



Aranesp[®]
(darbepoetin alfa)

EPOGEN[®]
(EPOETIN ALFA)
RECOMBINANT

PROCRIT[®]
EPOETIN ALFA



Assisting **P**roviders and cancer **P**atients with
Risk Information for the **S**afe use of **ESA**s

Training Module for Hospital Designees

Training Module for Hospital Designees

Erythropoiesis Stimulating Agents (ESAs) are used to treat anemia for patients with cancer where anemia is due to the effect of concomitant myelosuppressive chemotherapy and include Aranesp® (darbepoetin alfa), Epogen® (epoetin alfa), and Procrit® (epoetin alfa). The Food and Drug Administration (FDA) has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for ESAs used to treat patients with cancer to ensure that the benefits of these drugs outweigh the risks of shortened overall survival and/or increased risk of tumor progression or recurrence as shown in clinical studies of patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers.

The ESA APPRISE (Assisting Providers and cancer Patients with Risk Information for the Safe use of ESAs) Oncology Program is part of the REMS. This Training Module is required for certification in the ESA APPRISE Oncology Program and is intended for Hospital Designees at hospitals that dispense ESAs for patients with cancer.

The goal of the REMS for Aranesp® and Epogen®/Procrit® is:

To support informed discussions between patients with cancer and their healthcare providers by:

- educating healthcare providers about the risks and safe use conditions of ESAs for patients with cancer.
- informing patients about the risk of shortened overall survival and/or increased risk of tumor progression or recurrence when ESAs are used to treat anemia due to concomitant myelosuppressive chemotherapy.

Failure to comply with the ESA APPRISE Oncology Program requirements will result in suspension of the hospital's access to ESAs

This training module, as a component of this REMS Program, presents the requirements for healthcare providers (HCPs) who prescribe, or prescribe and dispense, Aranesp®, Epogen®, or Procrit® for patients with cancer as well as the requirements for Hospital Designees who must oversee implementation of this safety program at their respective Hospitals.

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: 3429792
Strategy (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs

Training Module for Hospital Designees

This Training Module features four sections:

Section 1: Key safety information for the use of ESAs for patients with cancer

Section 2: Appropriate use of ESAs for patients with cancer

Section 3: HCP and Hospital Designee Program requirements and materials

Section 4: Enrollment

Please see the Aranesp®, Epogen®, and Procrit® prescribing information, including **Boxed WARNINGS** and Medication Guides available at www.esa-apprise.com.

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: 3429792
and REMS for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs

SECTION 1

KEY SAFETY INFORMATION FOR USE OF ESAs FOR PATIENTS WITH CANCER

Section 1

Key Safety Information for Use of ESAs for Patients With Cancer

ESAs resulted in decreased locoregional control/progression-free survival and/or overall survival.

As shown in the table below, these findings were observed in studies of patients with advanced head and neck cancer receiving radiation therapy (Studies 5 and 6), in patients receiving chemotherapy for metastatic breast cancer (Study 1) or lymphoid malignancy (Study 2), and in patients with non-small cell lung cancer or various malignancies who were not receiving chemotherapy or radiotherapy (Studies 7 and 8).

Study/Tumor/(n)	Hemoglobin Target	Hemoglobin (Median; Q1, Q3*)	Primary Efficacy Outcome	Adverse Outcome for ESA-Containing Arm
Chemotherapy				
Study 1 Metastatic breast cancer (n = 939)	12–14 g/dL	12.9 g/dL; 12.2, 13.3 g/dL	12-month overall survival	Decreased 12-month survival
Study 2 Lymphoid malignancy (n = 344)	13–15 g/dL (M) 13–14 g/dL (F)	11 g/dL; 9.8, 12.1 g/dL	Proportion of patients achieving a hemoglobin response	Decreased overall survival
Study 3 Early breast cancer (n = 733)	12.5–13 g/dL	13.1 g/dL; 12.5, 13.7 g/dL	Relapse-free and overall survival	Decreased 3-year relapse-free and overall survival
Study 4 Cervical cancer (n = 114)	12–14 g/dL	12.7 g/dL; 12.1, 13.3 g/dL	Progression-free and overall survival and locoregional control	Decreased 3-year progression-free and overall survival and locoregional control
Radiotherapy Alone				
Study 5 Head and neck cancer (n = 351)	≥ 15 g/dL (M) ≥ 14 g/dL (F)	Not available	Locoregional progression-free survival	Decreased 5-year locoregional progression-free and overall survival
Study 6 Head and neck cancer (n = 522)	14–15.5 g/dL	Not available	Locoregional disease control	Decreased locoregional disease control
No Chemotherapy or Radiotherapy				
Study 7 Non-small cell lung cancer (n = 70)	12–14 g/dL	Not available	Quality of life	Decreased overall survival
Study 8 Non-myeloid malignancy (n = 989)	12–13 g/dL	10.6 g/dL; 9.4, 11.8 g/dL	RBC transfusions	Decreased overall survival

