01. Early Post-Marketing Safety Signals of Anifrolumab in EudraVigilance: A Belimumab-Comparator Disproportionality Analysis

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Background: Anifrolumab is a type I interferon receptor antagonist approved for adults with moderate-to-severe systemic lupus erythematosus (SLE). Although clinical trials established its efficacy and expected safety profile, post-marketing analyses using public EudraVigilance data remain limited. Spontaneous-report pharmacovigilance may identify early signals of disproportionate reporting after approval, particularly for infection-related, immune-mediated, and rare adverse events. Aim: This study aimed to evaluate early post-marketing signals of disproportionate adverse-event reporting for anifrolumab in public EudraVigilance data. **Methods**: We performed a retrospective disproportionality analysis of public EudraVigilance suspected adverse drug reaction reports. Anifrolumab was the index drug, and belimumab was selected as an active comparator to partially address indication-related reporting differences. Reports were restricted to 14 February 2022, the EU marketing authorisation date of anifrolumab, through 1 May 2026. Each unique case was counted once per MedDRA Preferred Term (PT). Non-clinical and data-quality PTs were excluded from the primary clinical signal analysis. PT-level disproportionality was assessed using reporting odds ratio (ROR), proportional reporting ratio (PRR) with chi-square, Bayesian confidence propagation neural network information component (IC), and Multi-item Gamma Poisson Shrinker empirical Bayes geometric mean (EBGM). A robust signal was defined as a PT with at least three anifrolumab cases and positivity across all four methods. Prespecified reaction-group analyses were supportive and used ROR, PRR/chi-square, and IC. A sensitivity analysis included only cases in which anifrolumab was the sole suspect drug. **Results**: The study included 1,122 anifrolumab cases and 3,585 belimumab cases. Anifrolumab reports contained 2,734 reactions across 823 unique PTs, while belimumab reports contained 13,889 reactions across 1,877 unique PTs. All reports were spontaneous. Anifrolumab cases were predominantly female (931/1,122; 83.0%) and healthcare-professional reported (998/1,122; 89.0%). After excluding 13 non-clinical or data-quality PTs, 2,105 clinical PTs were evaluated. Herpes zoster was the only robust signal of disproportionate reporting, reported in 84 anifrolumab cases and 42 belimumab cases, with ROR 6.78 (95% CI 4.66–9.87), PRR 6.35, chi-square 130.81, IC025 1.31, EBGM 2.56, and EB05 2.14. Forty-eight additional candidate signals were positive in at least two methods but did not meet the full quadruple definition. These included hypersensitivity-, respiratory infection-, infusion reaction-, herpesvirus-, and SLE activity-related terms. In supportive reaction-group analysis, herpesvirus/zoster reactions showed the strongest disproportionality. In the sole-suspect sensitivity analysis, herpes zoster remained the only robust signal, with 80 cases, ROR 6.99, IC025 1.36, EBGM 2.66, and EB05 2.21. **Conclusion**: Herpes zoster was the only robust signal of disproportionate reporting for anifrolumab compared with belimumab and remained stable after restriction to sole-suspect cases. Other findings were exploratory and require cautious interpretation because spontaneous reports cannot establish causality and may reflect SLE activity, comorbidity, or reporting bias. These results support continued attention to herpes zoster monitoring in patients treated with anifrolumab.

~~Figure or Table:~~

Analysis	Preferred Term	Anifrolumab cases, n	Belimumab cases, n	ROR	95% CI	PRR	IC025	EBGM	EB05
Primary analysis	Herpes zoster	84	42	6.78	4.66–9.87	6.35	1.31	2.56	2.14
Sole-suspect sensitivity analysis	Herpes zoster	80	42	6.99	4.79–10.20	6.52	1.36	2.66	2.21

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