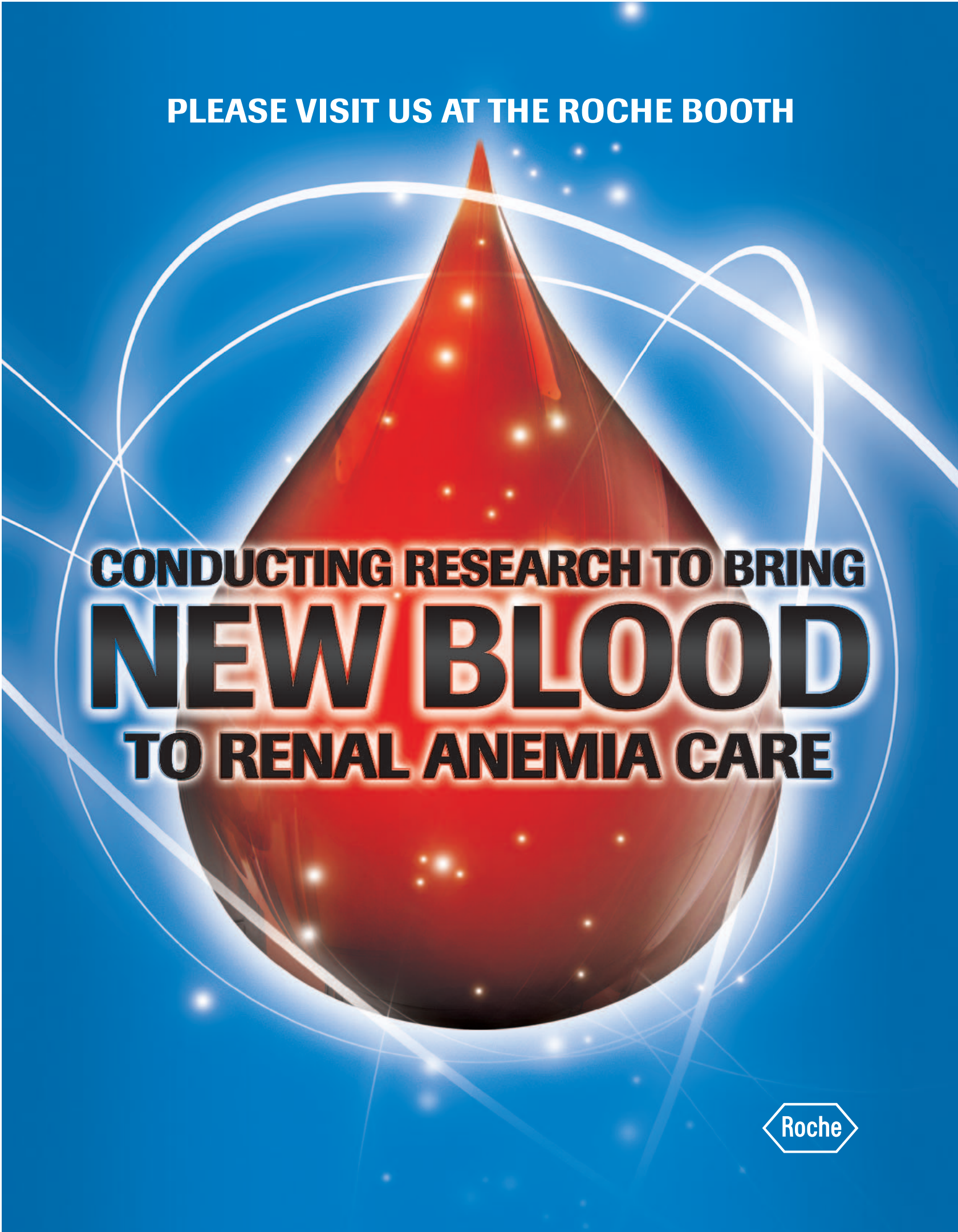
PLEASE VISIT US AT THE ROCHE BOOTH



Roche

***NEW** for the treatment of anemia associated with CKD*

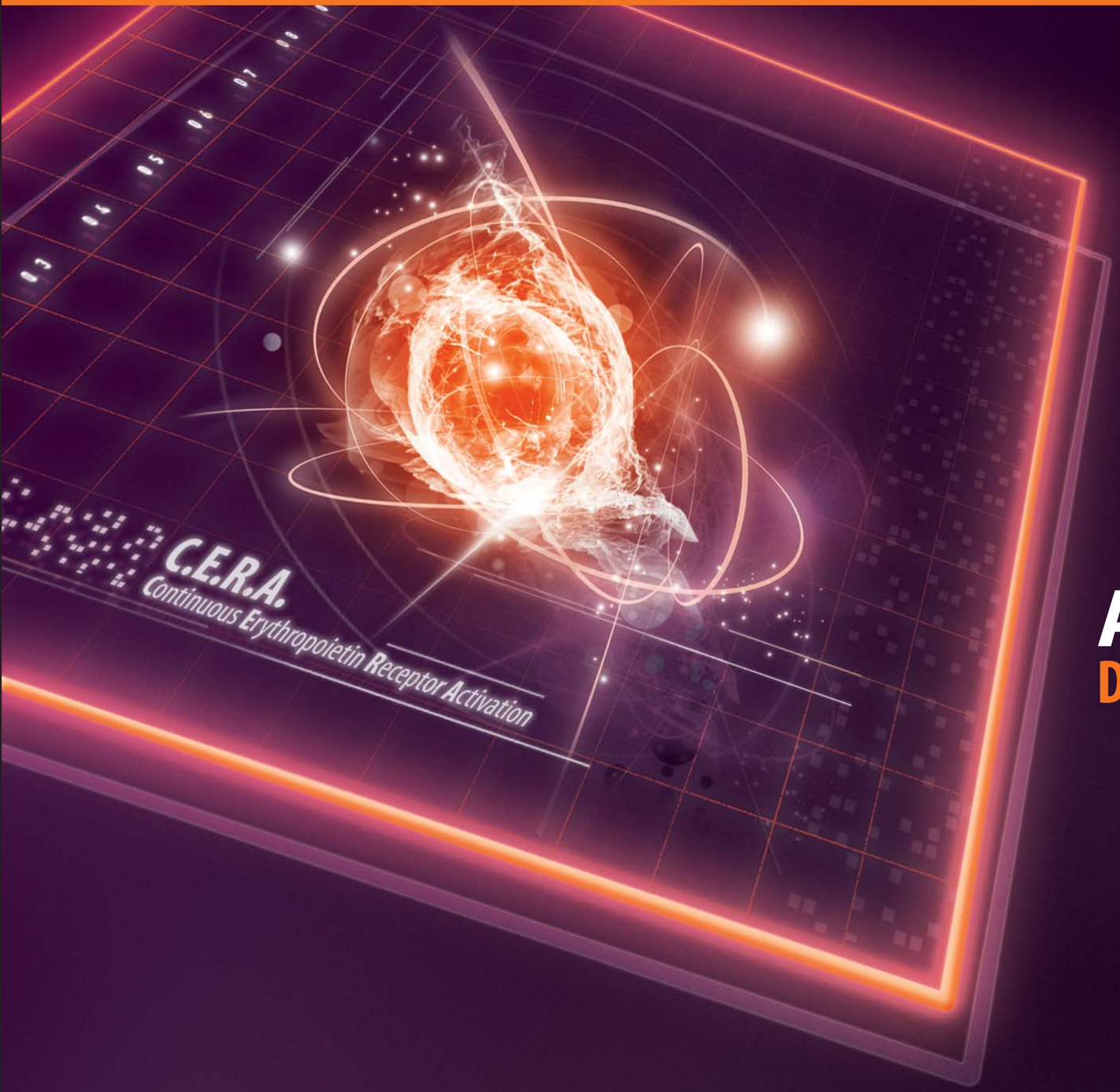
Now maintain Hb stability for

Fine-tuned patient care

***NEW** ONCE-MONTHLY*

MIRCERA®

***NEW** for CKD-related anemia*



A NOVEL FOUNDATION
DESIGNED FOR CONTINUOUS ACTIVATION

***NEW** ONCE-MONTHLY*
MIRCERA®

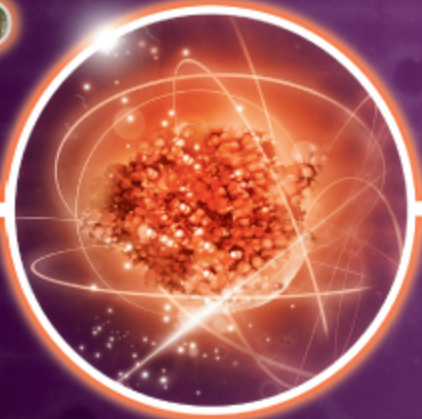
***NEW** for patients with CKD-related anemia*

***NEW** ONCE-MONTHLY*

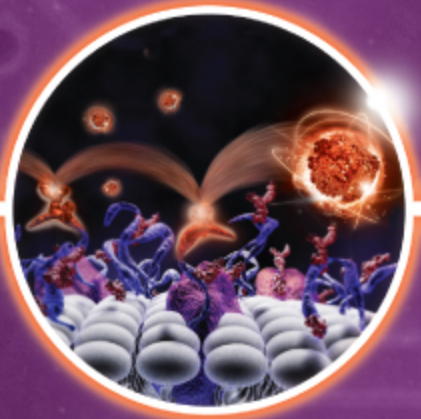
MIRCERA®

INNOVATION
THROUGH CONTINUOUS ACTIVATION

New MIRCERA maintains stable Hb levels within target range with once-monthly dosing



NOVEL, FIRST-IN-CLASS MOLECULE WITH A LONGER HALF-LIFE



UNIQUE CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATION

ONCE-MONTHLY DOSING TO DELIVER STABLE Hb CONTROL FOR ALL PATIENT TYPES

NEW ONCE-MONTHLY
MIRCERA®
pegzerepoetin alfa

NEW

MIRCERA®

methoxy polyethylene glycol-epoetin beta

Continuous activity. Targeted stability.

NOW AVAILABLE

FOR CKD-RELATED ANAEMIA

TARGETED Hb STABILITY

ONCE-MONTHLY MAINTENANCE FOR ALL ADULT PATIENTS[1-3*]

Introducing a new molecule for continuous activation[1,4,5]

*For medical contraindications, please refer to Prescribing Information.

Brief Prescribing Information

MIRCERA® (methoxy polyethylene glycol-epoetin beta)

50, 75, 100, 150, 200, 250 µg methoxy polyethylene glycol-epoetin beta. Solution for injection in prefilled syringes.

Indication: Treatment of anaemia associated with chronic kidney disease (CKD). The safety and efficacy of MIRCERA therapy in other indications has not been established.

Dosage: ***Correction/Patients not currently treated with an erythropoiesis stimulating agent (ESA):***

Starting dose is 0.6 µg/kg body weight, administered once every 2 weeks IV or SC in order to increase to a haemoglobin (Hb) level greater than 11 g/dL.

Dose may be increased by ~25% of previous dose if rate of rise in Hb is <1.0 g/dL (0.621 mmol/L) over a month. Further increases of ~25% may be made at monthly intervals until the individual target Hb level is obtained.

If rate of rise in Hb is >2 g/dL (1.24 mmol/L) in 1 month or if the Hb level is increasing and approaching 12 g/dL (7.45 mmol/L), the dose is to be reduced by ~25%.

If the Hb level continues to increase, therapy should be interrupted until Hb level begins to decrease, at which point therapy should be restarted at a dose ~25% below the previously administered dose.