*Q1 = 25th percentile Q3 = 75th percentile

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: 3429792 (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with Risk Information for the Safe use of ESAs

Section 1

Key Safety Information for Use of ESAs for Patients With Cancer

Decreased Overall Survival

Study 1 was a randomized, placebo-controlled study of 939 women with metastatic breast cancer receiving chemotherapy; patients received either weekly epoetin alfa or placebo for up to a year. This study was designed to show that survival was superior when epoetin alfa was administered to prevent anemia (maintain hemoglobin levels between 12 and 14 g/dL or hematocrit between 36% and 42%). This study was terminated prematurely when interim results demonstrated a higher mortality at 4 months (8.7% vs. 3.4%) and a higher rate of fatal thrombotic reactions (1.1% vs. 0.2%) in the first 4 months of the study among patients treated with epoetin alfa. The most common investigator-attributed cause of death within the first 4 months was disease progression; 28 of 41 deaths in the epoetin alfa arm and 13 of 16 deaths in the placebo arm were attributed to disease progression. Investigator-assessed time to tumor progression was not different between the 2 groups. Survival at 12 months was significantly lower in the epoetin alfa arm (70% vs. 76%, HR 1.37, 95% CI: 1.07, 1.75; $p = 0.012$).

Study 2 was a randomized, double-blind study (darbepoetin alfa vs. placebo) conducted in 344 anemic patients with lymphoid malignancy receiving chemotherapy. With a median follow-up of 29 months, overall mortality rates were significantly higher among patients randomized to darbepoetin alfa as compared to placebo (HR 1.36, 95% CI: 1.02, 1.82).

Study 7 was a multicenter, randomized, double-blind study (epoetin alfa vs. placebo) in which patients with advanced non-small cell lung cancer receiving only palliative radiotherapy or no active therapy were treated with epoetin alfa to achieve and maintain hemoglobin levels between 12 and 14 g/dL. Following an interim analysis of 70 patients (planned accrual 300 patients), a significant difference in survival in favor of the patients in the placebo arm of the study was observed (median survival 63 vs. 129 days; HR 1.84; $p = 0.04$).

Study 8 was a randomized, double-blind study (darbepoetin alfa vs. placebo) in 989 anemic patients with active malignant disease, neither receiving nor planning to receive chemotherapy or radiation therapy. There was no evidence of a statistically significant reduction in proportion of patients receiving RBC transfusions. The median survival was shorter in the darbepoetin alfa treatment group than in the placebo group (8 months vs. 10.8 months; HR 1.30, 95% CI: 1.07, 1.57).

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: 3429792
and Mitigation Strategy (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs

Section 1

Key Safety Information for Use of ESAs for Patients With Cancer

Decreased Progression-free Survival and Overall Survival

Study 3 was a randomized, open-label, controlled, factorial design study in which darbepoetin alfa was administered to prevent anemia in 733 women receiving neo-adjuvant breast cancer treatment. A final analysis was performed after a median follow-up of approximately 3 years. The 3-year survival rate was lower (86% vs. 90%; HR 1.42, 95% CI: 0.93, 2.18) and the 3-year relapse-free survival rate was lower (72% vs. 78%; HR 1.33, 95% CI: 0.99, 1.79) in the darbepoetin alfa-treated arm compared to the control arm.

Study 4 was a randomized, open-label, controlled study that enrolled 114 of a planned 460 cervical cancer patients receiving chemotherapy and radiotherapy. Patients were randomized to receive epoetin alfa to maintain hemoglobin between 12 and 14 g/dL or to RBC transfusion support as needed. The study was terminated prematurely due to an increase in thromboembolic adverse reactions in epoetin alfa-treated patients compared to control (19% vs. 9%). Both local recurrence (21% vs. 20%) and distant recurrence (12% vs. 7%) were more frequent in epoetin alfa-treated patients compared to control. Progression-free survival at 3 years was lower in the epoetin alfa-treated group compared to control (59% vs. 62%; HR 1.06, 95% CI: 0.58, 1.91). Overall survival at 3 years was lower in the epoetin alfa-treated group compared to control (61% vs. 71%; HR 1.28, 95% CI: 0.68, 2.42).

