Evrenzo™ roxadustat

20, 50, 70 mg film-coated tablet

EVRENZO (roxadustat) is indicated for treatment of adult patients with symptomatic anaemia associated with chronic kidney disease (CKD)[1]

Like a breath of fresh air, at high altitude

EVRENZO tackles the multiple causes of anaemia of CKD in a coordinated way, leveraging the HIF pathway to:[1]

- achieve and maintain target haemoglobin levels.[1]
  - irrespective of inflammation[2]
- with reduced use of IV iron compared with ESA[1]
- via an oral treatment taken just three days a week[1]

ESA, erythropoiesis-stimulating agent; HIF, hypoxia-inducible factor; IV, intravenous

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected Adverse Reactions using the tab below.

MAT-EG-EVZ-2022-00002
Date of preparation: December 2022

For Healthcare Professionals Only

References

1. EVRENZO EU SmPC, July 2022. Available at: https://www.medicines.org.uk/emc/product/12835/smpc#.
2. Provenzano R, Besarab A, Wright S, et al. Roxadustat (FG-4592) Versus Epoetin Alfa for Anemia in Patients Receiving Maintenance Hemodialysis: A Phase 2, Randomized, 6- to 19-Week, Open-Label, Active-Comparator, Dose-Ranging, Safety and Exploratory Efficacy Study. *Am J Kidney Dis*. 2016;67(6):912-924.

Adverse event reporting (AER)

For reporting any adverse event or safety information related to Astellas products, please contact immediately pharmacovigilance.ae@astellas.com or call +201115910444

Evrenzo™
roxadustat
20, 50, 70 mg film-coated tablet

UNMET NEED

Anemia of CKD has a multi-factorial etiology.[1]

CKD, chronic kidney disease; EPO, erythropoietin;
ESA, erythropoiesis-stimulating agent

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Challenges with standard of care therapies

- The current management of anemia in patients with advanced CKD consists of a combination of injectable ESAs with oral or IV iron supplementation.[2]
- The efficacy of oral iron may be limited by gastrointestinal side effects and variable GI absorption.[4]
- IV iron occasionally induces hypersensitivity reactions, and must be given by an HCP.[1,7,5]
- Relative resistance to the effect of ESAs is a common problem in the management of patients with anaemia of CKD.[4]
  - A number of studies have highlighted the association between inflammation, ESA hyporesponsiveness, and the requirement for higher ESA doses.[6]

In your experience, how many patients respond inadequately to the current standard of care?

Please use the slider to show your estimate

See evidence

EPO, erythropoietin; ESA, erythropoiesis-stimulating agent; HCPs, healthcare providers; CKD, chronic kidney disease; IV, intravenous; NDD, non-dialysis-dependent

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Challenges with standard of care therapies

- The current management of anemia in patients with advanced CKD consists of a combination of injectable ESAs with oral or IV iron supplementation.[2]
- The efficacy of oral iron may be limited by gastrointestinal side effects and variable GI absorption.[4]
- IV iron occasionally induces hypersensitivity reactions, and must be given by an HCP.[5]
- Relative resistance to the effect of ESAs is a common problem in the management of patients with anaemia of CKD.[4]

ESA hypo-responsiveness is seen in ~15% of patients with NDD-CDK and DD-CDK.[7]

The individual response to ESAs may vary greatly on the basis of various determinants.[8]

ESA hyporesponders were associated with increased mortality and hospitalization for CV disease.[9]

HD, haemodialysis; IV, intravenous; NDD, non-dialysis-dependent

evrenzo™
roxadustat
20, 50, 70 mg film-coated tablet

References

1. Li ZL, Tu Y, Liu BC. Treatment of Renal Anemia with Roxadustat: Advantages and Achievement. *Kidney Dis (Basel)*. 2020;6(2):65-73.
2. Locatelli F, Fishbane S, Block GA, Macdougall IC. Targeting Hypoxia-Inducible Factors for the Treatment of Anemia in Chronic Kidney Disease Patients. *Am J Nephrol*. 2017;45(3):187-199.
3. Barratt J, Andric B, Tataradze A, et al. Roxadustat for the treatment of anaemia in chronic kidney disease patients not on dialysis: a Phase 3, randomized, open-label, active-controlled study (DOLOMITES). *Nephrol Dial Transplant*. 2021;36(9):1616-1628.
4. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. *Kidney Int Suppl*. 2012;2:279–335.
5. Macdougall IC, Bircher AJ, Eckardt KU, et al. Iron management in chronic kidney disease: conclusions from a "Kidney Disease: Improving Global Outcomes" (KDIGO) Controversies Conference. *Kidney Int*. 2016;89(1):28-39.
6. Chawla LS, Krishnan M. Causes and consequences of inflammation on anemia management in hemodialysis patients. *Hemodial Int*. 2009;13(2):222-234.
7. Minutolo R, Conte G, Cianciaruso B, et al. Hyporesponsiveness to erythropoiesis-stimulating agents and renal survival in non-dialysis CKD patients. *Nephrol Dial Transplant*. 2012;27(7):2880-2886.
8. Rosati A, Ravaglia F, Panichi V. Improving Erythropoiesis Stimulating Agent Hyporesponsiveness in Hemodialysis Patients: The Role of Hepcidin and Hemodiafiltration Online. *Blood Purif*. 2018;45:139–146.
9. Cizman B, Smith HT, Camejo RR, et al. Clinical and Economic Outcomes of Erythropoiesis-Stimulating Agent Hyporesponsiveness in the Post-Bundling Era. *Kidney Med*. 2020;2(5):589-599.e1.

INTRODUCING EVRENZO

EVRENZO addresses the multifactorial pathophysiology of anaemia of CKD[1]

...to generate a coordinated erythropoietic response.[1]

Increases endogenous EPO production.[1] + **Reduces hepcidin levels.[1]** + **Improves iron bioavailability.[1]** = **Increases Hb and red blood cell production.[1]**

CKD, chronic kidney disease; EPO, erythropoietin; Hb, haemoglobin

EVRENZO acts by affecting the HIF pathway.[1]

See how oxygen levels affect HIF-PH (hypoxia-inducible factor-prolyl hydroxylase)[2]

HIF, hypoxia-inducible factor; HIF-PH, hypoxia-inducible factor-prolyl hydroxylase

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

EVRENZO acts by affecting the HIF pathway.[1]

See how oxygen levels affect HIF-PH (hypoxia-inducible factor-prolyl hydroxylase)[2]

HIF, hypoxia-inducible factor; HIF-PH, hypoxia-inducible factor-prolyl hydroxylase

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

EVRENZO acts by affecting the HIF pathway.[1]

EVRENZO reversibly inhibits HIF-PH, but at normal oxygen levels[1]

- Increases EPO[1]
- Regulates iron transporter proteins[1]
- Reduces hepcidin[1]

See how EVRENZO works

EPO, erythropoietin; HIF, hypoxia-inducible factor; HIF-PH, hypoxia-inducible factor-prolyl hydroxylase

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

EVRENZO can be used from the start of the treatment journey[1]

EVRENZO can be initiated after ensuring adequate iron stores[1]

It increases haemoglobin with reduced use of IV iron compared with ESA,[1] and is effective in patients with underlying inflammation.[4]

EVRENZO offers oral treatment that can be administered at home instead of hospital.[1]

EVRENZO addresses multiple aspects of anaemia of CKD[1]

EVRENZO can help patients achieve and maintain their Hb goals[1] - with less use of IV iron compared with ESA[1] - regardless of inflammation status[4]

EVRENZO offers oral treatment[1]

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IV, intravenous

Evrenzo can benefit a broad range of patients with anaemia across the CKD continuum[1]

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IV, intravenous

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

References

1. EVRENZO EU SmPC, July 2022. Available at: https://www.medicines.org.uk/emc/product/12835/smpc#.
2. Locatelli F, Fishbane S, Block GA, Macdougall IC. Targeting Hypoxia-Inducible Factors for the Treatment of Anemia in Chronic Kidney Disease Patients. *Am J Nephrol*. 2017;45(3):187-199.
3. Barratt J, Andric B, Tataradze A, et al. Roxadustat for the treatment of anaemia in chronic kidney disease patients not on dialysis: a Phase 3, randomized, open-label, active-controlled study (DOLOMITES). *Nephrol Dial Transplant*. 2021;36(9):1616-1628.
4. Provenzano R, Besarab A, Wright S, et al. Roxadustat (FG-4592) Versus Epoetin Alfa for Anemia in Patients Receiving Maintenance Hemodialysis: A Phase 2, Randomized, 6- to 19-Week, Open-Label, Active-Comparator, Dose-Ranging, Safety and Exploratory Efficacy Study. *Am J Kidney Dis*. 2016;67(6):912-924.
5. Gafter-Gvili A, Schechter A, Rozen-Zvi B. Iron Deficiency Anemia in Chronic Kidney Disease. *Acta Haematol*. 2019;142(1):44-50.

