Procrit based on required nonclinical study results[9]
ANALYTICAL	RETACRIT is highly similar in structure and function to Epogen/Procrit[9]

PD=pharmacodynamic; PK=pharmacokinetic.

Click to view full evidence

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

Using the totality of evidence, including extrapolation, RETACRIT was granted the same indications as Epogen/Procrit by the FDA.[1,8]

SELECTED SAFETY INFORMATION

RISK IN PATIENTS WITH PHENYLKETONURIA

- Phenylalanine can be harmful to patients with phenylketonuria (PKU). RETACRIT® single-dose vials contain phenylalanine, a component of aspartame. Each 1 mL single-dose vial of 2,000, 3,000, 4,000, 10,000, and 40,000 Units of epoetin alfa-epbx injection contains 0.5 mg of phenylalanine. Before prescribing RETACRIT® single-dose vials to a patient with PKU, consider the combined daily amount of phenylalanine from all sources, including RETACRIT®

DIALYSIS MANAGEMENT

- Patients may require adjustments in their dialysis prescriptions after initiation of RETACRIT®. Patients receiving RETACRIT® may require increased anticoagulation with heparin to prevent clotting of the extracorporeal circuit during hemodialysis

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CLINICAL STUDIES	**RETACRIT demonstrated no clinically meaningful differences in efficacy compared to Epogen/Procrit at a similar dose[9]** • In 2 clinical studies (SC and IV) of patients with CKD on hemodialysis, RETACRIT showed no clinically meaningful differences from Epogen/Procrit in efficacy and safety • No clinically meaningful differences in immunogenicity risk were observed between RETACRIT and Epogen/Procrit in healthy subjects and those with CKD on hemodialysis*
CLINICAL PHARMACOLOGY (PK/PD)	**RETACRIT met all PK/PD equivalence requirements in 2 studies[9]** • The studies showed that PK and PD parameters for RETACRIT fell within the prespecified bioequivalence window of 80% to 125% (90% confidence intervals)
NONCLINICAL	**RETACRIT is similar to Epogen/Procrit based on required nonclinical study results[9]** • Sufficient nonclinical pharmacology and toxicology studies compared RETACRIT and Epogen/Procrit
ANALYTICAL	**RETACRIT is highly similar in structure and function to Epogen/Procrit[9]** • Multiple orthogonal physicochemical and functional methods—in addition to biological activity analyses—confirm similarity • Amino acid sequences are the same

AE=adverse event; PD=pharmacodynamic; PK=pharmacokinetic.
*No samples tested positive for neutralizing antibodies. There was no apparent impact of antidrug antibody status on reported AEs in patients from either study.[9]

CLOSE

- Phenylalanine can be harmful to patients with phenylketonuria (PKU). RETACRIT® single-dose vials contain phenylalanine, a component of aspartame. Each 1 mL single-dose vial of 2,000, 3,000, 4,000, 10,000, and 40,000 Units of epoetin alfa-epbx injection contains 0.5 mg of phenylalanine. Before prescribing RETACRIT® single-dose vials to a patient with PKU, consider the combined daily amount of phenylalanine from all sources, including RETACRIT®

DIALYSIS MANAGEMENT

- Patients may require adjustments in their dialysis prescriptions after initiation of RETACRIT®. Patients receiving RETACRIT® may require increased anticoagulation with heparin to prevent clotting of the extracorporeal circuit during hemodialysis

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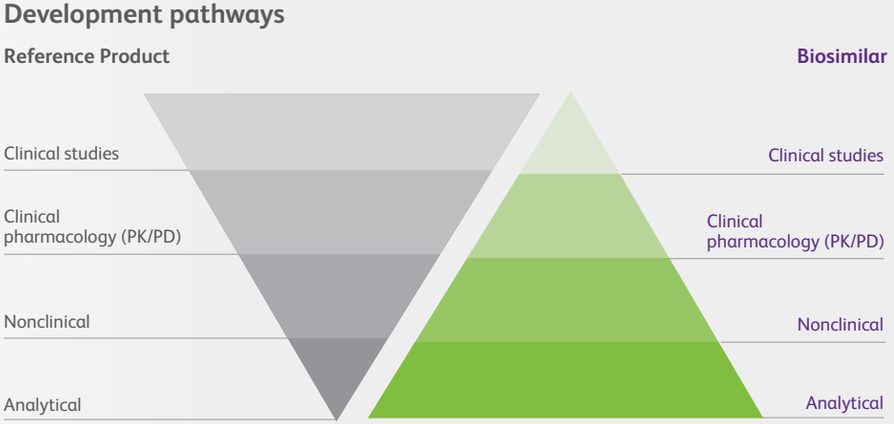
Biosimilars: Highly similar versions of existing biologic medicines[8]

- According to the FDA, a biosimilar is a medicine highly similar to another biological medicine or reference product already marketed in the United States
  - Biosimilars have no clinically meaningful differences in terms of safety, purity, and potency from their reference products

The FDA evaluates biosimilars based on a totality of evidence approach[8,10]



- The goal of biosimilar development is to demonstrate that there are no clinically meaningful differences based on the totality of evidence[8,10]
- Analytical studies are the foundation of biosimilar development and provide the greatest sensitivity for detecting differences between a biosimilar and its reference product[8,10]

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Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

ANEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE

- Adverse reactions in ≥5% of epoetin alfa-treated patients on dialysis were hypertension, arthralgia, muscle spasm, pyrexia, dizziness, medical device malfunction, vascular occlusion and upper respiratory tract infection

ANEMIA DUE TO CHEMOTHERAPY IN PATIENTS WITH CANCER

- Adverse reactions in ≥5% of epoetin alfa-treated patients in clinical studies were nausea, vomiting, myalgia, arthralgia, stomatitis, cough, weight decrease, leukopenia, bone pain, rash, hyperglycemia, insomnia, headache, depression, dysphagia, hypokalemia, and thrombosis

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- According to the FDA, a biosimilar is a medicine highly similar to another biological medicine or reference product already marketed in the United States
  - Biosimilars have no clinically meaningful differences in terms of safety, purity, and potency from their reference products

The FDA evaluates biosimilars based on a totality of evidence approach[8,10]

Development pathways

- The goal of biosimilar development is to demonstrate that there are no clinically meaningful differences based on the totality of evidence[8,10]
- Analytical studies are the foundation of biosimilar development and provide the greatest sensitivity for detecting differences between a biosimilar and its reference product[8,10]

CLOSE

ANEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE

- Adverse reactions in ≥5% of epoetin alfa-treated patients on dialysis were hypertension, arthralgia, muscle spasm, pyrexia, dizziness, medical device malfunction, vascular occlusion and upper respiratory tract infection

ANEMIA DUE TO CHEMOTHERAPY IN PATIENTS WITH CANCER

- Adverse reactions in ≥5% of epoetin alfa-treated patients in clinical studies were nausea, vomiting, myalgia, arthralgia, stomatitis, cough, weight decrease, leukopenia, bone pain, rash, hyperglycemia, insomnia, headache, depression, dysphagia, hypokalemia, and thrombosis