After dose interruption a Hb decrease of ~0.35 g/dL per week is expected. Dose adjustments should not be made more frequently than once a month.

If Hb level >11 g/dL (6.83 mmol/L) is reached for the individual patient, MIRCERA may be continued once monthly using the dose equal to twice the previous once every 2 weeks dose.

Patients currently treated with an ESA:

Patients currently treated with an ESA can be directly converted to MIRCERA administered once a month as a single IV or SC injection. The starting dose of methoxy polyethylene glycol-epoetin beta is described in the table below. The first injection should start at the next scheduled dose of the previously administered darbepoetin alfa or epoetin dose.

MIRCERA once monthly starting doses

Previous weekly darbepoetin alfa IV or SC dose (µg/week)	Previous weekly epoetin IV or SC dose (IU/week)	Monthly MIRCERA starting dose IV or SC dose (µg/once monthly)
<40	<8000	120
40–80	8000–16,000	200
>80	>16,000	360

If a dose adjustment is required to maintain the target Hb level >11 g/dL (6.83 mmol/L), the monthly dose may be increased by ~25%. For dose adjustments follow the detailed recommendations described under correction.

Since the treatment experience is limited in *patients on peritoneal dialysis*, regular Hb monitoring and strict adherence to dose adjustment guidance is recommended in these patients.

Missed dose: If one dose of MIRCERA is missed, the missed dose is to be administered as soon as possible and administration of MIRCERA is to be restarted at the prescribed dosing frequency.

Special Populations: MIRCERA is not recommended for use in children and adolescents below 18 years. Safety and efficacy data have not been established in patients with severe liver disease.

Administration: The solution can be administered SC or IV. MIRCERA can be injected SC in the abdomen, arm or thigh. All 3 injection sites are equally suitable.

Contraindication: Hypersensitivity to the active substance or any of the excipients. Patients with uncontrolled hypertension.

Special warnings and precautions: Supplementary iron therapy recommended for all patients with serum ferritin below 100 µg/L or transferrin saturation <20%. Iron status to be evaluated for all patients prior to and during treatment.

Failure to respond to MIRCERA therapy should prompt for a search for causative factors. Deficiencies (iron, vitamin B12, folic acid) reduce the effectiveness of ESAs and should therefore be corrected. Intercurrent infections, inflammatory or traumatic episodes, occult blood loss, haemolysis, severe aluminium toxicity, underlying haematologic diseases, or bone marrow fibrosis may also compromise the erythropoietic response.

A reticulocyte count should be considered as part of the evaluation. If all the conditions mentioned are excluded and the patient has a sudden drop of Hb associated with reticulocytopenia and anti-erythropoietin antibodies, examination of the bone marrow for the diagnosis of Pure Red Cell Aplasia (PRCA) should be considered. In case PRCA is diagnosed, therapy with MIRCERA must be discontinued and patients should not be switched to another ESA.

Pure Red Cell Aplasia caused by anti-erythropoietin antibodies has been reported in association with ESAs. These antibodies have been shown to cross-react with all ESAs, and patients suspected or confirmed to have antibodies to erythropoietin should not be switched to MIRCERA.

Blood pressure monitoring: As with other ESAs, blood pressure should be adequately controlled in all patients before, at initiation of, and during treatment with MIRCERA. If high blood pressure is difficult to control by medical treatment or dietary measures, the dose must be reduced or withheld.

Effect on tumour growth: MIRCERA, like other ESAs, is a growth factor that primarily stimulates red blood cell production. Erythropoietin receptors may be expressed on the surface of a variety of tumour cells. As with all growth factors, there is a concern that ESAs could stimulate the growth of any type of malignancy. Two controlled clinical studies in which epoetins were administered to patients with various cancers including head and neck cancers, and breast cancer, have shown an unexplained excess mortality.

MIRCERA is not approved for the treatment of anaemia in patients with cancer.