Time
00:00 - 00:10

Evrenzo™

roxadustat

20 mg, 50 mg, 70 mg film-coated tablet

Voice over

Screen

Time
00:10 - 00:15

CKD, chronic kidney disease.

Voice over

Screen

Time
00:16 - 00:22

Voice over

Screen

Time
00:23 - 00:28

EVRENZO reversibly inhibits HIF-PH enzymes,[1]

HIF-PH, hypoxia-inducible factor prolyl hydroxylase.

Voice over

allowing HIF-alpha to translocate to the nucleus, where it forms a heterodimer with HIF-beta, activating gene transcription.[2]

Screen

Time
00:28 - 00:34

HIF-α, hypoxia-inducible factor alpha; **HIF- β,** hypoxia-inducible factor beta.

Voice over

EVRENZO thereby mimics the body's natural response to hypoxia.[3]

Screen

Time
00:35 - 00:41

HIF, hypoxia-inducible factor; **EPO,** erythropoietin; **DMT1**, divalent metal-ion transporter-1.

Voice over

Activation of HIF also causes a reduction in hepcidin,[1] negating the effects of chronic inflammation, and consequently increases iron mobilization.[2]

Screen

Time
00:42 - 00:52

HIF, hypoxia-inducible factor.

Voice over

By stimulating a coordinated erythropoietic response, EVRENZO increases endogenous production of erythropoietin and improves iron bioavailability – ultimately leading to increased red blood cell production and haemoglobin levels.[1]

Screen

Time
00:53 - 01:08

EPO, erythropoietin.

Voice over

EVRENZO allows this multifactorial condition[2] to be treated in a coordinated way, through a three times weekly oral tablet.[1]

Screen

Time
01:09 - 01:17

Evrenzo™
roxadustat

20 mg, 50 mg, 70 mg film-coated tablet

Time
01:17 - 01:20

References

1. EVRENZO EU SmPC, December 2022. Available at: https://www.medicines.org.uk/emc/product/12835/smpc#. Last accessed December 2022.
2. Locatelli F, Fishbane S, Block GA, Macdougall IC. Targeting Hypoxia-Inducible Factors for the Treatment of Anemia in Chronic Kidney Disease Patients. *Am J Nephrol*. 2017;45(3):187-199.
3. Del Vecchio L, Locatelli F. Roxadustat in the treatment of anaemia in chronic kidney disease. Expert Opin Investig Drugs. 2018;27(1):125-133.

Time
01:21 - 01:29

Prescribing Information

Presentation: EVRENZO 20 mg, 50 mg and 70 mg, film-coated tablets roxadustat.
Composition: Each tablet contains 20 mg, 50 mg and 70 mg of roxadustat.
The other ingredients are:
Tablet core: lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, povidone, magnesium stearate.
Film-coating: polyvinyl alcohol, talc, macrogol, Allura Red Aluminium Lake AC, titanium dioxide, lecithin (soya).
Indication(s): **What EVRENZO is:** EVRENZO is a medicine that increases the number of red blood cells and haemoglobin level in your blood. It contains the active substance roxadustat. **What EVRENZO is used for:** EVRENZO is used to treat adults with symptomatic anaemia that occurs in patients with chronic kidney disease. Anaemia is when you have too few red blood cells and your haemoglobin level is too low. As a result, your body might not receive enough oxygen. Anaemia can cause symptoms such as tiredness, weakness, or shortness of breath. **How EVRENZO works:** Roxadustat, the active substance in EVRENZO, works by increasing the level of HIF, a substance in the body which increases the production of red blood cells when oxygen levels are low. By raising HIF levels, the medicine increases the production of red blood cells and raises the levels of haemoglobin (the oxygen-carrying protein in red blood cells). This improves the oxygen supply to your body and may reduce your symptoms of anaemia.
Posology and Method of Administration: Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. Your doctor will tell you what dose of EVRENZO to take. Your doctor will check your haemoglobin levels regularly and increase or lower your dose based on your haemoglobin levels. EVRENZO is taken by mouth as tablets.
Taking EVRENZO: •Take your EVRENZO dose three times per week unless your doctor told you otherwise. •Never take EVRENZO on consecutive days. •Take EVRENZO on the same three days every week. •EVRENZO can be taken with food or between meals. •Swallow the tablets whole. •Do not chew, break or crush the tablets. Take EVRENZO at least 1 hour after you have taken medicines that reduce phosphate levels in your blood (called phosphate binders) or other medicines or supplements that contain calcium, iron, magnesium or aluminum (called multivalent cations).
Dosing Schedule:
3 times a week dosing schedule: EVRENZO comes in a blister pack containing medicine for 4 weeks (12 tablets), divided into 4 rows. Each row contains 1 week of medicine (3 tablets). Make sure you take tablets from the same row for each week. Your dose ranges from 20 mg three times per week up to a maximum 400 mg three times per week.
Different dosing frequencies: In exceptional cases (based upon your haemoglobin levels), your doctor may decide to lower your EVRENZO dose to 20 mg two times or one time per week. In this case your doctor will explain which days week you need to take your dose.
More than 1 tablet needed to make up a dose: In most cases you will have 1 blister package per month. If your dose requires more than 1 blister package, you will need to take a tablet from each blister per dosing day. Your doctor will explain when and how many tablets to take. Your doctor will monitor your haemoglobin level and may temporarily stop your treatment if your haemoglobin level becomes too high. Do not restart your treatment until your doctor tells you to. Your doctor will tell you what dose of EVRENZO to take and when to start taking it again.
If you take more EVRENZO than you should: If you take more tablets or a higher dose than you should, contact your doctor straight away.
If you forget to take EVRENZO: •Never take a double dose to make up for a forgotten dose. •If more than 24 hours (1 day) remains before your next scheduled dose, take the missed dose as soon as possible and take the next dose on the next scheduled day. • If less than 24 hours (1 day) remains before your next scheduled dose: skip the missed dose and take the next dose on the next scheduled day.
If you stop taking EVRENZO: Do not stop taking this medicine unless your doctor tells you to do so. If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

Time
01:30 - 01:36

Prescribing Information

Possible Side Effects: Like all medicines, this medicine can cause side effects, although not everybody gets them. Some possible side effects may be serious. Contact your doctor straight away if you get any of the following: •blood clot in the veins of your legs (deep vein thrombosis or DVT) (may affect up to 1 in 10 people). •blood clot in the lungs (pulmonary embolism) (may affect up to 1 in 100 people). •blood clot in your haemodialysis access (vascular access thrombosis or VAT) that causes the vascular access to close up or stop working if you are using a fistula or graft for dialysis access (may affect more than 1 in 10 people). •seizures and warning signs of seizures (convulsions or fits) (may affect up to 1 in 10 people). •sepsis, a serious or in rare cases, life-threatening infection (may affect up to 1 in 10 people).
Other possible side effects: Very common (may affect more than 1 in 10 people): •increased amount of potassium •high blood pressure (hypertension) •feeling sick (nausea) •diarrhoea •swelling due to fluid retention in the extremities (peripheral oedema) Common (may affect up to 1 in 10 people): •difficulty in sleeping (insomnia) •headache •vomiting •constipation. Uncommon (may affect up to 1 in 100 people): •increased amount of bilirubin in your blood.
Reporting of side effects: If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. By reporting side affects you can help provide more information on the safety of this medicine.
Contraindications, Precautions and Warnings: Do not take EVRENZO •if you are allergic to peanut or soya, do not use this medicine. EVRENZO contains soya lecithin. •if you are allergic to roxadustat or any of the other ingredients of this medicine. •if you are more than 6 months pregnant, (It is also better to avoid this medicine in early pregnancy - see pregnancy section). •if you are breastfeeding. Talk to your doctor, or pharmacist before taking EVRENZO: •if you have epilepsy or have ever had convulsions or fits. •if you have signs and symptoms of an infection, which may include fever, sweating or chills, sore throat, runny nose, shortness of breath, feeling weak, confusion, cough, vomiting, diarrhoea or stomach pain, feeling of burning when you pass urine, red or painful skin or sores on your body. •if you have a liver disorder. Chronic kidney disease and anaemia may increase the risk of cardiovascular events and death. Managing your anaemia is important. Your doctor will monitor your haemoglobin and also consider your treatment regimen as anaemia treatment and switching between anaemia treatments may also have a negative impact on your cardiovascular health. **Talk to your doctor, or pharmacist straight away:** •if you get blood clots: •in the veins of your legs (deep vein thrombosis or DVT), signs of which can include pain and/or swelling in the legs, cramping or a feeling of warmth in the affected leg; •in the lungs (pulmonary embolism or PE), signs of which can include sudden shortness of breath, chest pain (usually worse with breathing), feeling of anxiety, dizziness, lightheadedness, or fainting; heart racing, coughing (sometimes with blood); •in your haemodialysis access (vascular access thrombosis or VAT) that stop the vascular access from working; signs of this can include swelling, redness, hardening or thickening of the skin around your access, oozing at the access site, not feeling a vibration ("thrill") over the access area; •if you have a seizure (convulsion or fit) or possible warning signs that a seizure may occur, such as headache, irritability, fear, confusion or unusual feelings; •if you have signs and symptoms of an infection, which include fever, sweating or chills, sore throat, runny nose, shortness of breath, feeling weak or faint, confusion, cough, vomiting, diarrhoea, or stomach pain, burning when you pass urine, red or painful skin or sores on your body. Misuse can lead to an increase in blood cells and consequently thicken the blood. This can cause life threatening problems with the heart or blood vessels.
Children and adolescents: Do not give EVRENZO to children and adolescents aged under 18 years because there is not enough information about its use in this age group.
Other medicines and EVRENZO: Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. EVRENZO may affect the way these medicines work, or these medicines may affect how EVRENZO works. In particular tell your doctor or pharmacist if you have or are taking any of the following medicines: •medicines to reduce phosphate levels in your blood (called phosphate binders) or other medicines or supplements that contain calcium, iron, magnesium or aluminum (called multivalent cations), such as sevelamer carbonate or calcium acetate.