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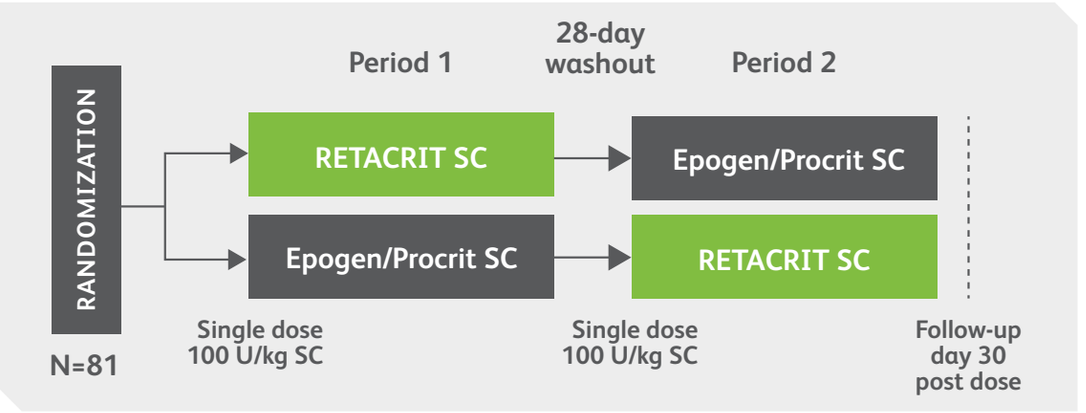
A single-dose crossover study evaluated PK/PD similarity in healthy male subjects[11]

Study design for single-dose PK/PD study in healthy male subjects



- **Single-dose, crossover study in healthy male subjects:** A single-center, randomized, open-label, crossover, phase 1 study evaluated PK/PD equivalence of a single SC dose of 100 U/kg of RETACRIT or Epogen®/Procrit® (epoetin alfa) in healthy male subjects (N=81). The study was designed to determine the PK (epoetin concentration) and PD (reticulocyte count) of RETACRIT and Epogen/Procrit. The predefined PK endpoints were baseline-adjusted epoetin alfa $AUC_{0\text{-}t}$ and C_{max}. The predefined PD endpoints were reticulocyte count (expressed as a percentage of erythrocytes) $AUC_{0\text{-}t}$ and C_{max}. The washout period was 28 days

$AUC_{0\text{-}t}$=area under the curve from the time of dosing to the last measurable concentration; C_{max}=maximum serum concentration.

Single-Dose Study

Multiple-Dose Study

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

SURGERY/PERISURGERY

- Adverse reactions in ≥5% of epoetin alfa-treated patients in clinical studies were nausea, vomiting, pruritus, headache, injection site pain, chills, deep vein thrombosis, cough, and hypertension

ANEMIA DUE TO ZIDOVUDINE IN PATIENTS WITH HIV INFECTION

- Adverse reactions in ≥5% of epoetin alfa-treated patients in clinical studies were pyrexia, cough, rash, and injection site irritation

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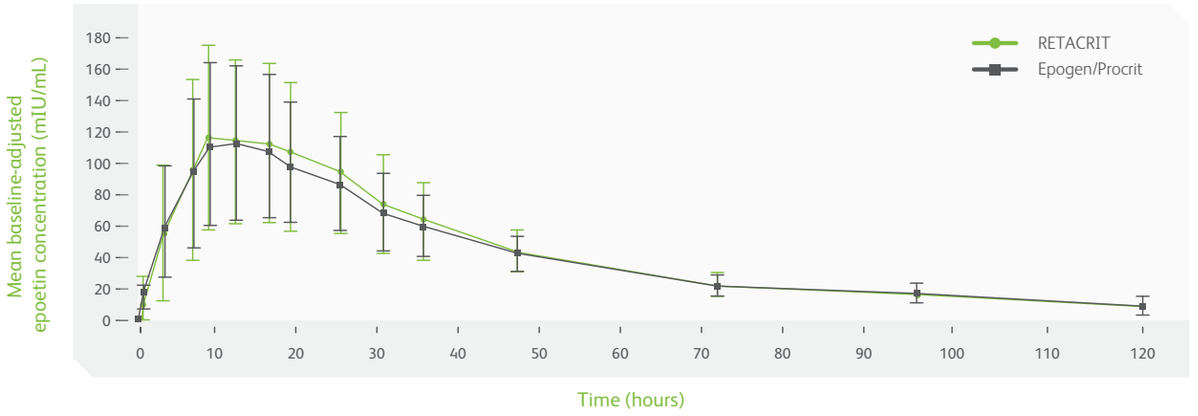
*Similar PK profile to Epogen®/Procrit®(epoetin alfa) in healthy male subjects[11]**

PK profiles of mean serum concentration following a 100 U/kg SC single dose of RETACRIT or Epogen/Procrit in healthy male subjects

Mean serum concentration of RETACRIT vs Epogen/Procrit



*The single-dose study is considered the pivotal study for evaluating PK similarity by the FDA.[9]
Adapted from Stalker D, Reid S, Ramaiya A, et al. *Clin Ther*. 2016;38(8):1778-1788.

Single-Dose Study

Multiple-Dose Study

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS: 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

(continued on next page)

Click to view full ISI

*Similar PK profile to Epogen®/Procrit®(epoetin alfa) in healthy male subjects[11]**

Statistical analyses of PK parameters[11]

Parameter	RETACRIT (n=71)	Epogen/Procrit (n=71)	GMR	90% CI†
$AUC_{0\text{-}120h}$ (mIU x h/mL)	4998.51	4754.33	1.05	1.01–1.11
C_{max} (mIU/mL)	120.52	110.86	1.09	1.01–1.18

CI=confidence interval; GMR=geometric mean ratio.
*The single-dose study is considered the pivotal study for evaluating PK similarity by the FDA.[9]
†PK equivalence was concluded if 90% CIs for geometric mean ratios of $AUC_{0\text{-}t}$ and C_{max} were completely contained within the acceptance limits of 0.80 to 1.25.

Single-Dose Study
Multiple-Dose Study

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

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

CHRONIC KIDNEY DISEASE (CONTINUED)

- Use the lowest RETACRIT® dose sufficient to reduce the need for red blood cell (RBC) transfusions

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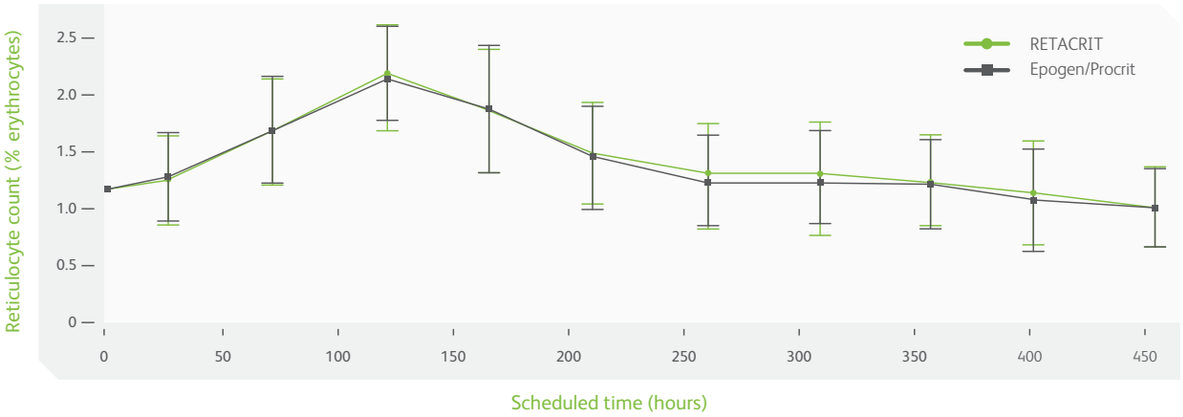
Similar PD profile to Epogen®/Procrit® (epoetin alfa) in healthy male subjects[11]

PD profiles of mean reticulocyte counts following a 100 U/kg SC single dose of RETACRIT or Epogen/Procrit in healthy male subjects

Reticulocyte counts over time with RETACRIT vs Epogen/Procrit



Adapted from Stalker D, Reid S, Ramaiya A, et al. *Clin Ther*. 2016;38(8):1778-1788.

