Public Assessment Report

(Variation, New Posology)

EFESA

INFORMASI PRODUK

Nama obat	:	Efesa
Bentuk sediaan	:	Injeksi
Zat aktif	:	Tiap ml mengandung : Efepoetin alfa 1 mg
Kemasan	:	Dus, 1 prefilled syringe @ 0,3 mL Dus, 1 prefilled syringe @ 0,6 mL
Pendaftar	:	PT. Kalbio Global Medika, Bekasi
Produsen	:	PT. Kalbio Global Medika, Bekasi
Kategori Registrasi	:	Registrasi produk biologi yang sudah terdaftar dengan indikasi dan posologi baru
Indikasi yang disetujui	:	*EFESA is indicated for the treatment of anemia in non-dialysis Chronic Kidney Disease (CKD) patients.*
Posologi yang diajukan	:	*In adult patients, EFESA is administered with recommended* ***starting dose*** *for anemia in CKD not on dialysis;* ● ***4 mcg/kg body weight*** *administered subcutaneously, subsequent doses will be* ***titrated to optimal hemoglobin target and will be administered once every two weeks****.* ● *When initiating or adjusting therapy, monitor hemoglobin levels at least* ***biweekly until stable, then monitor at least monthly. Administer Efesa subcutaneously in the abdomen, arm or thigh.*** ● *If the* ***increase in Hb is less than 1.0 g/dL over 4 weeks and iron stores are adequate****, the dose may* ***be increased by approximately 25% of the previous dose. Further increases may be made at 4-week intervals when the Hb is in the specified target Hb range. The maximum dose of Efepoetin alfa is 8 mcg/kg BW, which may be given when it is necessary.*** ● *If the rate of rise in Hb is greater than 2 g/dL in one month or the Hb increases by more than 1.0 g/dL in a 2-week period, the dose should be decreased by approximately 25%.* ● *If the Hb is increasing and exceeds 11.5 g/dL, the dose should be reduced by approximately 25%.* ● *If the Hb continues to increase and exceeds 12 g/dL, dosing should be temporarily withheld until the Hb begins to decrease and restart dosing when Hb level falls back to the predetermined Hb level for restarting (ie ≤11.5 g/dL) based on the next scheduled Hb test results, at which point therapy should* ***be reinitiated at a dose approximately 25% below the previous dose.*** ● *During maintenance period, dosage of Efesa should be adjusted to maintain the Hb within the target range* ***(10 g/dL to 12 g/dL). Efesa could be administered using the same everytwo-week dose. It could also be administered every-four-week at double the two weekly dosage (GXE4KGbio-001).***

PENGANTAR

Efepoetin alfa merupakan novel long-acting recombinant erythropoietin (EPO)-hybrid Fc fusion protein (rhEPO-hyFc) yang dikembangkan oleh PT. Kalbe Genexine Biologics bekerja sama dengan Genexine, Inc

dan Green Cross Corporation, South Korea. Efesa Injeksi telah disetujui izin edarnya di Indonesia sejak 12 Oktober 2023. Efesa diindikasikan untuk mengobati *anemia in non-dialysis Chronic Kidney Disease (CKD).* Dilakukan pengajuan registrasi variasi penambahan posologi baru.

ASPEK MUTU
Tidak ada evaluasi data mutu pada pengajuan registrasi ini.

ASPEK KHASIAT DAN KEAMANAN
Studi Non Klinik
Tidak ada evaluasi data mutu pada pengajuan registrasi ini.