Time
01:36 - 01:42

Prescribing Information

You must take EVRENZO at least 1 hour after these medicines or supplements. Otherwise roxadustat will not be properly absorbed by your body. • a medicine to treat gout called probenecid. • medicines used to lower cholesterol, such as simvastatin, atorvastatin, or rosuvastatin (also called "statins"), or gemfibrozil. •other medicines used to treat anaemia such as erythropoiesis-stimulating agents (ESAs). If you normally take any of these medicines, your doctor might change it and prescribe a different medicine for you during your treatment with EVRENZO. EVRENZO contains lactose, soya sugar (lactose), traces of peanut and soya (soya lecithin), and an azo colouring agent (Allura Red AC aluminium lake). If you have been told by your doctor that you have an intolerance to some sugars or are allergic to peanut, soya or azo colouring agents, contact your doctor before taking this medicine.
Pregnancy, Breast-feeding and lactation: If you are pregnant, think you may be pregnant or are planning to have a baby, contact your doctor. EVRENZO may harm your unborn baby. EVRENZO is not recommended in the first 6 months of pregnancy and must not be taken in the last 3 months of pregnancy. Women taking EVRENZO who are able to become pregnant should use an effective method of contraception during treatment with EVRENZO and for at least one week after the last dose of EVRENZO. If you use a hormonal contraceptive, you must also use a barrier method, such as a condom, or a diaphragm. Do not breastfeed if you are on treatment with EVRENZO. It is not known if EVRENZO passes into your breast milk and could harm your baby.
Driving and using machines: This medicine may affect your ability to drive or use machines. Seizures can occur as a side effect.

For more detailed information, please refer to the full Prescribing Information as available with Astellas Medical Representative. Legal category: POM; **MA Holder:** Astellas Pharma Europe B.V., Sylviusweg 62, 2333 BE Leiden, NL.
Further information available upon request from: Astellas Pharma DMCC, P.O. Box 282872, Dubai, UAE.
Version: 1.0.

For reporting any adverse event or safety information related to Astellas products, please contact immediately pharmacovigilance.ae@astellas.com or call +201115910444.

- **Always read the full prescribing information.**
- **Healthcare professionals are asked to report any suspected adverse drug reaction to Egyptian Pharmacovigilance Center (EPVC).**
- **Egyptian drug authority EVRENZO leaflet approval date 6/7/2022.**

Time
01:43 - 01:50

Evrenzo™ roxadustat

20 mg, 50 mg, 70 mg film-coated tablet

astellas

Astellas Pharma International B.V. Scientific
Office, Star Capital F2, Floor 8, Office 81
8th Omar Ibn El Khattab, Masaken El
Mohandesin, Heliopolis, Cairo, Egypt

CLINICAL TRIALS & EFFICACY

ALPINE - A global clinical trial programme

The above image is for illustrative purpose only

ALPINE - A global clinical trial programme[1]

ALPS[1]

(N=594)

Non-dialysis-dependent
ESA-untreated patients
Placebo-controlled
Hb correction and maintenance

ANDES[1]

(N=916)

Non-dialysis-dependent
ESA-untreated patients
Placebo-controlled
Hb correction and maintenance

OLYMPUS[1]

(N=2,760)

Non-dialysis-dependent
ESA-untreated patients
Placebo-controlled
Hb correction and maintenance

DOLOMITES[1]

(N=616)

Non-dialysis-dependent
ESA-untreated patients
ESA-controlled
Hb correction and maintenance

HIMALAYAS[1]

(N=1,039)

Incident-dialysis-dependent
ESA-untreated patients
ESA-controlled
Hb correction and maintenance

ROCKIES[1]

(N=2,101)

Incident and stable dialysis-dependent
ESA-untreated & treated patients
ESA-controlled
Hb correction and maintenance

SIERRAS[1]

(N=740)

Incident and stable dialysis-dependent
ESA-untreated & treated patients
ESA-controlled
Hb correction and maintenance

PYRENEES[1]

(N=834)

Stable dialysis-dependent
ESA-treated patients
ESA-controlled
Hb maintenance

ESA, erythropoiesis-stimulating agent;
Hb, haemoglobin; IV, intravenous

Evrenzo™
oxadustat
20, 50, 70 mg film-coated tablet

Comprehensive clinical trial programme including 9,600 patients[1]

The efficacy and safety profile of EVRENZO has been established in a broad range of patients.[1]

The key efficacy endpoint was achieving and maintaining Hb target. Other efficacy endpoints included use of rescue therapy, IV iron use and change in LDL cholesterol.[1]

- Increase in Hb level comparable to ESA, with reduced use of IV iron[1]
- Maintenance dose was irrespective of baseline inflammation.[2]
- Safety profile comparable to ESA for the majority of variables evaluated and reflective of the underlying CKD population[1]

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IDD, incident dialysis-dependent; IV, intravenous; LDL, low-density lipoprotein; NDD, non-dialysis-dependent; SDD, stable dialysis-dependent

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Evidence of Hb efficacy and iron utilisation

	Patients not on dialysis (NDD)	Patients on dialysis (DD)
Primary endpoint	Hb control comparable to ESA[3]	Hb control comparable to ESA[1]
Secondary endpoint	Reduced use of IV iron compared with ESA[1]	Reduced use of IV iron compared with ESA[1]

DD, dialysis-dependent; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IV, intravenous; NDD, non-dialysis-dependent

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Patients treated with EVRENZO achieved and maintained Hb levels comparable to ESA[3]

NDD vs. active comparator: DOLOMITES

See response rates

This was a Phase 3, multicentre, randomized, open-label, active-controlled study conducted from March 2014 to June 2018, to compare the efficacy, safety and tolerability of roxadustat with darbepoetin alfa (DA) for treatment of anaemia in NDD CKD patients. After a ≤ 6-week screening period, eligible patients were randomized (1:1) to receive roxadustat (n=286) or DA (n=273) for up to 104 weeks during the treatment period. An initial correction period to achieve Hb ≥ 11.0 g/dL and Hb change from baseline (BL; CFB) ≥1.0 g/dL (measured at two consecutive visits separated by ≥5 days) occurred in both groups. This was followed by a maintenance period with dosing aimed at achieving Hb levels between 10.0 and 12.0 g/dL. During a 4-week follow up period, anaemia treatment was at the discretion of study investigators.[3]

CI, confidence interval; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IV, intravenous; NDD, non-dialysis-dependent; PPS, per protocol set

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Patients treated with EVRENZO achieved and maintained Hb levels comparable to ESA[3]

Proportion of patients achieving correction of Hb levels during the first 24 weeks of treatment[3]

89.5% versus 78.0%, difference 11.51%, 95% confidence interval 5.66–17.36%[3]

ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IV, intravenous; NDD, non-dialysis-dependent; PPS, per protocol set

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Japanese patients converted from ESA to EVRENZO maintained effective Hb control[4]

- Study in 334 Japanese patients with CKD not on dialysis[4]
- EVRENZO was non-inferior to ESA[4]
- EVRENZO doses required to maintain Hb control were not affected by inflammation, while ESA doses were higher in patients with high CRP[4]

This was a phase III, active-controlled, multicenter, partially randomized, open-label study in Japanese patients with NDD CKD. Patients who had used recombinant human erythropoietin or darbepoetin alfa (DA) before conversion were randomized to roxadustat or DA (comparative arms). Patients who had used epoetin beta pegol before conversion were allocated to roxadustat (reference arm). The primary endpoint was change in average hemoglobin (Hb) level from baseline during the evaluation period (Weeks 18–24). Longer term efficacy and safety were evaluated in roxadustat-treated patients over 52 weeks. For patients who received roxadustat, treatment was continued until Week 52. Treatment was ended at Week 24 for patients who were randomized to the DA treatment arm.[4]

*Data from Japanese patients.

Conversion of non-dialysis patients otherwise stable on ESA treatment has not been investigated in European cohorts. A decision to treat these patients with EVRENZO should be based on a benefit-risk consideration for the individual patient.[1]

CKD, chronic kidney disease; CRP, C-reactive protein; EOW, end of week; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; SD, standard deviation; SmPC, summary of product characteristics

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

EVRENZO raises Hb with less use of IV iron compared with ESA[1]

NDD vs. active comparator:
DOLOMITES

How did the serum iron levels compare?

ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; HIF-PHI, hypoxia-inducible factor-prolyl hydroxylase inhibitor; IV, intravenous; NDD, non-dialysis-dependent

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

EVRENZO raises Hb with less use of IV iron compared with ESA[1]

EVRENZO achieved serum iron levels comparable to ESA...[3]

...but only half as many patients on EVRENZO used IV iron, reflecting improved iron bioavailability[1]

ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IV, intravenous; NDD, non-dialysis-dependent

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Patients maintained target Hb levels on a stable dose of EVRENZO[1]

Mean (SE) Hb (g/dL) over time up to week 52 (FAS); NDD pool (Hb correction)

EVRENZO	2368	2279	2229	2200	2162	2136	2104	2069	2060	2021	2028	1994	1947	1907	1850	1845	1799	1766	1730
Placebo	1865	1865	1751	1706	1686	1645	1597	1558	1519	1470	1451	1385	1340	1265	1216	1160	1115	1060	1041

NDD pool
ALPS
ANDES
OLYMPUS

Hb, haemoglobin; IV, intravenous; NDD, non-dialysis-dependent; SE, standard error; FAS, full analysis set.

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Patients recently started on dialysis and treated with EVRENZO achieved and maintained target Hb levels comparable to those treated with ESA[1]

IDD pool
HIMALAYAS
SIERRAS (subset)
ROCKIES (subset)

See response rates

ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IDD, incident-dialysis-dependent; SE, standard error

Patients recently started on dialysis and treated with EVRENZO achieved and maintained target Hb levels comparable to those treated with ESA[1]

Proportion of patients who achieved Hb response at weeks 28-52[1]

P value was not done

ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IDD, non-dialysis-dependent; SE, standard error

Patients stable on dialysis and converted to EVRENZO achieved and maintained target Hb levels comparable to those treated with ESA[1]

Mean (SE) Hb (g/dL) over time up to Week 52 (FAS): stable subpool (ESA conversion)[1]

See response rates

ESA, erythropoiesis-stimulating agent;
FAS, full analysis set; Hb, haemoglobin; SE, standard error

Patients stable on dialysis and converted to EVRENZO achieved and maintained target Hb levels comparable to those treated with ESA[1]

Proportion of patients who achieved Hb response at weeks 28–36[1]

P value was not done

ESA, erythropoiesis-stimulating agent;
FAS, full analysis set; Hb, haemoglobin; SE, standard error

EVRENZO raises Hb with less use of IV iron compared with ESA[1]

Patients who had been on dialysis ≥2 weeks and ≤4 months (FAS)[1]

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; FAS, full analysis set; Hb, haemoglobin; HIF-PHI, hypoxia-inducible factor-prolyl hydroxylase inhibitor; IDD, incident dialysis dependent; IV, intravenous

Fewer IV iron infusions administered in patients treated with EVRENZO vs. those treated with ESA[5]

Mean number of IV iron administrations per PEY during Weeks 1–52 (FAS)[5]

DD pool
HIMALAYAS
PYRENEES
ROCKIES
SIERRAS

EVRENZO improves iron metabolism by decreasing hepcidin and increasing iron absorption[1]

DD, dialysis-dependent; ESA, erythropoiesis-stimulating agent; FAS, full analysis set; IV, intravenous; PEY, patient-exposure year

EVRENZO efficacy does not appear to depend on inflammation status[2]

- EVRENZO reduces levels of hepcidin, the master regulator of iron metabolism, which is elevated in patients with inflammation[1]
- Exploratory studies suggest that the erythropoietic response of EVRENZO is independent of baseline inflammation[2]

EVRENZO is significantly more effective than ESA at reducing hepcidin[2]

Design: Phase 2, randomized (3:1), open-label, active-comparator, safety and efficacy study.
Setting & Participants: Patients with stable end-stage renal disease treated with hemodialysis who previously had hemoglobin (Hb) levels maintained with epoetin alfa.
Intervention: Part 1: 6-week dose-ranging study in 54 individuals of thrice weekly oral roxadustat dose versus continuation of intravenous epoetin alfa. Part 2: 19-week treatment in 90 individuals in 6 cohorts with various starting doses and adjustment rules (1.0-2.0 mg/kg or tiered weight based) in individuals with a range of epoetin alfa responsiveness. Intravenous iron was prohibited.
Outcomes: Primary end point was Hb level response, defined as end-of-treatment Hb level change of 20.5 g/dL or greater from baseline (part 1) and as mean Hb level ≥ 11.0 g/dL during the last 4 treatment weeks (part 2).

See More

ESA, erythropoiesis-stimulating agent; SE, standard error

EVRENZO is effective regardless of inflammation status[2]

- EVRENZO reduces levels of hepcidin, the master regulator of iron metabolism, which is elevated

Unlike ESA, dose requirements of EVRENZO are not correlated with CRP levels[2]

CRP, C-reactive protein; ESA, erythropoiesis-stimulating agent; IU, international unit

ESA, erythropoiesis-stimulating agent; SE, standard error

EVRENZO demonstrates efficacy irrespective of comorbidities.[8]

- In the DOLOMITES trial, EVRENZO was effective in patients not on dialysis with a wide range of comorbidities[*3]
- Patients in the ALPINE clinical trial programme were representative of the general clinical profile of patients with anaemia of CKD. The most common CKD aetiologies were diabetic and hypertensive nephropathy [1]

Diabetes 34%

Cardiovascular, cerebrovascular or thromboembolic disease 47%

Hypertension 29%

Polycystic kidney disease 8%

Pyelonephritis 10%

Statin therapy 49%

*CKD etiology included Diabetic nephropathy, Hypertensive nephropathy, and Pyelonephritis. at baseline, 47% of patients had history of cardiovascular, cerebrovascular or thromboembolic diseases.

CKD, chronic kidney disease

EVRENZO significantly reduced LDL cholesterol from baseline vs. ESA[1]

The cardiovascular benefit of this effect in patients not on dialysis has not been established

DD, dialysis-dependent; ESA, erythropoiesis-stimulating agent; IDD, incident dialysis-dependent; LDL, low-density lipoprotein; LS, least squares; NDD, non-dialysis dependent

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

EVRENZO can help patients with anaemia of CKD...

- To achieve and maintain their target Hb levels[1]
- with a reduced use of IV iron compared with ESA[1]
- and with an oral treatment that can be taken at home[1]

Helps patients achieve and maintain their Hb goals[1]

Effective across the CKD spectrum (NDD, IDD & SDD)[1]

Effective in patients with inflammation or raised hepcidin[2]

Oral treatment[1] avoids the challenges of parenteral therapy

Can be taken at home, saving the time and cost of hospital administration*

*This benefit only applies to non-dialysis dependent and peritoneal dialysis patients.

†Patients currently treated with an ESA can be converted to roxadustat, however, conversion of dialysis patients otherwise stable on ESA treatment is only to be considered when there is a valid clinical reason[1]

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IDD, incident dialysis-dependent; IV, intravenous; NDD, non-dialysis-dependent; SDD, stable-dialysis-dependent

- EVRENZO gained Marketing Authorisation in Europe in August 2021[6]
- EVRENZO has been licensed in China and Japan since 2019[7]

References

1. EVRENZO EU SmPC, July 2022. Available at: https://www.medicines.org.uk/emc/product/12835/smpc#.
2. Provenzano R, Besarab A, Wright S, et al. Roxadustat (FG-4592) Versus Epoetin Alfa for Anemia in Patients Receiving Maintenance Hemodialysis: A Phase 2, Randomized, 6- to 19-Week, Open-Label, Active-Comparator, Dose-Ranging, Safety and Exploratory Efficacy Study. *Am J Kidney Dis*. 2016;67(6):912-924.
3. Barratt J, Andric B, Tataradze A, et al. Roxadustat for the treatment of anaemia in chronic kidney disease patients not on dialysis: a Phase 3, randomized, open-label, active-controlled study (DOLOMITES). *Nephrol Dial Transplant*. 2021;36(9):1616-1628.
4. Akizawa T, Iwasaki M, Otsuka T, Yamaguchi Y, Reusch M. Phase 3 Study of Roxadustat to Treat Anemia in Non-Dialysis-Dependant CKD. *Kidney Int Rep*. 2021;6(7):1810-1828.
5. Barratt J, Sulowicz W, Schömig M, et al. Efficacy and Cardiovascular Safety of Roxadustat in Dialysis-Dependent Chronic Kidney Disease: Pooled Analysis of Four Phase 3 Studies. *Adv Ther*. 2021;38(10):5345-5360.
6. European Medicines Agency. Evrenzo. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/evrenzo. Last accessed: November 2022.
7. Japanese Pharmaceuticals and Medical Devices Agency. Report on the Deliberation Results. Available at: https://www.pmda.go.jp/files/000234811.pdf. Last accessed: November 2022.