Single-Dose Study

Multiple-Dose Study

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SELECTED SAFETY INFORMATION

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

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

(continued on next page)

Click to view full ISI

Similar PD profile to Epogen®/Procrit®(epoetin alfa) in healthy male subjects[11]

Statistical analyses of PD parameters

Parameter	RETACRIT (n=73)	Epogen/Procrit (n=73)	GMR	95% CI*
$AUC_{0\text{-}t}$ (% x h)	644.25	635.28	1.01	0.98–1.05
C_{max} (%)	2.18	2.13	1.02	0.98–1.06

*PD equivalence concluded if both 95 % CIs were completely contained within the acceptance limits of 0.80 and 1.25.

Single-Dose Study

Multiple-Dose Study

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

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

CANCER (CONTINUED)

- 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

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Single-Dose Study
Multiple-Dose Study

A multiple-dose parallel group study evaluated PK/PD similarity in healthy male subjects[12]

Study design for multiple-dose study in healthy male subjects

- **Multiple-dose, parallel-group study in healthy male subjects:** A multiple-dose, parallel-group study (single-center, randomized, open-label) was also performed to evaluate PK/PD similarity following multiple SC doses of 100 U/kg 3 times weekly for 4 weeks in healthy male subjects (N=129). The predefined PD endpoint was $AUEC_{Hb}$ over 28 days. Multiple-dose PK equivalence was evaluated as a supportive measure of Hb levels. The predefined PK endpoints were $AUC_{0\text{-}48h}$ and C_{max} post final dose on day 26. The multiple-dose, pairwise comparison established the PD (Hb level) similarity of RETACRIT and Epogen®/Procrit® (epoetin alfa)

$AUEC_{Hb}$=area under the effect (Hb concentration) curve; Hb=hemoglobin.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

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

PERISURGERY

- Due to increased risk of deep venous thrombosis (DVT), DVT prophylaxis is recommended

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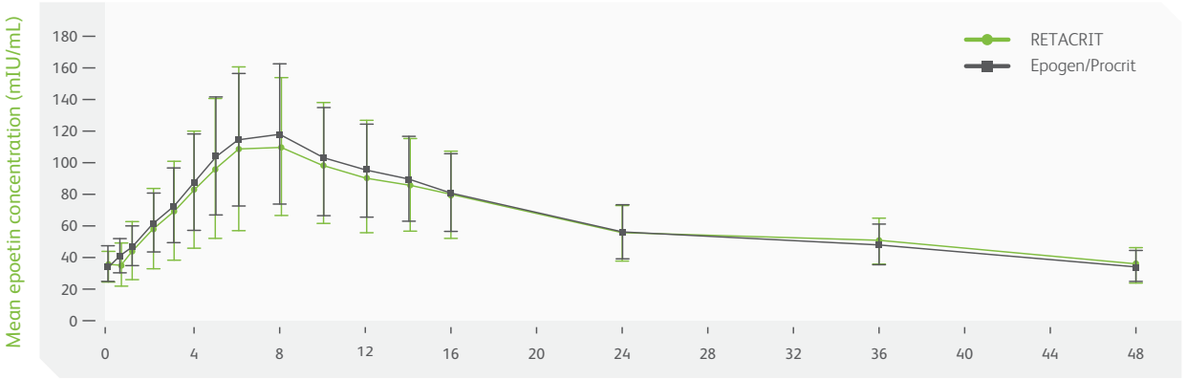
Similar PK profile to Epogen®/Procrit® (epoetin alfa) in healthy male subjects[12]

PK profiles of serum epoetin concentration following SC administration of 100 U/kg RETACRIT or Epogen/Procrit in healthy male subjects 3 times a week for 4 weeks*

Mean epoetin concentration after day 26 dosing with RETACRIT vs Epogen/Procrit



*Dosing was at time 0 on day 26.
Adapted from Stalker D, Ramaiya A, Kumbhat S, et al. *Clin Ther*. 2016;38(5):1090-1101.

Single-Dose Study
Multiple-Dose Study

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION
CONTRAINDICATIONS
RETACRIT® is contraindicated in patients with:
- Uncontrolled hypertension
- Pure red cell aplasia (PRCA) that begins after treatment with RETACRIT® or other erythropoietin protein drugs
- Serious allergic reactions to RETACRIT® or other epoetin alfa products

(continued on next page)

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Similar PK profile to Epogen®/Procrit® (epoetin alfa) in healthy male subjects[12]

Statistical analyses of PK parameters

Parameter	RETACRIT (n=61)	Epogen/Procrit (n=62)	GMR*	90% CI†
$AUC_{0\text{-}48}$ (mIU x h/mL) Geometric mean	2917.85	2995.71	0.974	0.896–1.059
LS mean (SE)	2917.85 (1.036)	2995.71 (1.036)		
C_{max} (mIU/mL) Geometric mean	111.47	118.83	0.938	0.839–1.049
LS mean (SE)	111.47 (1.049)	118.83 (1.049)		

LS=least squares; SE=standard error.
*The GMR is the ratio (RETACRIT/Epogen/Procrit) of the LS means.
†PK equivalence was concluded if both 90% CIs were completely contained within the acceptance limits of 0.80 to 1.25.

Single-Dose Study
Multiple-Dose Study

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

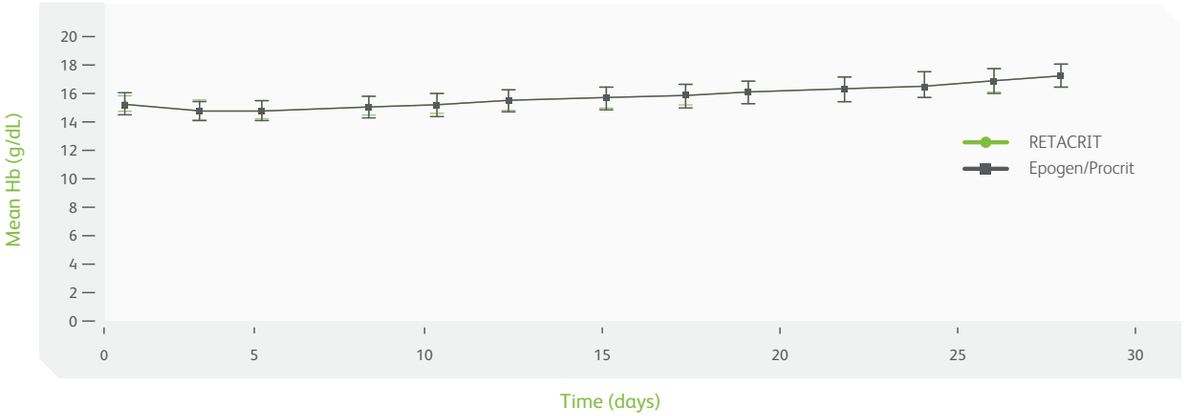
SELECTED SAFETY INFORMATION
CONTRAINDICATIONS (CONTINUED)
RETACRIT® from multiple-dose vials contains benzyl alcohol and is contraindicated in:
- Neonates, infants, pregnant women, and lactating women. When therapy with RETACRIT® is needed in these patient populations, use single-dose vials; do not admix with bacteriostatic saline containing benzyl alcohol

Click to view full ISI

Similar PD profile to Epogen®/Procrit® (epoetin alfa) in healthy male subjects[12]

PD profiles following multiple 100 U/kg SC doses 3 times per week for 4 weeks in healthy male subjects*†

Mean Hb levels for RETACRIT vs Epogen/Procrit



*The multiple-dose, pairwise comparison established the PD (Hb level) similarity of RETACRIT and Epogen/Procrit.
†Dosing was at time 0 on day 1.
Adapted from Stalker D, Ramaiya A, Kumbhat S, et al. *Clin Ther.* 2016;38(5):1090-1101.