Study 5 was a randomized, placebo-controlled study in 351 head and neck cancer patients where epoetin beta or placebo was administered to achieve target hemoglobins ≥ 14 and ≥ 15 g/dL for women and men, respectively. Locoregional progression-free survival was significantly shorter in patients receiving epoetin beta (HR 1.62, 95% CI: 1.22, 2.14; $p = 0.0008$) with medians of 406 days and 745 days in the epoetin beta and placebo arms respectively. Overall survival was significantly shorter in patients receiving epoetin beta (HR 1.39, 95% CI: 1.05, 1.84; $p = 0.02$).

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: 3429792
and Mitigation Strategy (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs

Section 1

Key Safety Information for Use of ESAs for Patients With Cancer

Decreased Locoregional Control

Study 6 was a randomized, open-label, controlled study conducted in 522 patients with primary squamous cell carcinoma of the head and neck receiving radiation therapy alone (no chemotherapy) who were randomized to receive darbepoetin alfa to maintain hemoglobin levels of 14 to 15.5 g/dL or no darbepoetin alfa. An interim analysis performed on 484 patients demonstrated that locoregional control at 5 years was significantly shorter in patients receiving darbepoetin alfa (RR 1.44, 95% CI: 1.06, 1.96; p = 0.02). Overall survival was shorter in patients receiving darbepoetin alfa (RR 1.28, 95% CI: 0.98, 1.68; p = 0.08).

Please see the full prescribing information for Aranesp® (darbepoetin alfa), Epogen® (epoetin alfa), or Procrit® (epoetin alfa) for other risks associated with these ESAs, including other Warnings and Precautions, and Adverse Reactions.

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

and Mitigation Strategy (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with Risk Information for the Safe use of ESAs

SECTION 2

APPROPRIATE USE OF ESAs FOR PATIENTS WITH CANCER

Section 2

Appropriate Use of ESAs for Patients With Cancer

- ESAs are indicated for the treatment of anemia in patients with non-myeloid 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.
- ESAs are 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.
 - as a substitute for RBC transfusions in patients who require immediate correction of anemia.
- ESAs have not been shown to improve quality of life, fatigue, or patient well-being.

Important Dosing and Treatment Information

- Initiate ESAs in patients on cancer chemotherapy only if the hemoglobin is less than 10 g/dL.
- Use the lowest dose of ESAs necessary to avoid RBC transfusions.
- Discontinue ESAs following the completion of a chemotherapy course.

Please see the Aranesp®, Epogen®, and Procrit® prescribing information, including **Boxed WARNINGS** and Medication Guides available at www.esa-apprise.com.

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: 3429792
and Mitigation Strategy (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs

Section 2

Hospital Designee Knowledge Check

Answer true or false to the following statements:

- 1** **True or False:** ESAs are not indicated for the treatment of anemia in patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
- 2** **True or False:** Initiate ESAs in patients with cancer receiving myelosuppressive chemotherapy only when hemoglobin level is less than 11 g/dL.
- 3** **True or False:** ESAs should be discontinued following the completion of a chemotherapy course.

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: 3429792 (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs

Section 2

Answers to the Hospital Designee Knowledge Check

- 1 TRUE** The correct statement is: ESAs are not indicated for the treatment of anemia in patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
- 2 FALSE** The correct statement is: Initiate ESAs in patients with cancer receiving myelosuppressive chemotherapy only when hemoglobin level is less than 10 g/dL.
- 3 TRUE** The correct statement is: ESAs should be discontinued following the completion of a chemotherapy course.

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

and Mitigation Strategy (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs

SECTION 3
PROGRAM REQUIREMENTS
AND MATERIALS FOR
HEALTHCARE PROVIDERS
AND HOSPITAL DESIGNEES



Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs

Section 3

Program Requirements and Materials for Healthcare Providers and Hospital Designees

HCP requirements for patient counseling

The ESA APPRISE Oncology Program requires HCPs to counsel patients in the following manner:

- Counsel each patient on the risks (increased risk of mortality and increased risk of tumor progression or recurrence) of Aranesp® or Epogen®/Procrit® before each new course of ESA therapy by reviewing the Acknowledgment Form.
- Discuss each patient's questions or concerns about ESAs.
- Document that the risk:benefit discussion with each patient has occurred by completing the Acknowledgment Form with each patient and providing each patient a copy of the signed form.
 - Completed Acknowledgment Forms (or modified version consistent with the allowable changes) must be available to the ESA APPRISE Oncology Program for auditing purposes in a manner that does not require disclosure of the patient's medical record.
 - In a private practice-based clinic, store the forms on-site and/or archive them through an electronic medical records system as long as they are retrievable.
 - In a hospital, provide the completed Acknowledgment Form (or modified version consistent with the allowable changes) to the Hospital Designee responsible for maintaining and storing the forms.