DOSING

ON TOP of their anaemia.
AT HOME with their treatment.[1]

EVRENZO offers an oral treatment that can be taken in the home setting, avoiding the time and cost of IV administration.[1]

IV, intravenous

Starting patients on EVRENZO

EVRENZO is taken 3 times a week, on non-consecutive days[1]

Three times weekly dosing reduces the pill burden compared with dosing every day

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Starting dose[1]

For patients not currently treated with an ESA:

Body weight	EVRENZO dosage
<100 kg	70 mg, three times per week
≥100kg	100 mg, three times per week

Tablet strengths

Monitoring haemoglobin

- Hb levels should be monitored every two weeks until the desired Hb level of 10 to 12 g/dL is achieved and stabilised, and every 4 weeks thereafter, or as clinically indicated[1]

- Hb values more than 12 g/dL and a Hb rise of more than 2 g/dL over 4 weeks may increase the risk of thrombosis[1]

- Individualise dose to achieve and maintain target Hb levels of 10–12 g/dL[1]

Please consult the Summary of Product Characteristics for guidance on dose adjustment, Hb monitoring, and other dosing information.[1]

ESA, erythropoiesis-stimulating agent; Hb, haemoglobin

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

EVRENZO dosing for patients converting from ESA[1]

The recommended starting dose of EVRENZO is based on the average prescribed ESA dose in the 4 weeks before conversion[1]

Darbepoetin alfa IV or SC dose (micrograms/week)	Epoetin IV or SC dose (IU/week)	Methoxy polyethylene glycol-epoetin beta IV or SC dose (micrograms/month)	EVRENZO dose (mg three times per week)
Less than 25	Less than 5,000	Less than 80	70
25 to less than 40	5,000 up to 8,000	80 up to and including 120	100
40 up to and including 80	More than 8,000 up to and including 16,000	More than 120 up to and including 200	150
More than 80	More than 16,000	More than 200	200

The first dose of EVRENZO should replace the next scheduled dose of the current ESA[1]

Conversion of non-dialysis patients otherwise stable on ESA treatment has not been investigated. A decision to treat these patients with roxadustat should be based on a benefit_risk consideration for the individual patient.[1]

Conversion of dialysis patients otherwise stable on ESA treatment should only be considered when there is a valid clinical reason[1]

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

ESA, erythropoiesis-stimulating agent; IV, intravenous; SC, subcutaneous

Dose adjustment [1]

The stepwise dose adjustments up or down should follow the sequence of the available doses: 20 mg — 40 mg — 50 mg — 70 mg — 100 mg — 150 mg — 200 mg — 250 mg — 300 mg — 400 mg (only for CKD patients on dialysis).[1]

Change in Hb over the previous 4 weeks*	Current Hb level (g/dL)			
	<10.5	10.5–11.9	12.0–12.9	≥13.0
> +1.0	No change	↓ 1 step	↓ 1 step	**Withhold dosing, monitor Hb and resume dosing when Hb <12.0 g/dL, at a dose reduced by 2 steps**
-1.0 to +1.0	↑ 1 step	No change	↓ 1 step	
< -1.0	↑ 1 step	↑ 1 step	No change	

The dose of EVRENZO should not be adjusted more frequently than once every 4 weeks, except if Hb increases by more than 2 g/dL at any time within a 4-week period, in which case the dose should be reduced by one step immediately.[1]

*Change in Hb over the previous 4 weeks = (present Hb value) – (previous Hb value drawn 4 weeks ago).

Maintenance dose[1]

After stabilisation to target Hb levels between 10 to 12 g/dL, the Hb levels should continue to be monitored regularly and the dose adjustment rules followed.

CKD, chronic kidney disease; Hb, haemoglobin

Supporting patients taking EVRENZO

3 days a week dosing gives your patients four days every week when they can take a break from treatment with EVRENZO[1]

References

1. EVRENZO EU SmPC, July 2022. Available at: https://www.medicines.org.uk/emc/product/12835/smpc#.

Evrenzo™
roxadustat
20, 50, 70 mg film-coated tablet

SAFETY

Raising the standard of care with a well studied safety profile

The safety profile of EVRENZO has been evaluated in over 6,800 patients[1]

- The general safety profile of EVRENZO was overall comparable to ESA for the majority of safety variables evaluated and is reflective of the studied CKD populations[1]

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent

EVZ_2022_0110_ABC Date of preparation: September 2022

Adverse events profile

The safety of Evrenzo was evaluated in 3542 non-dialysis dependent (NDD) and 3353 dialysis dependent (DD) patients with anaemia and CKD who have received at least one dose of Evrenzo.[1]

Adverse reactions observed during clinical studies[1]

(very common ≥1/10; common ≥1/100 to <1/10; uncommon ≥1/1,000 to <1/100)

MedDRA System organ class (SOC)	Frequency	Adverse reaction
Infections and infestations	Common	Sepsis
Metabolism and nutrition disorders	Very common	Hyperkalaemia
Psychiatric disorders	Common	Insomnia
Nervous system disorders	Common	Seizures, headache
Vascular disorders	Very common	Hypertension, vascular access thrombosis (VAT)*
	Common	Deep vein thrombosis (DVT)

*Associated with CKD patients who were on dialysis while receiving EVRENZO.
†Based on global post-marketing experience.

CKD, chronic kidney disease; DD, dialysis-dependent; ESA, erythropoiesis-stimulating agent; MedDRA, Medical Dictionary tor Regulatory Activities; NDD, non-dialysis-dependent

Adverse events profile

- Adverse events listed in the SmPC were derived from the whole ALPINE programme, including trials in NDD patients vs. placebo or vs. ESA, as well as trials in DD patients vs. ESA[1]

Adverse reactions observed during clinical studies[1]
(very common ≥1/10; common ≥1/100 to <1/10; uncommon ≥1/1,000 to <1/100)

MedDRA System organ class (SOC)	Frequency	Adverse reaction
Gastrointestinal disorders	Very common	Nausea, diarrhoea
	Common	Constipation, vomiting
Skin and subcutaneous tissue disorders	Not known†	Dermatitis Exfoliative Generalised (DEG)
Hepatobiliary disorders	Uncommon	Hyperbilirubinaemia
Respiratory, thoracic, mediastinal disorders	Uncommon	Pulmonary embolism
General disorders and administration site conditions	Very common	Peripheral oedema

*Associated with CKD patients who were on dialysis while receiving EVRENZO.
†Based on global post-marketing experience.

CKD, chronic kidney disease; DD, dialysis-dependent; ESA, erythropoiesis-stimulating agent; MedDRA, Medical Dictionary tor Regulatory Activities; NDD, non-dialysis-dependent

Adverse events frequency

Patients not on dialysis

Incidence of TEAE (≥5% in any treatment group) in DOLOMITES trial[2]

	EVRENZO	ESA
End Stage Renal Disease	33.4%	36.2%
Hypertension	29.7%	33.8%
Decreased EGFR	17.0%	16.7%
Peripheral oedema	15.2%	12.3%
Hyperkalaemia	11.8%	14.4%
Nausea	10.8%	8.5%

Patients on dialysis

Pooled analysis of adverse events in patients with DD-CKD[5.1]

	EVRENZO	ESA
Vascular access thrombosis	12.8%	10.2%
Seizures	2.0%	1.6%
Sepsis	3.4%	3.4%
Pulmonary embolism	0.6%	0.5%
Deep-vein thrombosis	1.3%	0.3%

CKD, chronic kidney disease; DD, dialysis-dependent; ESA, erythropoiesis-stimulating agent; EGFR, estimated glomerular filtration rate; TEAE, treatment-emergent adverse event

Cardiovascular safety profile

A meta-analysis, of adjudicated major adverse cardiovascular events (MACE; a composite of all-cause mortality [ACM], myocardial infarction, stroke) and MACE+ (a composite of ACM, myocardial infarction, stroke, and hospitalization for either unstable angina or congestive heart failure), from the phase 3 study program was conducted in 8984 patients.[1]

No evidence of increased risk of major cardiovascular events or ACM with EVRENZO compared to ESA in a pool of patients not on dialysis and those just started on dialysis[1]

- Overall, the cardiovascular and mortality risk for treatment with EVRENZO has been estimated to be comparable to the cardiovascular and mortality risk for ESA therapy based on data from direct comparison of both therapies[1]
- Since, for patients with anaemia associated with CKD and not on dialysis, this risk could not be estimated with sufficient confidence versus placebo, a decision to treat these patients with EVRENZO should be based on similar considerations that would be applied before treating with an ESA[1]

ACM, all-cause mortality; CI, confidence interval; CKD, chronic kidney disease; CV, cardiovascular; ESA, erythropoiesis-stimulating agent; HR, hazard ratio; IDD, incident dialysis dependent; MI, myocardial infarction; NDD, non-dialysis-dependent

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Cardiovascular safety profile

Findings for patients on dialysis

Overall, EVRENZO was comparable with ESA for MACE, MACE+ and ACM[3]

	Patients new to dialysis (<4 months)	Patients stable on dialysis (>4 months) and stable on ESA
MACE	HR 0.83 (95% CI 0.61–1.13)	HR 1.18 (95% CI 1.00, 1.38)
MACE+	HR 0.76 (95% CI 0.57–1.00)	HR 1.03 (95% CI 0.90, 1.19)
ACM	HR 0.83 (95% CI 0.57–1.19)	HR 1.23 (95% CI 1.02, 1.49)
	Numerically lower risk compared with ESA, favourable trend towards EVRENZO	Comparison of treatment effects cannot be reliably established due to the inherent risks of switching patients from ESA to EVRENZO

Patients currently treated with an ESA can be converted to Evrenzo, however, conversion of dialysis patients otherwise stable on ESA treatment is only to be considered when there is a valid clinical reason.[1]

ESA, erythropoiesis-stimulating agent; **MACE,** major adverse cardiovascular events; **MACE+,** MACE + congestive, heart failure or unstable angina requiring hospitalisation; **ACM,** all cause mortality; **HR,** hazard ratio.