Single-Dose Study
Multiple-Dose Study

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

INCREASED MORTALITY, MYOCARDIAL INFARCTION, STROKE, AND THROMBOEMBOLISM

- In controlled clinical trials of patients with chronic kidney disease (CKD) comparing higher hemoglobin targets (13 - 14 g/dL) to lower targets (9 - 11.3 g/dL), epoetin alfa increased the risk of death, myocardial infarction, stroke, congestive heart failure, thrombosis of hemodialysis vascular access, and other thromboembolic events in the higher target groups
- Using ESAs to target a hemoglobin level of greater than 11 g/dL increases the risk of serious adverse cardiovascular reactions and has not been shown to provide additional benefit. 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 greater than 1 g/dL over 2 weeks may contribute to these risks

(continued on next page)

Click to view full ISI

Similar PD profile to Epogen®/Procrit® (epoetin alfa) in healthy male subjects[12]

Statistical analyses of PD parameters

Parameter	RETACRIT (n=62)	Epogen/Procrit (n=62)	GMR*	95% CI†
$AUEC_{Hb}$ (g x h/dL) Geometric mean	10238.11	10199.66	1.006	0.996–1.016
LS mean (SE)	10251.11 (1.004)	10186.73 (1.004)		

*The GMR is the ratio (RETACRIT/Epogen/Procrit) of the LS means.
†PD equivalence was concluded if the 95% CI was completely contained within the acceptance limits of 0.965 to 1.035.

Single-Dose Study
Multiple-Dose Study

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION
INCREASED MORTALITY, MYOCARDIAL INFARCTION, STROKE, AND THROMBOEMBOLISM (CONTINUED)

- In controlled clinical trials of patients with cancer, epoetin alfa increased the risks for death and serious adverse cardiovascular reactions. These adverse reactions included myocardial infarction and stroke
- 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

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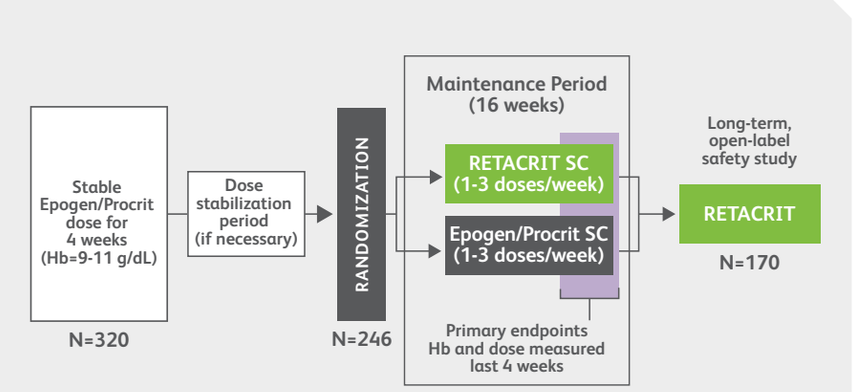
Two comparative clinical studies evaluated the efficacy and safety profile of SC and IV administration of RETACRIT in patients with CKD on hemodialysis[13,14]

Co-primary endpoints for both studies included the comparison between RETACRIT and Epogen®/Procrit® (epoetin alfa) in mean weekly Hb level and mean weekly dosage per kg body weight during the last 4 weeks of the double-blind maintenance period

Study design for SC administration in patients with CKD on hemodialysis[4,14,15]



Subject eligibility determined during the Screening Period, within 4 weeks prior to randomization. Stable subjects taking IV Epogen/Procrit were randomized to receive either RETACRIT or Epogen/Procrit by SC injection 1 to 3 times per week, for 12 to 18 weeks. All subjects must have been optimally titrated and stable with SC administration for entry into Maintenance Period.

16-week SC study in patients with CKD on hemodialysis: Randomized, double-blind, parallel-group study that enrolled patients with CKD on hemodialysis (N=320) who received SC administration of RETACRIT or Epogen/Procrit maintenance treatment for 16 weeks. In the dose-stabilization period of the study, patients who previously received IV Epogen/Procrit were randomized to SC RETACRIT or Epogen/Procrit for 12 to 18 weeks to achieve 4 weeks of stable dosing. Patients who had been on SC Epogen/Procrit were randomized directly into the Maintenance Period.[14]

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

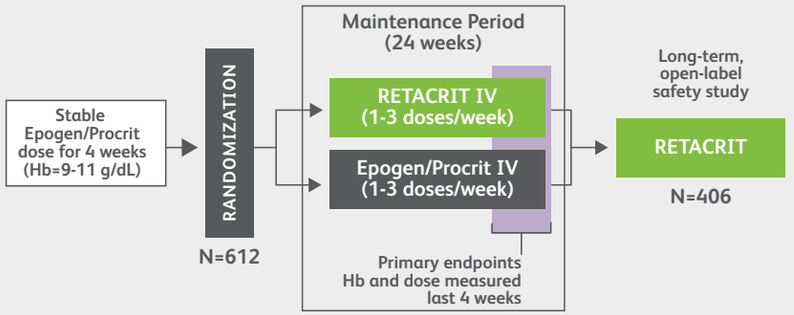
INCREASED MORTALITY AND/OR INCREASED RISK OF TUMOR PROGRESSION OR RECURRENCE IN PATIENTS WITH CANCER

- ESAs resulted in decreased locoregional control/progression-free survival (PFS) and/or overall survival (OS). Adverse effects on PFS and/or OS were observed in studies of patients receiving chemotherapy for breast cancer, lymphoid malignancy, and cervical cancer; in patients with advanced head and neck cancer receiving radiation therapy; and in patients with non-small cell lung cancer or various malignancies who were not receiving chemotherapy or radiotherapy

Click to view full ISI

Two comparative clinical studies evaluated the efficacy and safety profile of SC and IV administration of RETACRIT in patients with CKD on hemodialysis[13,14]

Study design for IV administration in patients with CKD on hemodialysis[4,13,15]



24-week IV study in patients with CKD on hemodialysis: Randomized, double-blind, parallel-group study that enrolled patients with CKD on hemodialysis (N=612). Patients on prior IV Epogen/Procrit were randomized to IV RETACRIT or Epogen/Procrit in the Maintenance Period for up to 24 weeks. Subject eligibility was determined during the Screening Period, within 4 weeks prior to randomization.[13]

Comparative study populations for both RETACRIT and Epogen®/Procrit® (epoetin alfa) were diverse and balanced in terms of gender, race, age, and weight[13,14]

In both clinical studies, patient demographics and baseline disease characteristics were evenly distributed between arms, with only minor imbalances. Subject disposition was balanced between treatment arms.[13,14]

Key inclusion criteria: Patients with CKD and anemia, ≥12 weeks stable dialysis, adequate iron stores (plasma ferritin >100 mcg/L and TSAT >20%), and stable on Epogen/Procrit treatment (Hb and dose).[13,14]

Key exclusion criteria: Patients experiencing cardiovascular serious adverse events ≤3 months, a folic acid or vitamin B12 deficiency, or history of disorders that affect RBC, such as anti-rhEPO antibodies.[4]

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

HYPERTENSION

- RETACRIT® is contraindicated in patients with uncontrolled hypertension. Following initiation and titration of epoetin alfa, approximately 25% of patients on dialysis required initiation of or increases in antihypertensive therapy; hypertensive encephalopathy and seizures have been reported in patients with CKD receiving RETACRIT®
- Appropriately control hypertension prior to initiation of and during treatment with RETACRIT®. Reduce or withhold RETACRIT® if blood pressure becomes difficult to control. Advise patients of the importance of compliance with antihypertensive therapy and dietary restrictions