ESA APPRISE Oncology Program Patient and Healthcare Provider Acknowledgment Form (Acknowledgment Form)

Aranesp® (darbepoetin alfa), Epogen® (epoetin alfa), and Procrit® (epoetin alfa) are Erythropoiesis Stimulating Agents (ESAs) used for patients with cancer.

Instructions for Healthcare Providers

- 1 Counsel the patient on the risks and benefits of Aranesp® or Epogen®/Procrit® before each new course of ESA therapy.
- 2 Complete each section of the form as required with the patient.
- 3 Provide a copy of the signed form to the patient.
- 4 Make completed Acknowledgment Forms available to the ESA APPRISE Oncology Program (Program) for auditing purposes.
 - In a private practice-based clinic, store and archive the completed forms so that they are retrievable.
 - In a hospital, provide the completed forms to the Hospital Designee responsible for maintaining and storing the forms.

Patient Acknowledgment of ESA Benefits and Risks

Aranesp® and Epogen®/Procrit® are prescription medicines used to treat anemia. They are in a class of medicines called erythropoiesis stimulating agents, or ESAs. These medicines are different from each other, so your healthcare provider will decide which one is right for you.

Benefits: People with anemia have a lower-than-normal number of red blood cells (RBCs). ESAs work like the human protein called erythropoietin to help your body make more RBCs. ESAs are used to reduce or avoid the need for RBC transfusions.

Risks: ESAs may make my tumor grow faster and I may die sooner.

By signing this form, I acknowledge that my healthcare provider did the following before I received my first dose of an ESA:

- Told me about the benefits and risks of ESA therapy
- Answered all of my questions or concerns about my treatment with an ESA

Written Permission to Share Information

I permit my healthcare provider to share this form with Amgen and Janssen Products, LP (the Sponsors) and their contractors that manage certain aspects of the ESA APPRISE Oncology Program (the Contractors). The Program Sponsors and Contractors agree to keep my information secure. They will use it only to make sure Program rules are being followed.

I understand that:

- If I do not sign this form, I will not receive an ESA
- After my information has been shared with the Program Sponsors and Contractors, federal privacy laws no longer protect it. This means that the Sponsors and Contractors can give it to others, such as the Food and Drug Administration, to learn about Program effectiveness, as required by law
- I can cancel my permission at any time by providing written notice to my healthcare provider
- My permission lasts until the Program ends

Signature of patient or patient representative _____ Printed name of patient representative _____ Date (MM/DD/YYYY) _____

Printed patient name _____ Relationship to patient (if applicable) _____

Healthcare Provider Acknowledgment

I acknowledge that prior to the initiation of this new course of ESA therapy:

- I counseled the patient on the risks and benefits of ESAs by reviewing the Acknowledgment Form.
- I discussed all concerns and answered all questions the patient had about treatment with ESAs to the best of my ability.
- The patient or patient representative signed the Acknowledgment Form in my presence and I provided a copy of the signed Acknowledgment Form to the patient.

*Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules. Or modified version consistent with the allowable changes. Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP. VS 10/13

Healthcare Provider Enrollment ID#

Signature of Healthcare Provider _____

Printed name of Healthcare Provider _____

Date (MM/DD/YYYY) _____ (Pre-populated information) Site ID _____ Site Name _____ Site Address (Address, City, State, Zip) _____

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: A29792 (REMS) for Aranesp®, Epogen®, and Procrit®.