AC
erythropoiesis-stimulating agent; HR, hazard ratio; IDD, incident dialysis dependent; MI, myocardial infarction; NDD, non-dialysis-dependent

Evrenzo™
roxadustat
20, 50, 70 mg film-coated tablet

Contraindications, special warnings and precautions for use

SmPC

Contraindications[1]

EVRENZO is contraindicated in the following conditions:

- Hypersensitivity to the active substance, peanut, soya or to any of the excipients
- Third trimester of pregnancy
- Breast-feeding

Special warnings and precautions for use[1]

- Cardiovascular safety
- Thrombotic vascular events
- Seizures
- Serious infections
- Sepsis
- Inadequate response to therapy
- Hepatic impairment
- Pregnancy and contraception
- Misuse
- Excipients
- Drug interactions

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Cardiovascular and mortality risk[1]

SmPC

- Overall, the cardiovascular and mortality risk for treatment with EVRENZO has been estimated to be comparable to the cardiovascular and mortality risk for ESA therapy based on data from direct comparison of both therapies
- Since, for patients with anaemia associated with CKD and not on dialysis, this risk could not be estimated with sufficient confidence versus placebo, a decision to treat these patients with EVRENZO should be based on similar considerations that would be applied before treating with an ESA
- Further, several contributing factors have been identified that may impose this risk, including treatment non-responsiveness, and converting stable ESA treated dialysis patients
- In the case of non-responsiveness, treatment with EVRENZO should not be continued beyond 24 weeks after the start of treatment
- Conversion of dialysis patients otherwise stable on ESA treatment is only to be considered when there is a valid clinical reason
- For stable ESA treated patients with anaemia associated with CKD and not on dialysis, this risk could not be estimated as these patients have not been studied. A decision to treat these patients with EVRENZO should be based on a benefit risk consideration for the individual patient

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Thrombotic vascular events[1]

SmPC

- The reported risk of thrombotic vascular events (TVEs) should be carefully weighed against the benefits to be derived from treatment with EVRENZO particularly in patients with pre-existing risk factors for TVE, including obesity and prior history of TVEs (e.g., deep vein thrombosis [DVT] and pulmonary embolism [PE]). Deep vein thrombosis was reported as common and pulmonary embolism as uncommon amongst the patients in clinical studies. The majority of DVT and PE events were serious.
- Vascular access thrombosis (VAT) was reported as very common amongst the CKD patients on dialysis in clinical studies
- In CKD patients on dialysis, rates of VAT in EVRENZO-treated patients were highest in the first 12 weeks following initiation of treatment, at Hb values more than 12 g/dL and in the setting of Hb rise of more than 2 g/dL over 4 weeks. It is recommended to monitor Hb levels and adjust the dose using the dose adjustment rules to avoid Hb levels of more than 12 g/dL and Hb rise of more than 2 g/dL over 4 weeks
- Patients with signs and symptoms of TVEs should be promptly evaluated and treated according to standard of care. The decision to interrupt or discontinue treatment should be based on a benefit-risk consideration for the individual patient

CKD, chronic kidney disease; Hb, haemoglobin

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Seizures[1]

SmPC

- Seizures were reported as common amongst the patients in clinical studies receiving EVRENZO
- EVRENZO should be used with caution in patients with a history of seizures (convulsions or fits), epilepsy or medical conditions associated with a predisposition to seizure activity such as central nervous system (CNS) infections
- The decision to interrupt or discontinue treatment should be based on a benefit-risk consideration of the individual patient

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Serious infections[1]

SmPC

- The most commonly reported serious infections were pneumonia and urinary tract infections. Patients with signs and symptoms of an infection should be promptly evaluated and treated according to standard of care

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Sepsis[1]

SmPC

- Sepsis was one of the most commonly reported serious infections and included fatal events
- Patients with signs and symptoms of sepsis (e.g., an infection that spreads throughout the body with low blood pressure and the potential for organ failure) should be promptly evaluated and treated according to standard of care

Evrenzo™
roxadustat
20, 50, 70 mg film-coated tablet

Inadequate response to therapy[1]

SmPC

- Inadequate response to therapy with EVRENZO should prompt a search for causative factors. Nutrient deficiencies should be corrected
- Intercurrent infections, 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 typical causes of non-response are excluded, and the patient has reticulocytopenia, an examination of the bone marrow should be considered
- In the absence of an addressable cause for an inadequate response to therapy, EVRENZO should not be continued beyond 24 weeks of therapy

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Hepatic impairment[1]

SmPC

- Caution is warranted when EVRENZO is administered to patients with moderate hepatic impairment (Child-Pugh class B)
- EVRENZO is not recommended for use in patients with severe hepatic impairment (Child-Pugh class C)

Pregnancy and contraception[1]

SmPC

- EVRENZO should not be initiated in women planning on becoming pregnant, during pregnancy or when anaemia associated with CKD is diagnosed during pregnancy
- In such cases, alternative therapy should be started, if appropriate
- If pregnancy occurs while EVRENZO is being administered, treatment should be discontinued and alternative treatment started, if appropriate
- Women of childbearing potential must use highly effective contraception during treatment and for at least one week after the last dose of EVRENZO

CKD, chronic kidney disease

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Misuse[1]

SmPC

- Misuse may lead to an excessive increase in packed cell volume. This may be associated with life-threatening complications of the cardiovascular system

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Excipients[1]

SmPC

- EVRENZO contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product
- EVRENZO contains Allura Red AC aluminium lake which may cause allergic reactions
- EVRENZO contains traces of soya lecithin. Patients who are allergic to peanut or soya, should not use this medicinal product

Interaction with other medicinal products[1]

SmPC

Effect of other medicinal products on EVRENZO

Phosphate binders and other products containing multivalent cations

- Co-administration of EVRENZO with phosphate binders sevelamer carbonate or calcium acetate in healthy subjects decreased EVRENZO AUC by 67% and 46% and C_{max} by 66% and 52%, respectively. EVRENZO may form a chelate with multivalent cations such as in phosphate binders or other products containing calcium, iron, magnesium or aluminium. Staggered administration of phosphate binders (at least 1 hour apart) had no clinically significant effect on EVRENZO exposure in patients with CKD. EVRENZO should be taken at least 1 hour after administration of phosphate binders or other medicinal products or supplements containing multivalent cations. This restriction does not apply to lanthanum carbonate, as the co-administration of EVRENZO with lanthanum carbonate did not result in a clinically meaningful change in the plasma exposure of EVRENZO.

Modifiers of CYP2C8 or UGT1A9 activity

- EVRENZO is a substrate of CYP2C8 and UGT1A9. Co-administration of EVRENZO with gemfibrozil (CYP2C8 and OATP1B1inhibitor) or probenecid (UGT and OAT1/OAT3 inhibitor) in healthy subjects increased EVRENZO AUC by 2.3-fold and C_{max} by 1.4-fold. Monitor Hb levels when initiating or discontinuing concomitant treatment with gemfibrozil, probenecid, other strong inhibitors or inducers of CYP2C8 or other strong inhibitors of UGT1A9. Adjust the dose of EVRENZO following dose adjustment rules based on Hb monitoring.

AUC, area under curve; CKD, chronic kidney disease; Hb, haemoglobin

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Interaction with other medicinal products[1] cont.

SmPC

Effects of EVRENZO on other medicinal products

OATP1B1 or BCRP Substrates

- EVRENZO is an inhibitor of BCRP and OATP1B1. These transporters play an important role in the intestinal and hepatic uptake and efflux of statins. Co-administration of 200 mg of EVRENZO with simvastatin in healthy subjects increased the AUC and C_{max} of simvastatin 1.8- and 1.9-fold, respectively, and the AUC and C_{max} of simvastatin acid (the active metabolite of simvastatin) 1.9- and 2.8-fold, respectively. The concentrations of simvastatin and simvastatin acid also increased when simvastatin was administered 2 hours before or 4 or 10 hours after EVRENZO. Co-administration of 200 mg of EVRENZO with rosuvastatin increased the AUC and C_{max} of rosuvastatin 2.9- and 4.5-fold, respectively. Co-administration of 200 mg of EVRENZO with atorvastatin increased the AUC and C_{max} of atorvastatin 2.0- and 1.3-fold, respectively
- Interactions are also expected with other statins. When co-administered with EVRENZO, consider this interaction, monitor for adverse reactions associated with statins and for the need of statin dose reduction. Refer to statin prescribing information when deciding on the appropriate statin dose for individual patients
- EVRENZO may increase the plasma exposure of other medicinal products that are substrates of BCRP or OATP1B1. Monitor for possible adverse reactions of co-administered medicinal products and adjust dose accordingly.