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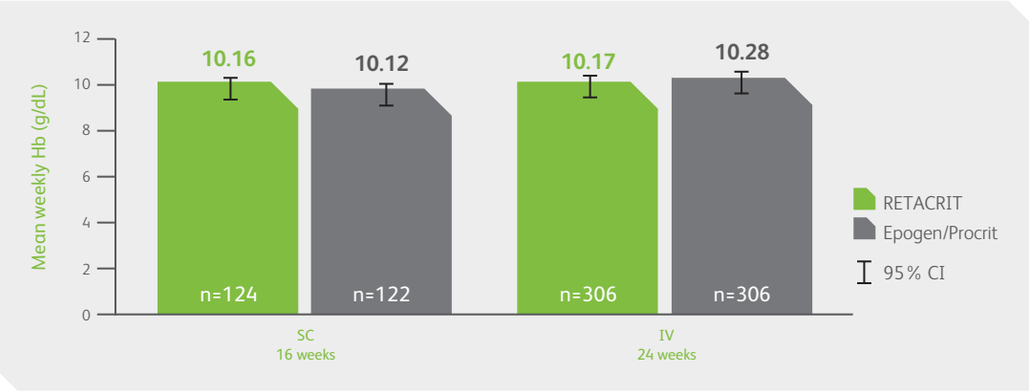
RETACRIT demonstrated no clinically meaningful differences in efficacy compared to Epogen®/Procrit® (epoetin alfa)[4,13,14]

No clinically meaningful differences were noted between RETACRIT and Epogen/Procrit in mean weekly Hb level achieved in CKD patients during the last 4 weeks of treatment

Mean weekly Hb levels with RETACRIT vs Epogen/Procrit (co-primary endpoint of ITT population)*



ITT=intent to treat.
*Statistical analysis supporting biosimilarity: 95% confidence interval for LS mean for the difference between RETACRIT and Epogen/Procrit treatment groups during last 4 weeks of maintenance was -0.17 to 0.24 g/dL/week (SC study) and -0.25 to 0.01 g/dL/week (IV study) and was contained within prespecified acceptance limits of +/-0.5 g/dL/week.[4]

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

SEIZURES

- Epoetin alfa products, including RETACRIT®, increase the risk of seizures in patients with CKD. During the first several months following initiation of RETACRIT®, monitor patients closely for premonitory neurologic symptoms. Advise patients to contact their healthcare practitioner for new-onset seizures, premonitory symptoms or change in seizure frequency

LACK OR LOSS OF HEMOGLOBIN RESPONSE TO RETACRIT®

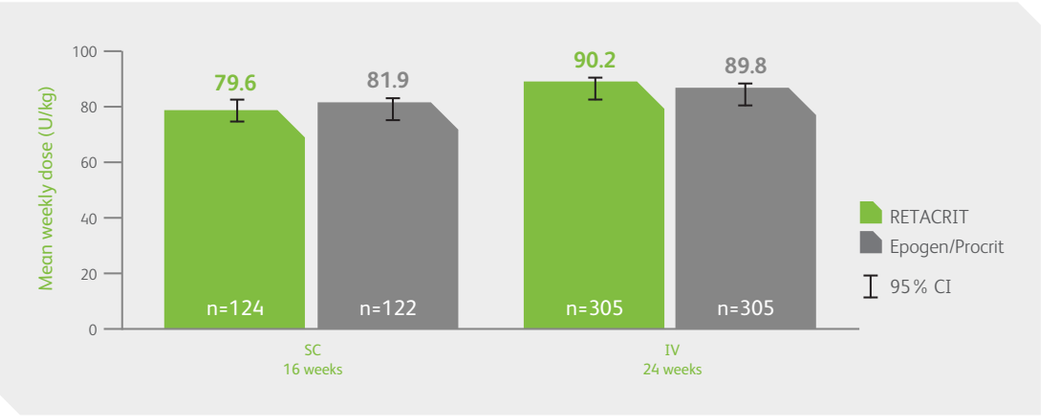
- For lack or loss of hemoglobin response to RETACRIT®, initiate a search for causative factors (eg, iron deficiency, infection, inflammation, bleeding). If typical causes of lack or loss of hemoglobin response are excluded, evaluate for PRCA. In the absence of PRCA, follow dosing recommendations for management of patients with an insufficient hemoglobin response to RETACRIT® therapy

Click to view full ISI

RETACRIT showed no clinically meaningful differences in mean weekly dose versus Epogen®/Procrit® (epoetin alfa)[4,13,14]

The mean weekly dose needed to maintain Hb target levels in CKD patients during the last 4 weeks of treatment had no clinically meaningful difference between treatment groups in either study

Mean weekly dose of RETACRIT vs Epogen/Procrit (co-primary endpoint of ITT population)*



*Statistical analysis supporting biosimilarity: 95% confidence interval for LS mean for the difference between RETACRIT and Epogen/Procrit treatment groups during last 4 weeks of maintenance was -14.51 to 9.82 U/kg/week (SC study) and -10.40 to 11.13 U/kg/week (IV study) and was contained within prespecified acceptance limits of +/-45 U/kg/week.[4]

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SELECTED SAFETY INFORMATION

PURE RED CELL APLASIA

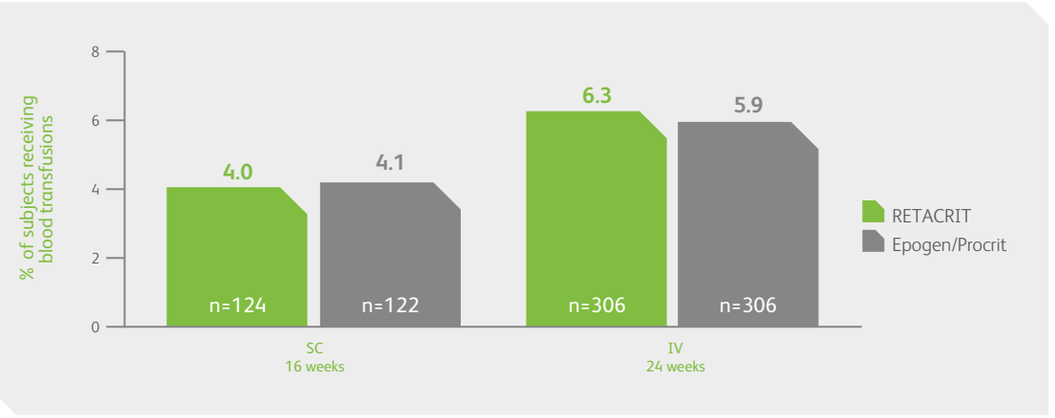
- Cases of PRCA and of severe anemia, with or without other cytopenias that arise following the development of neutralizing antibodies to erythropoietin have been reported in patients treated with epoetin alfa. This has been reported predominantly in patients with CKD receiving ESAs by subcutaneous administration. PRCA has also been reported in patients receiving ESAs for anemia related to hepatitis C treatment (an indication for which RETACRIT® is not approved)
- If severe anemia and low reticulocyte count develop during treatment with RETACRIT®, withhold RETACRIT® and evaluate patients for neutralizing antibodies to erythropoietin. **Contact Pfizer Inc. at 1-800-438-1985 to perform assays for binding and neutralizing antibodies.** Permanently discontinue RETACRIT® in patients who develop PRCA following treatment with RETACRIT® or other erythropoietin protein drugs. Do not switch patients to other ESAs

Click to view full ISI

RETACRIT displayed similar transfusion rates to Epogen®/Procrit® (epoetin alfa)[4,13,14]

In 2 comparative studies, the incidence of transfusion was not statistically different between treatment groups in either study

Transfusion rates with RETACRIT vs Epogen/Procrit in patients with CKD (secondary endpoint of ITT population)*



*Prespecified secondary efficacy endpoint. Other secondary efficacy analyses conducted on the ITT population (7 endpoints) provided supportive results for the conclusion of no statistically significant difference between treatment groups.