VS 10/13



Assisting Providers and cancer Patients with Risk Information for the Safe use of ESAs

Section 3

Program Requirements and Materials for Healthcare Providers and Hospital Designees

Hospital Designee Requirements

- Assume the authority and responsibility to internally coordinate and oversee implementation of the ESA APPRISE Oncology Program requirements in the hospital(s) for which you are responsible.
- Complete the Training Module for Hospital Designees.
- Understand that if HCPs in the hospital prescribe Aranesp® or Epogen®/Procrit® to patients with cancer, failure to comply with Program requirements will lead to suspension of access to ESAs for the hospital.
- Inform all HCPs who prescribe Aranesp® or Epogen®/Procrit® for patients with cancer at the hospital of the Program training and certification requirements.
- Establish or oversee the establishment of a system, order sets, protocols, or other measures designed to ensure that the hospital is in compliance with the ESA APPRISE Oncology Program, such that:
 - ESAs are only dispensed to patients with cancer after verifying:
 - that the HCP who prescribes ESAs for patients with cancer is certified in the Program; and
 - that the discussion between the patient and the Program-certified provider on the risks of ESA therapy is documented by patient and provider signatures on the ESA APPRISE Oncology Program Patient and Healthcare Provider Acknowledgment Form (Acknowledgment Form) prior to initiation of each new course of ESA therapy.
 - If an HCP who prescribes ESAs is not certified in the ESA APPRISE Oncology Program, the provider will be notified that they are not able to prescribe ESAs for patients with cancer.

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: 3429792 (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs

Section 3

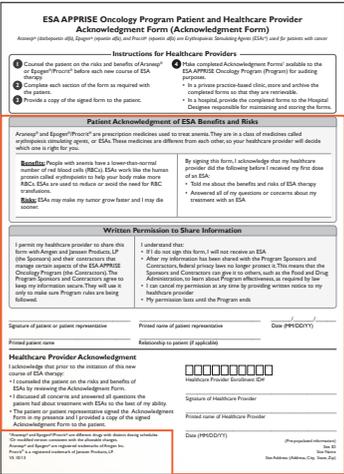
Program Requirements and Materials for Healthcare Providers and Hospital Designees

- To learn more about allowable changes to the Acknowledgment Form, please refer to the Guidelines for Acknowledgment Form Integration Within Healthcare Systems and Clinics flashcard accessible at www.esa-apprise.com in the Forms & Resources section.



Guidelines for Acknowledgment Form Integration Within Healthcare Systems and Clinics





The screenshot shows the Acknowledgment Form with several sections highlighted in red boxes. A red box around the top section (Instructions for Healthcare Providers) is linked to a text box on the right. Another red box around the bottom section (Healthcare Provider Acknowledgment) is linked to a text box at the bottom.

Hospitals and healthcare providers in private practice-based clinics that are certified in the ESA APPRISE Oncology Program may modify the ESA APPRISE Oncology Program Patient and Healthcare Provider Acknowledgment Form (Acknowledgment Form) and present the modified form to patients in either paper or electronic form, provided that the Acknowledgment Form conforms with the following criteria:

Allowable formatting-related changes include:

- Removal of title, instructions, and footnoted text
- Addition of patient identifier and/or clinic/hospital identifiers (eg, name and/or logo, barcodes)
- Changes to make the form compatible with existing systems, including electronic- and paper-based systems

NO changes should be made to boxed content

The hospital or private practice-based clinic must maintain evidence of compliance that the Acknowledgment Form was signed by both the patient or patient representative and the healthcare provider prior to the initiation of each new course of ESA therapy.

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP. This document has been required by the US Food and Drug Administration as part of a Risk Evaluation and Mitigation Strategy (REMS) for Aranesp®, Epogen®, and Procrit®.

V3 10/13



Assisting Providers and cancer Patients with Risk Information for the Safe Use of ESAs

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP. Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules. This document has been required by the US Food and Drug Administration as part of a Risk Evaluation and Mitigation Strategy (REMS) for Aranesp®, Epogen®, and Procrit®.

Section 3

Program Requirements and Materials for Healthcare Providers and Hospital Designees

- Oversee compliance with Program auditing to assess the effectiveness of the Program.
- Maintain evidence of compliance with the Program for auditing purposes, as follows:
 - Documentation (ie, unique enrollment ID number) that each HCP in the hospital who prescribes ESAs for patients with cancer is certified in the Program.
 - Documentation of the risk:benefit discussion between certified provider and patient on the Acknowledgment Form for each patient with cancer for whom an Aranesp® or Epogen®/Procrit® prescription was filled; the Acknowledgment Forms are to be stored on-site and/or archived in a retrievable manner.
 - Completed Acknowledgment Forms (or modified version consistent with the allowable changes) must be available to the ESA APPRISE Oncology Program for auditing purposes in a manner that does not require disclosure of the patient's medical record.