EVRENZO and ESAs

- It is not recommended to combine administration of EVRENZO and ESAs as the combination has not been studied

AUC, area under curve; ESA, erythropoiesis-stimulating agent

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

References

1. EVRENZO EU SmPC, July 2022. Available at: https://www.medicines.org.uk/emc/product/12835/smpc#.
2. Barratt J, Andric B, Tataradze A, et al. Roxadustat for the treatment of anaemia in chronic kidney disease patients not on dialysis: a Phase 3, randomized, open-label, active-controlled study (DOLOMITES). *Nephrol Dial Transplant*. 2021;36(9):1616-1628.
3. Barratt J, Sulowicz W, Schömig M, et al. Efficacy and Cardiovascular Safety of Roxadustat in Dialysis-Dependent Chronic Kidney Disease: Pooled Analysis of Four Phase 3 Studies. *Adv Ther*. 2021;38(10):5345-5360.

Raise your expectations with EVRENZO

Demonstrated Efficacy

- EVRENZO can help your patients achieve and maintain their target Hb levels[1]
- EVRENZO is effective in patients with underlying inflammation.[2]
- Patients treated with EVRENZO use less IV iron than those treated with ESA[1]

Added benefit for your patient

- Oral administration means patients can avoid parenteral therapy[1]
- Treatment just 3 days per week[1]

An oral treatment for anaemia of CKD

- EVRENZO raises Hb levels without increasing CV risk compared to ESA in patients not on dialysis and those just started on dialysis[1]
- The safety profile of EVRENZO has been evaluated in a clinical trial programme involving over 6,800 patients, and was overall comparable to ESA for the majority of safety variables[1]

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions using the tab below.

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IV, intravenous

Summary of discussion

- Anaemia of CKD is a complex, multifactorlal disease[3]
- EVRENZO has the potential to change the treatment paradigm, addressing the multifactorial pathophysiology of anaemia of CKD with the convenience of an oral tablet[1]
- Roxadustat is a first-in-class HIF-PH inhibitor[4] which harnesses the HIF pathway – the natural process that stimulates erythropoiesis in response to low oxygen[1]
- EVRENZO stimulates a coordinated erythropoietic response, increasing endogenous EPO, reducing hepcidin levels, improving iron bioavailability and increasing Hb and red blood cell production[1]
- EVRENZO can benefit a broad range of patients with anaemia across the CKD continuum, and may be initiated as soon as patients need additional treatment after iron[1]

Send information

What would you like to discuss at our next call?

- ☐ EVRENZO mechanism of action
- ☐ Anaemia of CKD
- ☐ Efficacy of EVRENZO
- ☐ Dosing and administration
- ☐ Suitable patients
- ☐ Starting patients on EVRENZO

1. How confident are you about prescribing EVRENZO for patients who are not on dialysis?

Not confident | Fairly confident | Very confident

2. How confident are you about prescribing EVRENZO for patients on dialysis?

Not confident | Fairly confident | Very confident

Future content

Evrenzo™ roxadustat

20, 50, 70 mg film-coated tablet

CKD, chronic kidney disease; EPO, erythropoietin; Hb, haemoglobin; HIF, hypoxia-inducible factor; HIF-PH, hypoxia-inducible factor-prolyl hydroxylase

Summary of discussion

- EVRENZO has been investigated in a comprehensive clinical trial programme involving more than 9,600 patients[1]
- Patients treated with EVRENZO achieved and maintained Hb levels comparable to ESA, with less use of IV iron compared with ESA[1]
- EVRENZO is effective regardless of inflammation status and comorbidities[5]
- No increased cardiovascular risk in patients not on dialysis and those just started on dialysis with EVRENZO compared to ESA[1]
  - Conversion of dialysis patients otherwise stable on ESA treatment is only to be considered when there is a valid clinical reason.

What would you like to discuss at our next call?

- ☐ EVRENZO mechanism of action
- ☐ Anaemia of CKD
- ☐ Efficacy of EVRENZO
- ☐ Dosing and administration
- ☐ Suitable patients
- ☐ Starting patients on EVRENZO

1. How confident are you about prescribing EVRENZO for patients who are not on dialysis?

2. How confident are you about prescribing EVRENZO for patients on dialysis?

Send information

Future content

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IV, intravenous

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

Summary of discussion

- The general safety profile of EVRENZO was overall comparable to ESA for the majority of safety variables evaluated[1]
- EVRENZO can help patients with anaemia of CKD…
  - To achieve and maintain their target Hb levels[1]
  - with a reduced use of IV iron compared with ESA[1]
  - and an oral treatment that can be taken at home[1]

What would you like to discuss at our next call?

- ☐ EVRENZO mechanism of action
- ☐ Anaemia of CKD
- ☐ Efficacy of EVRENZO
- ☐ Dosing and administration
- ☐ Suitable patients
- ☐ Starting patients on EVRENZO

1. How confident are you about prescribing EVRENZO for patients who are not on dialysis?

2. How confident are you about prescribing EVRENZO for patients on dialysis?

Send information

Future content

Evrenzo™ roxadustat

20, 50, 70 mg film-coated tablet

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IV, intravenous

Summary of discussion

[Cont.]

- The general safety profile of EVRENZO was overall co
safety va
- EVRENZO
of CKD..
  - To
Hb
  - wit
wit
  - anc
tha

What would you like to discuss at our next call?

☐ EVRENZO mechanism of action

ribing
dialysis?

Not confident | Fairly confident | Very confident

2. How confident are you about prescribing EVRENZO for patients on dialysis?

Not confident | Fairly confident | Very confident

Send information

Future content

Future content

What would you like to discuss at our next call?

- ☐ Clinical trial summaries
- ☐ Efficacy data summary
- ☐ EVRENZO safety profile
- ☐ Mechanism of action explanation

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; IV, intravenous

Evrenzo™ roxadustat
20, 50, 70 mg film-coated tablet

References

1. EVRENZO EU SmPC, July 2022. Available at: https://www.medicines.org.uk/emc/product/12835/smpc#.
2. Provenzano R, Besarab A, Wright S, et al. Roxadustat (FG-4592) Versus Epoetin Alfa for Anemia in Patients Receiving Maintenance Hemodialysis: A Phase 2, Randomized, 6- to 19-Week, Open-Label, Active-Comparator, Dose-Ranging, Safety and Exploratory Efficacy Study. *Am J Kidney Dis*. 2016;67(6):912-924.
3. Li ZL, Tu Y, Liu BC. Treatment of Renal Anemia with Roxadustat: Advantages and Achievement. *Kidney Dis (Basel)*. 2020;6(2):65-73.
4. European Medicines Agency. Summary of opinion1 (initial authorisation). EVRENZO. Available at: https://www.ema.europa.eu/en/documents/smop-initial/chmp-summary-positive-opinion-evrenzo_en.pdf. Last accessed: December 2022.
5. Barratt J, Andric B, Tataradze A, et al. Roxadustat for the treatment of anaemia in chronic kidney disease patients not on dialysis: a Phase 3, randomized, open-label, active-controlled study (DOLOMITES). *Nephrol Dial Transplant*. 2021;36(9):1616-1628.