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SELECTED SAFETY INFORMATION

SERIOUS ALLERGIC REACTIONS

- Serious allergic reactions, including anaphylactic reactions, angioedema, bronchospasm, skin rash, and urticaria may occur with epoetin alfa products. Immediately and permanently discontinue RETACRIT® and administer appropriate therapy if a serious allergic or anaphylactic reaction occurs

SEVERE CUTANEOUS REACTIONS

- 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 epoetin alfa) in the postmarketing setting. Discontinue RETACRIT® therapy immediately if a severe cutaneous reaction, such as SJS/TEN, is suspected

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RETACRIT displayed similar transfusion rates to Epogen®/Procrit® (epoetin alfa)[4,13,14]

Secondary analyses of 7 endpoints conducted on the ITT population provided supportive results for the conclusion of no clinically meaningful differences between RETACRIT and Epogen/Procrit*

- Mean weekly Hb level†
- Mean weekly epoetin dose per kg body weight†
- Mean weekly Hb level over each 4-week interval‡
- Mean weekly epoetin dose per kg body weight over each 4-week interval‡
- Total epoetin dose†
- Proportion of subjects within and outside the target range for mean weekly Hb of 9.0 g/dL to 11.0 g/dL†
- Proportion of subjects who received blood transfusions†

*For SC (16-week Treatment Period) and IV (24-week Treatment Period) clinical studies.
†No statistically significant difference was observed between treatment groups.
‡Results were comparable; no test for statistical significance was performed.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

RISK OF SERIOUS ADVERSE REACTIONS DUE TO BENZYL ALCOHOL PRESERVATIVE

- RETACRIT® from multiple-dose vials contains benzyl alcohol and is contraindicated for use in neonates, infants, pregnant women, and lactating women. In addition, do not mix RETACRIT® with bacteriostatic saline (which also contains benzyl alcohol) when administering RETACRIT® to these patient populations
- Serious and fatal reactions including "gasping syndrome" can occur in neonates and infants treated with benzyl alcohol-preserved drugs, including RETACRIT® multiple-dose vials. The "gasping syndrome" is characterized by central nervous system depression, metabolic acidosis, and gasping respirations. There is a potential for similar risks to fetuses and infants exposed to benzyl alcohol in utero or in breastfed milk, respectively. RETACRIT® multiple-dose vials contain 8.5 mg of benzyl alcohol per mL. The minimum amount of benzyl alcohol at which serious adverse reactions may occur is not known

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RETACRIT showed a comparable incidence of AEs of special interest[9]

No clinically meaningful differences were noted between RETACRIT and Epogen®/Procrit® (epoetin alfa) in the incidence of AEs of special interest, including severe and serious AEs

Incidence of AEs of special interest

AE of Special Interest Category	SC and IV Studies	
	Epogen/Procrit Randomized (n=426) [n (%)]	RETACRIT Randomized (n=423) [n (%)]
Thromboembolic events	26 (6.1%)	32 (7.6%)
Cerebrovascular events	6 (1.4%)	4 (0.9%)
Myocardial infarction	3 (0.7%)	4 (0.9%)

- No new safety signals were identified in RETACRIT compared to the known AE profile of Epogen/Procrit

FDA-approved RETACRIT is similar to Epogen/Procrit, with no clinically meaningful differences in terms of safety, purity, or potency.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

RISK IN PATIENTS WITH PHENYLKETONURIA

- Phenylalanine can be harmful to patients with phenylketonuria (PKU). RETACRIT® single-dose vials contain phenylalanine, a component of aspartame. Each 1 mL single-dose vial of 2,000, 3,000, 4,000, 10,000, and 40,000 Units of epoetin alfa-epbx injection contains 0.5 mg of phenylalanine. Before prescribing RETACRIT® single-dose vials to a patient with PKU, consider the combined daily amount of phenylalanine from all sources, including RETACRIT®

DIALYSIS MANAGEMENT

- Patients may require adjustments in their dialysis prescriptions after initiation of RETACRIT®. Patients receiving RETACRIT® may require increased anticoagulation with heparin to prevent clotting of the extracorporeal circuit during hemodialysis

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RETACRIT showed a similar safety profile to Epogen®/Procrit® (epoetin alfa) across AE categories[9,13,14]

In comparative studies, RETACRIT showed comparable incidence of most common AEs

Frequency of common AEs (≥5%) across SC and IV studies

System Class	SC Study in CKD		IV Study in CKD	
	Epogen/Procrit Randomized (n=122) [n (%)]	RETACRIT Randomized (n=122) [n (%)]	Epogen/Procrit Randomized (n=304) [n (%)]	RETACRIT Randomized (n=301) [n (%)]
Subjects with ≥1 TEAE	86 (71%)	85 (70%)	229 (75%)	232 (77%)
Nausea	8 (7%)	10 (8%)	25 (8%)	30 (10%)
Fall	3 (2%)	8 (7%)	–	–
Pyrexia	4 (3%)	8 (7%)	–	–
AV fistula	4 (3%)	6 (5%)	25 (8%)	26 (9%)
Headache	3 (2%)	6 (5%)	16 (5%)	23 (8%)
Pain in extremity	5 (4%)	6 (5%)	17 (6%)	10 (3%)

TEAE=treatment-emergent adverse event.

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SELECTED SAFETY INFORMATION

ANEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE

- Adverse reactions in ≥5% of epoetin alfa-treated patients on dialysis were hypertension, arthralgia, muscle spasm, pyrexia, dizziness, medical device malfunction, vascular occlusion and upper respiratory tract infection

ANEMIA DUE TO CHEMOTHERAPY IN PATIENTS WITH CANCER

- Adverse reactions in ≥5% of epoetin alfa-treated patients in clinical studies were nausea, vomiting, myalgia, arthralgia, stomatitis, cough, weight decrease, leukopenia, bone pain, rash, hyperglycemia, insomnia, headache, depression, dysphagia, hypokalemia, and thrombosis

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RETACRIT showed a similar safety profile to Epogen®/Procrit® (epoetin alfa) across AE categories[9,13,14]

In comparative studies, RETACRIT showed comparable incidence of most common AEs

Frequency of common AEs (≥5%) across SC and IV studies

System Class	SC Study in CKD		IV Study in CKD	
	Epogen/Procrit Randomized (n=122) [n (%)]	RETACRIT Randomized (n=122) [n (%)]	Epogen/Procrit Randomized (n=304) [n (%)]	RETACRIT Randomized (n=301) [n (%)]
Dizziness	9 (7%)	3 (2%)	15 (5%)	20 (7%)
Injection site pain	8 (7%)	3 (2%)	–	–
Vomiting	6 (5%)	4 (3%)	15 (5%)	28 (9%)
Hyperkalemia	6 (5%)	3 (2%)	12 (4%)	14 (5%)
Hypoglycemia	6 (5%)	1 (1%)	–	–
Muscle spasms	–	–	24 (8%)	27 (9%)
Dyspnea	–	–	21 (7%)	22 (7%)
Diarrhea	–	–	27 (9%)	21 (7%)

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

SURGERY/PERISURGERY

- Adverse reactions in ≥5% of epoetin alfa-treated patients in clinical studies were nausea, vomiting, pruritus, headache, injection site pain, chills, deep vein thrombosis, cough, and hypertension

ANEMIA DUE TO ZIDOVUDINE IN PATIENTS WITH HIV INFECTION

- Adverse reactions in ≥5% of epoetin alfa-treated patients in clinical studies were pyrexia, cough, rash, and injection site irritation