The safety and efficacy of MIRCERA therapy has not been established in patients with haemoglobinopathies, seizures, bleeding or a recent history of bleeding requiring transfusions or with platelet levels greater than 500 x 10^9/L. Therefore, caution should be used in these patients.

Drug interactions: No interaction studies have been performed. There is no evidence that MIRCERA alters the metabolism of other medicinal products.

Use in pregnancy and lactation: There is no adequate experience in human pregnancy and lactation. Caution should be exercised when prescribing to pregnant women.

Side-effects and adverse reactions: See SmPC for full listing. The most frequent reported adverse reaction was hypertension (common). Headache, vascular access thrombosis (uncommon). Hypersensitivity, hot flush, maculopapular rash, hypertensive encephalopathy (rare). A slight decrease in platelet counts remaining within the normal range was observed in clinical studies.

Legal Category: POM

Presentations, Marketing Authorization Numbers: Packs of 1 prefilled syringe: 50 µg solution in 0,3 mL EU/1/07/400/008, 75 µg solution in 0,3 mL EU/1/07/400/009, 100 µg solution in 0,3 mL EU/1/07/400/010, 150 µg solution in 0,3 mL EU/1/07/400/011, 200 µg solution in 0,3 mL EU/1/07/400/012, 250 µg solution in 0,3 mL EU/1/07/400/013

Marketing Authorisation Holder: Roche Registration Limited, 6 Falcon Way, Shire Park, Welwyn Garden City, AL 7 1TW, UK.

MIRCERA is a registered trademark.

Consult SmPC for additional information on pediatric use, hepatic impairment, overdose, list of excipients and storage.

Adverse events should be reported to F. Hoffmann-La Roche Ltd.

Date of preparation: October 2007. J600031C

F. Hoffmann-La Roche Ltd
4070 Basel, Switzerland

Roche

Information about adverse event reporting can be found at www.yellowcard.gov.uk. Adverse events should also be reported to Roche Products Limited. Please contact UK Drug Safety Centre on 01707 367554.

References: 1. MIRCERA® Summary of Product Characteristics. F. Hoffmann-La Roche Ltd, 2007. **2.** Levin NW, Imbasciati C, Combe M, et al. Adequate Hb levels are maintained with IV C.E.R.A. (continuous erythropoietin receptor activator) administered up to once monthly in dialysis patients irrespective of age, gender or diabetic status. Abstract SA-PO206, presented at ASN Annual Meeting, November 14–19, 2006, San Diego, California. **3.** Sulowicz W, Locatelli F, Ryckelynck J-P, et al. Once-monthly subcutaneous C.E.R.A. maintains stable hemoglobin control in patients with chronic kidney disease on dialysis and converted directly from epoetin one to three times weekly. *Clin J Am Soc Nephrol. 2007;2:637-646.* **4.** Jarsch M, Brandt M, Haselbeck A. Consumption of C.E.R.A. and epoetin beta in cellular assay: UT-7 consumption model. Abstract presented at American Society of Hematology (ASH) 48th Meeting, December 9–12, 2006, Orlando, FL. **5.** Jarsch M, Kubbies M, Lanzendörfer M, Haselbeck A, Brandt M. C.E.R.A. acts differently at the erythropoietin (EPO) receptor compared with epoetin beta: UT-7 and CD34+ cell stimulation assays. Abstract SA-PO209, presented at ASN Annual Meeting, November 14–19, 2006, San Diego, California. *J Am Soc Nephrol.* 2006;17:619A.


CONTINUOUSLY CONNECTING
more patients to life
MIRCERA offers you and more of your patients the ability to achieve:
Sustained anemia management through a unique continuous erythropoietin receptor and a longer half-life
Stable Hb control for all patient types with once-monthly dosing
A smooth and steady rise in Hb levels to safely reach and maintain a target range of 11–12 g/dL
NEW ONCE-MONTHLY
MIRCERA®
pegzerepoetin alfa