API

ABBREVIATED PRESCRIBING INFORMATION

Prescribing Information

Presentation: EVRENZO 20 mg, 50 mg and 70 mg, film-coated tablets roxadustat.
Composition: Each tablet contains 20 mg, 50 mg and 70 mg of roxadustat.
The other ingredients are:
Tablet core: lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, povidone, magnesium stearate.
Film-coating: polyvinyl alcohol, talc, macrogol, Allura Red Aluminium Lake AC, titanium dioxide, lecithin (soya).
Indication(s): What EVRENZO is: EVRENZO is a medicine that increases the number of red blood cells and haemoglobin level in your blood. It contains the active substance roxadustat. What EVRENZO is used for: EVRENZO is used to treat adults with symptomatic anaemia that occurs in patients with chronic kidney disease. Anaemia is when you have too few red blood cells and your haemoglobin level is too low. As a result, your body might not receive enough oxygen. Anaemia can cause symptoms such as tiredness, weakness, or shortness of breath. How EVRENZO works: Roxadustat, the active substance in EVRENZO, works by increasing the level of HIF, a substance in the body which increases the production of red blood cells when oxygen levels are low. By raising HIF levels, the medicine increases the production of red blood cells and raises the levels of haemoglobin (the oxygen-carrying protein in red blood cells). This improves the oxygen supply to your body and may reduce your symptoms of anaemia.
Posology and Method of Administration: Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. Your doctor will tell you what dose of EVRENZO to take. Your doctor will check your haemoglobin levels regularly and increase or lower your dose based on your haemoglobin levels. EVRENZO is taken by mouth as tablets.
Taking EVRENZO: •Take your EVRENZO dose three times per week unless your doctor told you otherwise. •Never take EVRENZO on consecutive days. •Take EVRENZO on the same three days every week. •EVRENZO can be taken with food or between meals. •Swallow the tablets whole. •Do not chew, break or crush the tablets. Take EVRENZO at least 1 hour after you have taken medicines that reduce phosphate levels in your blood (called phosphate binders) or other medicines or supplements that contain calcium, iron, magnesium or aluminum (called multivalent cations).
Dosing Schedule:
3 times a week dosing schedule: EVRENZO comes in a blister pack containing medicine for 4 weeks (12 tablets), divided into 4 rows. Each row contains 1 week of medicine (3 tablets). Make sure you take tablets from the same row for each week. Your dose ranges from 20 mg three times per week up to a maximum 400 mg three times per week.
Different dosing frequencies: In exceptional cases (based upon your haemoglobin levels), your doctor may decide to lower your EVRENZO dose to 20 mg two times or one time per week. In this case your doctor will explain which days week you need to take your dose.
More than 1 tablet needed to make up a dose: In most cases you will have 1 blister package per month. If your dose requires more than 1 blister package, you will need to take a tablet from each blister per dosing day. Your doctor will explain when and how many tablets to take. Your doctor will monitor your haemoglobin level and may temporarily stop your treatment if your haemoglobin level becomes too high. Do not restart your treatment until your doctor tells you to. Your doctor will tell you what dose of EVRENZO to take and when to start taking it again.
If you take more EVRENZO than you should: If you take more tablets or a higher dose than you should, contact your doctor straight away.
If you forget to take EVRENZO: •Never take a double dose to make up for a forgotten dose. •If more than 24 hours (1 day) remains before your next scheduled dose, take the missed dose as soon as possible and take the next dose on the next scheduled day. • If less than 24 hours (1 day) remains before your next scheduled dose: skip the missed dose and take the next dose on the next scheduled day.
If you stop taking EVRENZO: Do not stop taking this medicine unless your doctor tells you to do so. If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

Prescribing Information

Possible Side Effects: Like all medicines, this medicine can cause side effects, although not everybody gets them. Some possible side effects may be serious. Contact your doctor straight away if you get any of the following: •blood clot in the veins of your legs (deep vein thrombosis or DVT) (may affect up to 1 in 10 people). •blood clot in the lungs (pulmonary embolism) (may affect up to 1 in 100 people). •blood clot in your haemodialysis access (vascular access thrombosis or VAT) that causes the vascular access to close up or stop working if you are using a fistula or graft for dialysis access (may affect more than 1 in 10 people). •seizures and warning signs of seizures (convulsions or fits) (may affect up to 1 in 10 people). •sepsis, a serious or in rare cases, life-threatening infection (may affect up to 1 in 10 people).
Other possible side effects: Very common (may affect more than 1 in 10 people): •increased amount of potassium •high blood pressure (hypertension) •feeling sick (nausea) •diarrhoea •swelling due to fluid retention in the extremities (peripheral oedema) Common (may affect up to 1 in 10 people): •difficulty in sleeping (insomnia) •headache •vomiting •constipation. Uncommon (may affect up to 1 in 100 people): •increased amount of bilirubin in your blood.
Reporting of side effects: If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. By reporting side affects you can help provide more information on the safety of this medicine.
Contraindications, Precautions and Warnings: Do not take EVRENZO •if you are allergic to peanut or soya, do not use this medicine. EVRENZO contains soya lecithin. •if you are allergic to roxadustat or any of the other ingredients of this medicine. •if you are more than 6 months pregnant, (It is also better to avoid this medicine in early pregnancy - see pregnancy section). •if you are breastfeeding. Talk to your doctor, or pharmacist before taking EVRENZO: •if you have epilepsy or have ever had convulsions or fits. •if you have signs and symptoms of an infection, which may include fever, sweating or chills, sore throat, runny nose, shortness of breath, feeling weak, confusion, cough, vomiting, diarrhoea or stomach pain, feeling of burning when you pass urine, red or painful skin or sores on your body. •if you have a liver disorder. Chronic kidney disease and anaemia may increase the risk of cardiovascular events and death. Managing your anaemia is important. Your doctor will monitor your haemoglobin and also consider your treatment regimen as anaemia treatment and switching between anaemia treatments may also have a negative impact on your cardiovascular health. **Talk to your doctor, or pharmacist straight away:** •if you get blood clots: •in the veins of your legs (deep vein thrombosis or DVT), signs of which can include pain and/or swelling in the legs, cramping or a feeling of warmth in the affected leg; •in the lungs (pulmonary embolism or PE), signs of which can include sudden shortness of breath, chest pain (usually worse with breathing), feeling of anxiety, dizziness, lightheadedness, or fainting; heart racing, coughing (sometimes with blood); •in your haemodialysis access (vascular access thrombosis or VAT) that stop the vascular access from working; signs of this can include swelling, redness, hardening or thickening of the skin around your access, oozing at the access site, not feeling a vibration ("thrill") over the access area; •if you have a seizure (convulsion or fit) or possible warning signs that a seizure may occur, such as headache, irritability, fear, confusion or unusual feelings; •if you have signs and symptoms of an infection, which include fever, sweating or chills, sore throat, runny nose, shortness of breath, feeling weak or faint, confusion, cough, vomiting, diarrhoea, or stomach pain, burning when you pass urine, red or painful skin or sores on your body. Misuse can lead to an increase in blood cells and consequently thicken the blood. This can cause life threatening problems with the heart or blood vessels.
Children and adolescents: Do not give EVRENZO to children and adolescents aged under 18 years because there is not enough information about its use in this age group.
Other medicines and EVRENZO: Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. EVRENZO may affect the way these medicines work, or these medicines may affect how EVRENZO works. In particular tell your doctor or pharmacist if you have or are taking any of the following medicines: •medicines to reduce phosphate levels in your blood (called phosphate binders) or other medicines or supplements that contain calcium, iron, magnesium or aluminum (called multivalent cations), such as sevelamer carbonate or calcium acetate.

Prescribing Information

You must take EVRENZO at least 1 hour after these medicines or supplements. Otherwise roxadustat will not be properly absorbed by your body. • a medicine to treat gout called probenecid. • medicines used to lower cholesterol, such as simvastatin, atorvastatin, or rosuvastatin (also called "statins"), or gemfibrozil. •other medicines used to treat anaemia such as erythropoiesis-stimulating agents (ESAs). If you normally take any of these medicines, your doctor might change it and prescribe a different medicine for you during your treatment with EVRENZO. EVRENZO contains lactose, soya sugar (lactose), traces of peanut and soya (soya lecithin), and an azo colouring agent (Allura Red AC aluminium lake). If you have been told by your doctor that you have an intolerance to some sugars or are allergic to peanut, soya or azo colouring agents, contact your doctor before taking this medicine.
Pregnancy, Breast-feeding and lactation: If you are pregnant, think you may be pregnant or are planning to have a baby, contact your doctor. EVRENZO may harm your unborn baby. EVRENZO is not recommended in the first 6 months of pregnancy and must not be taken in the last 3 months of pregnancy. Women taking EVRENZO who are able to become pregnant should use an effective method of contraception during treatment with EVRENZO and for at least one week after the last dose of EVRENZO. If you use a hormonal contraceptive, you must also use a barrier method, such as a condom, or a diaphragm. Do not breastfeed if you are on treatment with EVRENZO. It is not known if EVRENZO passes into your breast milk and could harm your baby.
Driving and using machines: This medicine may affect your ability to drive or use machines. Seizures can occur as a side effect.

For more detailed information, please refer to the full Prescribing Information as available with Astellas Medical Representative. Legal category: POM; **MA Holder:** Astellas Pharma Europe B.V., Sylviusweg 62, 2333 BE Leiden, NL.
Further information available upon request from: Astellas Pharma DMCC, P.O. Box 282872, Dubai, UAE.
Version: 1.0.
For reporting any adverse event or safety information related to Astellas products, please contact immediately pharmacovigilance.ae@astellas.com or call +201115910444

- **Always read the full prescribing information.**
- **Healthcare professionals are asked to report any suspected adverse drug reaction to Egyptian Pharmacovigilance Center (EPVC).**
- **Egyptian drug authority EVRENZO leaflet approval date 6/7/2022.**

astellas
Astellas Pharma International B.V. Scientific Office,
Star Capital F2, Floor 8, Office 81
8th Omar Ibn El Khattab, Masaken El Mohandesin,
Heliopolis, Cairo, Egypt

MAT-EG-EVZ-2022-00002
Date of preparation: December 2022