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RETACRIT showed a similar safety profile to Epogen®/Procrit® (epoetin alfa) across AE categories[9,13,14]

In comparative studies, RETACRIT showed comparable incidence of most common AEs

Frequency of common AEs (≥5%) across SC and IV studies

System Class	SC Study in CKD		IV Study in CKD	
	Epogen/Procrit Randomized (n=122) [n (%)]	RETACRIT Randomized (n=122) [n (%)]	Epogen/Procrit Randomized (n=304) [n (%)]	RETACRIT Randomized (n=301) [n (%)]
Hypertension	–	–	12 (4%)	19 (6%)
Cough	–	–	22 (7%)	16 (5%)
Hypotension	–	–	23 (8%)	14 (5%)
Noncardiac chest pain	–	–	17 (6%)	7 (2%)
Back pain	–	–	16 (5%)	12 (4%)

- In patients with CKD on hemodialysis, the incidence of the common (≥5%) TEAEs associated with epoetin alfa use showed no clinically meaningful differences between RETACRIT and Epogen/Procrit[4]

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS: 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**

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*No clinically meaningful differences in immunogenicity risk between RETACRIT and Epogen®/Procrit® (epoetin alfa)[9]**

No neutralizing ADAs were detected in the clinical confirmatory and PK/PD studies, and no apparent impact of ADA on safety, PK, or PD endpoints was observed

- Incidence of immunogenicity for RETACRIT vs Epogen/Procrit was compared in 3 clinical trials in patients with CKD and in healthy subjects
- No instances of PRCA were observed in either group

ADA=antidrug antibody; PRCA=pure red cell aplasia.
*No samples tested positive for neutralizing antibodies. There was no apparent impact of ADA status on reported AEs in patients from any of the studies.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

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

CHRONIC KIDNEY DISEASE (CONTINUED)

- Use the lowest RETACRIT® dose sufficient to reduce the need for red blood cell (RBC) transfusions

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Important Safety Information and Indications

WARNINGS: 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 RETACRIT® 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

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

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

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

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Important Safety Information and Indications

CONTRAINDICATIONS

RETACRIT® is contraindicated in patients with:

- Uncontrolled hypertension
- Pure red cell aplasia (PRCA) that begins after treatment with RETACRIT® or other erythropoietin protein drugs
- Serious allergic reactions to RETACRIT® or other epoetin alfa products

RETACRIT® from multiple-dose vials contains benzyl alcohol and is contraindicated in:

- Neonates, infants, pregnant women, and lactating women. When therapy with RETACRIT® is needed in these patient populations, use single-dose vials; do not admix with bacteriostatic saline containing benzyl alcohol

INCREASED MORTALITY, MYOCARDIAL INFARCTION, STROKE, AND THROMBOEMBOLISM

- In controlled clinical trials of patients with chronic kidney disease (CKD) comparing higher hemoglobin targets (13 - 14 g/dL) to lower targets (9 - 11.3 g/dL), epoetin alfa increased the risk of death, myocardial infarction, stroke, congestive heart failure, thrombosis of hemodialysis vascular access, and other thromboembolic events in the higher target groups
- Using ESAs to target a hemoglobin level of greater than 11 g/dL increases the risk of serious adverse cardiovascular reactions and has not been shown to provide additional benefit. 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 greater than 1 g/dL over 2 weeks may contribute to these risks
- In controlled clinical trials of patients with cancer, epoetin alfa increased the risks for death and serious adverse cardiovascular reactions. These adverse reactions included myocardial infarction and stroke
- 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

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

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

CANCER (CONTINUED)

- **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**

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Important Safety Information and Indications

INCREASED MORTALITY AND/OR INCREASED RISK OF TUMOR PROGRESSION OR RECURRENCE IN PATIENTS WITH CANCER

- ESAs resulted in decreased locoregional control/progression-free survival (PFS) and/or overall survival (OS). Adverse effects on PFS and/or OS were observed in studies of patients receiving chemotherapy for breast cancer, lymphoid malignancy, and cervical cancer; in patients with advanced head and neck cancer receiving radiation therapy; and in patients with non-small cell lung cancer or various malignancies who were not receiving chemotherapy or radiotherapy

HYPERTENSION

- RETACRIT® is contraindicated in patients with uncontrolled hypertension. Following initiation and titration of epoetin alfa, approximately 25% of patients on dialysis required initiation of or increases in antihypertensive therapy; hypertensive encephalopathy and seizures have been reported in patients with CKD receiving RETACRIT®
- Appropriately control hypertension prior to initiation of and during treatment with RETACRIT®. Reduce or withhold RETACRIT® if blood pressure becomes difficult to control. Advise patients of the importance of compliance with antihypertensive therapy and dietary restrictions

SEIZURES

- Epoetin alfa products, including RETACRIT®, increase the risk of seizures in patients with CKD. During the first several months following initiation of RETACRIT®, monitor patients closely for premonitory neurologic symptoms. Advise patients to contact their healthcare practitioner for new-onset seizures, premonitory symptoms or change in seizure frequency

LACK OR LOSS OF HEMOGLOBIN RESPONSE TO RETACRIT®

- For lack or loss of hemoglobin response to RETACRIT®, initiate a search for causative factors (eg, iron deficiency, infection, inflammation, bleeding). If typical causes of lack or loss of hemoglobin response are excluded, evaluate for PRCA. In the absence of PRCA, follow dosing recommendations for management of patients with an insufficient hemoglobin response to RETACRIT® therapy

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

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

PERISURGERY

- **Due to increased risk of deep venous thrombosis (DVT), DVT prophylaxis is recommended**

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Important Safety Information and Indications

PURE RED CELL APLASIA

- 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 epoetin alfa. 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 RETACRIT® is not approved)
- If severe anemia and low reticulocyte count develop during treatment with RETACRIT®, withhold RETACRIT® and evaluate patients for neutralizing antibodies to erythropoietin. **Contact Pfizer Inc. at 1-800-438-1985 to perform assays for binding and neutralizing antibodies.** Permanently discontinue RETACRIT® in patients who develop PRCA following treatment with RETACRIT® or other erythropoietin protein drugs. Do not switch patients to other ESAs

SERIOUS ALLERGIC REACTIONS

- Serious allergic reactions, including anaphylactic reactions, angioedema, bronchospasm, skin rash, and urticaria may occur with epoetin alfa products. Immediately and permanently discontinue RETACRIT® and administer appropriate therapy if a serious allergic or anaphylactic reaction occurs

SEVERE CUTANEOUS REACTIONS

- 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 epoetin alfa) in the postmarketing setting. Discontinue RETACRIT® therapy immediately if a severe cutaneous reaction, such as SJS/TEN, is suspected

RISK OF SERIOUS ADVERSE REACTIONS DUE TO BENZYL ALCOHOL PRESERVATIVE

- RETACRIT® from multiple-dose vials contains benzyl alcohol and is contraindicated for use in neonates, infants, pregnant women, and lactating women. In addition, do not mix RETACRIT® with bacteriostatic saline (which also contains benzyl alcohol) when administering RETACRIT® to these patient populations

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION
CONTRAINDICATIONS

RETACRIT® is contraindicated in patients with:

- Uncontrolled hypertension
- Pure red cell aplasia (PRCA) that begins after treatment with RETACRIT® or other erythropoietin protein drugs
- Serious allergic reactions to RETACRIT® or other epoetin alfa products

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Important Safety Information and Indications

- Serious and fatal reactions including "gasping syndrome" can occur in neonates and infants treated with benzyl alcohol-preserved drugs, including RETACRIT® multiple-dose vials. The "gasping syndrome" is characterized by central nervous system depression, metabolic acidosis, and gasping respirations. There is a potential for similar risks to fetuses and infants exposed to benzyl alcohol in utero or in breastfed milk, respectively. RETACRIT® multiple-dose vials contain 8.5 mg of benzyl alcohol per mL. The minimum amount of benzyl alcohol at which serious adverse reactions may occur is not known

