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Eflapegrastim-xnst (ROLVEDON)
Mini-Monograph
June 2023

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

FDA APPROVAL		
	Description/MOA	A novel, long-acting Granulocyte Colony-Stimulating Factor (G-CSF)
	Indication(s) Under Review	To decrease the incidence of infection (febrile neutropenia) in patients with non-myeloid malignancies receiving myelosuppressive cancer drugs. Not for mobilization for peripheral progenitor cells for stem cell transplantation
	Dosage Form(s)	13.2 ng/0.6mL pre-filled syringe for subcutaneous injection once each chemotherapy cycle

CLINICAL EVIDENCE		
	Study	ADVANCE[1] Study 1 N=406
	Design	P3, OL, MC, active control, non-inferiority; ECOG 0-2
	Population	Early-stage breast cancer; mAge 61; Female: >99%; White 78%; ECOG 0:71%; Adjuvant 83%
	Intervention	Eflapegrastim 13.2mg vs Pegfilgrastim 6 mg D2 of each cycle; 1°EP=DSN Cycle 1
	Results	C1 DSN: 0.2 vs 0.35 days (non-inferiority and superiority); C2-4 DSN: non-inferior; C1 FN: low; no difference
	Summary	In the adjuvant therapy of early breast cancer with chemotherapy (docetaxel and cyclophosphamide), eflapegrastim was non-inferiority to pegfilgrastim in reducing neutropenia in cycle 1 (primary) and throughout 4 cycles (secondary) with comparative safety.

CLINICAL EVIDENCE		
	Study	RECOVER[2] Study 2 N=237
	Design	P3, O, MC, active control, non-inferiority, ECOG 0-2
	Population	Early breast cancer, mAge 57; Female 100%; White 77%; ECOG=0 80%; Adjuvant 80%
	Intervention	Eflapegrastim 13.2mg vs Pegfilgrastim 6 mg D2 of each cycle; 1°EP=DSN Cycle 1
	Results	C1 DSN: 0.31vs 0.39 days (non-inferiority); C2-4 DSN: non-inferior; C1 FN: low, no difference; C2-4 FN: no difference
	Summary	In the adjuvant setting of early breast cancer treated with chemotherapy (docetaxel and cyclophosphamide), eflapegrastim was non-inferiority to pegfilgrastim in reducing severe neutropenia and febrile neutropenia complications in cycle 1 (primary) and throughout 4 cycles (secondary) with comparable safety.

P3=phase 3; OL=open-label; MC=multi-center; ECOG=Eastern Cooperative Oncology Group; DSN=duration of severe neutropenia; FN=febrile neutropenia

SAFETY		
	Boxed warnings	None
	Contraindications	serious allergic reaction to human G-CSF
	Warnings/Precautions	Splenic rupture, ARDS, serious allergic reactions, Sickle Cell crisis, glomerulonephritis, leukocytosis, thrombocytopenia, capillary leak syndrome, stimulation of tumor growth, MDS/AML in breast and lung cancer patients
	Adverse reactions	≥20%: fatigue, nausea, diarrhea, bone pain, headache, pyrexia, anemia, rash, myalgia, arthralgia, back pain

Drug	Formulary status	Clinical Guidance	Other Considerations
Eflapegrastim-xnst	TBD	None	Pre-filled syringe; administer SQ once per chemo cycle; application withdrawn in 2019 due to manufacturing issues
Pegfilgrastim-bmez	F	None	National Contract item; pre-filled syringe; administer SQ once per chemo cycle

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Projected Place in Therapy/Conclusions

- In 2 phase III clinical trials in patients with early breast cancer receiving myelosuppressive chemotherapy for 4 cycles in the adjuvant setting, eflapegrastim was non-inferior to pegfilgrastim in reducing the duration of severe neutropenia during cycle 1 (primary endpoint) and during cycles 2-4 (secondary endpoint). Pooled rates of febrile neutropenia for this chemotherapy combination without G-CSF prophylaxis are 29.1%.[3]
- Safety during the clinical trial (adverse reactions in ≥20%) was similar between eflapegrastim and pegfilgrastim despite the fact that eflapegrastim provides a lower dose of G-CSF compared to pegfilgrastim. The package labeling for both products contains the same contraindication and Warnings and Precautions.
- There is no clear place in therapy for eflapegrastim instead of pegfilgrastim.

References

[1] Schwarztberg LS, BhatG, Peguero J, et al. Eflapegrastim, a long-acting, granulocyte-colony stimulating factor for the management of chemotherapy-induced neutropenia: results of a Phase III trial. The Oncologist 2020; 25: e1233-e1241.

[2] Cobb PW, Moon YW, Mezei K, et al. A comparison of eflapegrastim to pegfilgrastim in the management of chemotherapy-induced neutropenia in patients with early-stage breast cancer undergoing cytotoxic chemotherapy (RECOVER): a Phase III study. Cancer Medicine 2020;9: 6234-6243.

[3] Younis T, Rayson D, Thompson K. Primary G-CSF prophylaxis for adjuvant TC or FEC-D chemotherapy outside of clinical trial settings: a systematic review and meta-analysis. Support Care Cancer 2012; 20: 2523-2530.