Studi Klinik
Diserahkan 1 studi klinik yang relevan dengan indikasi dan perubahan posologi baru yaitu studi fase III (GXE4KGBio-001) dengan disain studi *opel-label, randomized, mircera-controlled, parallel-group,* dimana hasil studi menunjukkan efikasi Efepoetin alfa terhadap pasien *non-dialysis Chronic Kidney Disease (CKD)* yang disimpulkan sebagai berikut:

1. Regimen pemberian dosis awal (starting dose), yaitu 4 mcg/kgBB, setiap 2 minggu, adalah sesuai dengan protokol studi klinik yang disetujui BPOM dan laporan hasil studi klinik GXE4KGbio-001.
2. Frekuensi monitoring kadar Hb, yaitu "sedikitnya setiap 2 minggu hingga Hb stabil, kemudian dimonitor sedikitnya setiap bulan"; dan pencantuman informasi lokasi pemberian (tempat injeksi), yaitu "secara subkutan pada abdomen, lengan atau paha", adalah sesuai dengan protokol studi klinik yang disetujui BPOM dan laporan hasil studi klinik GXE4KGbio-001.
3. Rewording terkait aturan penyesuaian dosis (peningkatan atau penurunan) yang diajukan adalah sesuai dengan yang dijelaskan pada protokol dan laporan studi klinik, dengan informasi yang lebih singkat dan jelas, serta tidak ada duplikasi informasi.
4. Untuk update informasi terkait maintenance period:
    a. Berdasarkan laporan final studi GXE4Kgbio-001 (versi 1.0 tanggal 22 Desember 2023), hasil penurunan titer Hb pada periode extension menunjukkan bahwa efepoetin Q2W non-inferior dari Mircera Q4W (perbedaan 0,195 g/dL; 95%CI -0,153; 0,543). Sedangkan untuk regimen efepoetin Q4W, efikasinya regimen Q4W terlihat sedikit lebih rendah dibanding regimen Q2W, tetapi masih masuk dalam kriteria non-inferioritas dibandingkan Mircera Q4W (perbedaan -0,39 g/dL; 95%CI -0,751; -0,030).
    b. Tidak ada analisa yang membandingkan head to head antara regimen Q2W vs Q4W.
    c. Regimen Q4W dapat mengurangi waktu kunjungan ke RS sehingga diharapkan dapat meningkatkan kepatuhan pasien terhadap pengobatan.
    d. Perlu ditambahkan informasi untuk merujuk pada informasi tentang studi klinik, agar klinis dapat lebih mencermati profil efikasi regimen Q2W dan Q4W sebagai pertimbangkan dalam menentukan strategi pengobatan pasiennya.

KEPUTUSAN:
Mempertimbangkan data khasiat dan keamanan tersebut di atas, diputuskan registrasi posologi baru Efesa Injeksi dapat diterima dengan perbaikan posologi menjadi sebagai berikut:
In adult patients, EFESA is administered with recommended starting dose for anemia in CKD not on dialysis:

- *4 mcg/kg body weight administered subcutaneously, subsequent doses will be titrated to optimal hemoglobin target and will be administered once every two weeks.*
- *When initiating or adjusting therapy, monitor hemoglobin levels at least biweekly until stable, then monitor at least monthly. Administer Efesa subcutaneously in the abdomen, arm or thigh.*

- *If the increase in Hb is less than 1.0 g/dL over 4 weeks and iron stores are adequate, the dose may be increased by approximately 25% of the previous dose. Further increases may be made at 4-week intervals when the Hb is in the specified target Hb range. The maximum dose of Efepoetin alfa is 8 mcg/kg BW, which may be given when it is necessary.*
- *If the rate of rise in Hb is greater than 2 g/dL in one month or the Hb increases by more than 1.0 g/dL in a 2-week period, the dose should be decreased by approximately 25%.*
- *If the Hb is increasing and exceeds 11.5 g/dL, the dose should be reduced by approximately 25%.*
- *If the Hb continues to increase and exceeds 12 g/dL, dosing should be temporarily withheld until the Hb begins to decrease and restart dosing when Hb level falls back to the predetermined Hb level for restarting (ie ≤11.5 g/dL) based on the next scheduled Hb test results, at which point therapy should be reinitiated at a dose approximately 25% below the previous dose.*
- *During maintenance period, dosage of Efesa should be adjusted to maintain the Hb within the target range (10 g/dL to 12 g/dL). Efesa could be administered using the same every-two-week dose. It could also be administered every-four-week at double the two weekly dosage* ***(see Clinical Studies section - study GXE4KGbio-001).***