RISK IN PATIENTS WITH PHENYLKETONURIA

- Phenylalanine can be harmful to patients with phenylketonuria (PKU). RETACRIT® single-dose vials contain phenylalanine, a component of aspartame. Each 1 mL single-dose vial of 2,000, 3,000, 4,000, 10,000, and 40,000 Units of epoetin alfa-epbx injection contains 0.5 mg of phenylalanine. Before prescribing RETACRIT® single-dose vials to a patient with PKU, consider the combined daily amount of phenylalanine from all sources, including RETACRIT®

DIALYSIS MANAGEMENT

- Patients may require adjustments in their dialysis prescriptions after initiation of RETACRIT®. Patients receiving RETACRIT® may require increased anticoagulation with heparin to prevent clotting of the extracorporeal circuit during hemodialysis

ANEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE

- Adverse reactions in ≥5% of epoetin alfa-treated patients on dialysis were hypertension, arthralgia, muscle spasm, pyrexia, dizziness, medical device malfunction, vascular occlusion and upper respiratory tract infection

ANEMIA DUE TO CHEMOTHERAPY IN PATIENTS WITH CANCER

- Adverse reactions in ≥5% of epoetin alfa-treated patients in clinical studies were nausea, vomiting, myalgia, arthralgia, stomatitis, cough, weight decrease, leukopenia, bone pain, rash, hyperglycemia, insomnia, headache, depression, dysphagia, hypokalemia, and thrombosis

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION
CONTRAINDICATIONS (CONTINUED)

RETACRIT® from multiple-dose vials contains benzyl alcohol and is contraindicated in:

- Neonates, infants, pregnant women, and lactating women. When therapy with RETACRIT® is needed in these patient populations, use single-dose vials; do not admix with bacteriostatic saline containing benzyl alcohol

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Important Safety Information and Indications

SURGERY/PERISURGERY

- Adverse reactions in ≥5% of epoetin alfa-treated patients in clinical studies were nausea, vomiting, pruritus, headache, injection site pain, chills, deep vein thrombosis, cough, and hypertension

ANEMIA DUE TO ZIDOVUDINE IN PATIENTS WITH HIV INFECTION

- Adverse reactions in ≥5% of epoetin alfa-treated patients in clinical studies were pyrexia, cough, rash, and injection site irritation

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

INCREASED MORTALITY, MYOCARDIAL INFARCTION, STROKE, AND THROMBOEMBOLISM

- In controlled clinical trials of patients with chronic kidney disease (CKD) comparing higher hemoglobin targets (13 - 14 g/dL) to lower targets (9 - 11.3 g/dL), epoetin alfa increased the risk of death, myocardial infarction, stroke, congestive heart failure, thrombosis of hemodialysis vascular access, and other thromboembolic events in the higher target groups
- Using ESAs to target a hemoglobin level of greater than 11 g/dL increases the risk of serious adverse cardiovascular reactions and has not been shown to provide additional benefit. 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 greater than 1 g/dL over 2 weeks may contribute to these risks

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Important Safety Information and Indications

INDICATIONS

ANEMIA DUE TO CHRONIC KIDNEY DISEASE

RETACRIT® is indicated for the treatment of anemia due to CKD, including patients on dialysis and not on dialysis, to decrease the need for RBC transfusion.

ANEMIA DUE TO ZIDOVUDINE IN PATIENTS WITH HIV INFECTION

RETACRIT® is indicated for the treatment of anemia due to zidovudine administered at ≤4,200 mg/week in patients with HIV infection with endogenous serum erythropoietin levels of ≤500 mUnits/mL.

ANEMIA DUE TO CHEMOTHERAPY IN PATIENTS WITH CANCER

RETACRIT® is indicated for the treatment of anemia in patients with nonmyeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

REDUCTION OF ALLOGENEIC RED BLOOD CELL TRANSFUSIONS IN PATIENTS UNDERGOING ELECTIVE, NONCARDIAC, NONVASCULAR SURGERY

RETACRIT® is indicated to reduce the need for allogeneic RBC transfusions among patients with perioperative hemoglobin >10 to ≤13 g/dL who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery. RETACRIT® is not indicated for patients who are willing to donate autologous blood preoperatively.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

INCREASED MORTALITY, MYOCARDIAL INFARCTION, STROKE, AND THROMBOEMBOLISM (CONTINUED)

- In controlled clinical trials of patients with cancer, epoetin alfa increased the risks for death and serious adverse cardiovascular reactions. These adverse reactions included myocardial infarction and stroke
- 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

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Important Safety Information and Indications

Limitations of Use

RETACRIT® has not been shown to improve quality of life, fatigue, or patient well-being.

RETACRIT® is not indicated for use:

- In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy
- In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure
- In patients with cancer receiving myelosuppressive chemotherapy in whom the anemia can be managed by transfusion
- In patients scheduled for surgery who are willing to donate autologous blood
- In patients undergoing cardiac or vascular surgery
- As a substitute for RBC transfusions in patients who require immediate correction of anemia

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

INCREASED MORTALITY AND/OR INCREASED RISK OF TUMOR PROGRESSION OR RECURRENCE IN PATIENTS WITH CANCER

- ESAs resulted in decreased locoregional control/progression-free survival (PFS) and/or overall survival (OS). Adverse effects on PFS and/or OS were observed in studies of patients receiving chemotherapy for breast cancer, lymphoid malignancy, and cervical cancer; in patients with advanced head and neck cancer receiving radiation therapy; and in patients with non-small cell lung cancer or various malignancies who were not receiving chemotherapy or radiotherapy

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Summary
References

RETACRIT: Pfizer Oncology's commitment to building onto the clinical experience of epoetin alfa

Pfizer

With the largest portfolio of oncology biosimilars—including RETACRIT—Pfizer is committed to expanding options for patient care[3]

Favorable coverage[4]

Potential savings[4]

Support for you and your patients

Approved for all eligible indications of Epogen®/Procrit® (epoetin alfa), with an identical dosing and administration schedule[2]

Realize the full potential of biosimilars. Ask about the Pfizer biosimilar portfolio.

Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

HYPERTENSION

- RETACRIT® is contraindicated in patients with uncontrolled hypertension. Following initiation and titration of epoetin alfa, approximately 25% of patients on dialysis required initiation of or increases in antihypertensive therapy; hypertensive encephalopathy and seizures have been reported in patients with CKD receiving RETACRIT®
- Appropriately control hypertension prior to initiation of and during treatment with RETACRIT®. Reduce or withhold RETACRIT® if blood pressure becomes difficult to control. Advise patients of the importance of compliance with antihypertensive therapy and dietary restrictions

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Summary

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Please see Important Safety Information and Indications on pages 39-46 and full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at RetacritHCP.com.

SELECTED SAFETY INFORMATION

SEIZURES

- Epoetin alfa products, including RETACRIT®, increase the risk of seizures in patients with CKD. During the first several months following initiation of RETACRIT®, monitor patients closely for premonitory neurologic symptoms. Advise patients to contact their healthcare practitioner for new-onset seizures, premonitory symptoms or change in seizure frequency

LACK OR LOSS OF HEMOGLOBIN RESPONSE TO RETACRIT®

- For lack or loss of hemoglobin response to RETACRIT®, initiate a search for causative factors (eg, iron deficiency, infection, inflammation, bleeding). If typical causes of lack or loss of hemoglobin response are excluded, evaluate for PRCA. In the absence of PRCA, follow dosing recommendations for management of patients with an insufficient hemoglobin response to RETACRIT® therapy

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