Please see the Aranesp®, Epogen® and Procrit® prescribing information, including **Boxed WARNINGS** and Medication Guides available at www.esa-apprise.com.

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: 3429792 (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs

Section 3

Program Requirements and Materials for Healthcare Providers and Hospital Designees

Failure to comply with the ESA APPRISE Oncology Program requirements will result in suspension of your access to ESAs

Upon completion of this enrollment process, you (and an alternate contact, if provided) will receive an email (or fax if no email address is provided) with the ESA APPRISE Oncology Program enrollment ID number unique to the hospital. This enrollment ID number allows you to identify HCPs enrolled at your location, by clicking “Login” at the top right of the ESA APPRISE Oncology Program website home page. You can also order more Program materials via www.esa-apprise.com using the hospital enrollment ID number.

Once you have enrolled, you will receive the following materials to assist HCPs in the hospital in implementing the Program:

- ESA APPRISE Oncology Program Patient and Healthcare Provider Acknowledgment Forms
- Guidelines for Acknowledgment Form Integration Within Healthcare Systems and Clinics
- Steps for Healthcare Providers who Prescribe, or Prescribe and Dispense, ESAs to Patients With Cancer
- Steps for Hospitals and Hospital/Institution-affiliated Outpatient Facilities That Dispense ESAs to Patients With Cancer

Should you have any questions during this training and enrollment process, call the ESA APPRISE Oncology Program Call Center at 1-866-284-8089 or contact your local Amgen or Janssen Products, LP Field Representative.

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: 3429792 (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with Risk Information for the Safe use of ESAs

SECTION 4

HOSPITAL DESIGNEE ENROLLMENT



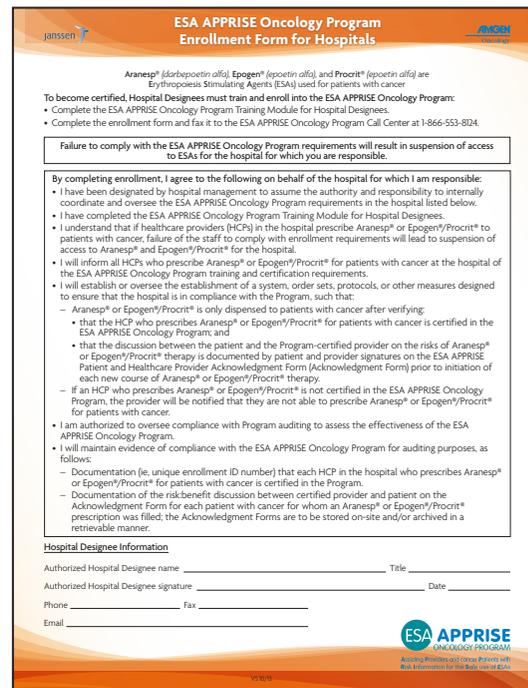
Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs

Section 4

Hospital Designee Enrollment

Now that you have completed the ESA APPRISE Oncology Program Training Module, you are ready to enroll. Enrollment confirms the fact that you have reviewed the safety and appropriate use information for ESAs for patients with cancer, and commits you to complying with the Program requirements.

Failure to comply with the ESA APPRISE Oncology Program requirements will result in suspension of your access to ESAs



The image shows a document titled "ESA APPRISE Oncology Program Enrollment Form for Hospitals". It includes the Janssen and Amgen logos at the top. The text defines Aranesp®, Epogen®, and Procrit® as Erythropoiesis Stimulating Agents (ESAs) used for cancer patients. It lists requirements for enrollment, such as completing training and the enrollment form. A prominent warning states that failure to comply will result in suspension of access. The form contains a large section for a declaration of compliance, followed by a "Hospital Designee Information" section with fields for name, title, signature, date, phone, fax, and email. The ESA APPRISE Oncology Program logo is at the bottom right.

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: 3429792 (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with Risk Information for the Safe use of ESAs

Aranesp® and Epogen® are registered trademarks of Amgen Inc. Procrit® is a registered trademark of Janssen Products, LP.

Aranesp® and Epogen®/Procrit® are different drugs with distinct dosing schedules.

This document has been required by the US Food and Drug Administration as part of a Risk Evaluation

Reference ID: A129792
and a REMS (REMS) for Aranesp®, Epogen®, and Procrit®.

V5 10/13



Assisting Providers and cancer Patients with
Risk Information for the Safe use of ESAs