Cureus
Part of SPRINGER NATURE

Open Access Original Article

Psychiatric Adverse Events Associated With Bimekizumab: A Disproportionality Analysis of the FDA Adverse Event Reporting System

Review began 10/01/2026
Review ended 10/14/2026
Published 10/23/2026

© **Copyright** 2026
De Souza et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.118465

Beatriz C. De Souza [1], Alana Leão [2], Augusto A. Manfredi [3], Julia Bastos M. Dos Santos [4], Giovana G. Dantas [5], Verônica M. Franco [6], Letícia C. Lopes [7], Nicole L. Bergman [4], Victoria de Oliveira C. Borges [8], Pedro Paulo Stozek F. De Oliveira [5]

1. School of Health Sciences, Universidade de Mogi das Cruzes, Mogi das Cruzes, BRA 2. Faculty of Medicine, Universidade Evangélica de Goiás, Anápolis, BRA 3. School of Medicine, Centro Universitário Fundação Assis Gurgacz, Cascavel, BRA 4. School of Medicine, Instituto de Educação Médica, Rio de Janeiro, BRA 5. School of Medicine, Centro Universitário de Volta Redonda, Volta Redonda, BRA 6. School of Medicine, Universidade de Ribeirão Preto, Ribeirão Preto, BRA 7. School of Medicine, Universidade de Rio Verde, Rio Verde, BRA 8. School of Medicine, Faculdade São Leopoldo Mandic, Campinas, BRA

Corresponding author: Alana Leão, alanaleaoo321@gmail.com

Abstract

Background and objective

Bimekizumab, a dual inhibitor of interleukin-17A and interleukin-17F, carries a US label warning for suicidal ideation and behavior. Whether postmarketing reporting is consistent with that warning has not been examined as a primary objective. In this study, we aimed to quantify the reporting of depression, suicidality, anxiety, and insomnia and to test whether any signal depended on the comparator and reporting channel.

Methods

We conducted a case/non-case disproportionality analysis of the FDA Adverse Event Reporting System (FAERS), accessed through openFDA, covering reports received from October 18, 2023, to June 30, 2026. Ten psychiatric preferred terms were assessed using reporting odds ratios (RORs) under four analyses: against all other FAERS reports, restricted to physician and pharmacist reports, against 11 other biologic agents indicated for the same diseases, and with both sides restricted to spontaneous reports. A signal required a lower 95% confidence limit above 1 and at least three exposed reports.

Results

Among 20,939 bimekizumab-associated reports, 702 (3.4%) contained a target term. Depression (349 reports (1.7%); ROR: 2.38; 95% confidence interval (CI): 2.14 to 2.65) met the signal criterion in all four analyses and survived Bonferroni correction for 40 comparisons in each. Suicidal ideation (142 reports (0.7%); ROR: 1.93; 95% CI: 1.63 to 2.28) met the criterion in all four analyses but survived correction in only three, not surviving in the analysis restricted to spontaneous reports (ROR: 1.27; 95% CI: 1.01 to 1.59). The magnitude of the signal depended on the comparator: when compared with other biologic agents, the ROR for depression fell to 1.24 (95% CI: 1.10 to 1.38) and that for suicidal ideation rose to 3.81 (95% CI: 3.14 to 4.63).

Conclusions

Bimekizumab was associated with disproportionate reporting of depression and suicidal ideation in FAERS. The association depended on both the comparator and the reporting channel, was concordant with the labeled warning, was equally compatible with that warning having shaped reporting, and does not establish causation.

Categories: Pharmacology, Health Policy, Dermatology
Keywords: axial spondyloarthritis, bimekizumab, dual inhibitor of interleukin-17, fda adverse event reporting system, hidradenitis suppurativa, interleukin-17a, interleukin-17f, psoriasis, psoriatic arthritis, psychiatric safety

Introduction

Bimekizumab is a humanized monoclonal antibody that simultaneously neutralizes interleukin-17A and interleukin-17F, producing more complete suppression of downstream inflammatory signaling than selective interleukin-17A inhibition and, in head-to-head trials, superior rates of complete skin clearance [1]. Since its first approval by the Food and Drug Administration (FDA) for moderate-to-severe plaque psoriasis in October 2023, its label has expanded to psoriatic arthritis, axial spondyloarthritis, and, in November 2024, moderate-to-severe hidradenitis suppurativa [2].

Psychiatric safety has been a recurring question for this drug class since brodalumab, an interleukin-17

receptor A antagonist, was approved with a boxed warning and a mandatory Risk Evaluation and Mitigation Strategy for suicidal ideation and behavior based on its pivotal trials; seven years of subsequent surveillance covering 7,845 patient-years recorded no completed suicide and a single attempt [3]. The concern was carried into the bimekizumab label: section 5.1 of the US prescribing information warns of new-onset or worsening suicidal ideation and behavior, directs prescribers to monitor for it, and advises weighing risk against benefit in patients with severe depression or prior suicidal ideation [2]. Whether postmarketing reporting is concordant with that warning has not been examined directly.

The question is not settled by mechanism or by observational data, and the uncertainty is specific. Patients with major depressive disorder show peripheral overactivation of the interleukin-23/Th17 axis, including elevated circulating interleukin-17A, which would predict that inhibiting that axis relieves rather than causes depressive symptoms [4]; yet the same prediction is hard to reconcile with a suicidality warning derived from the trials of two agents acting on it. Observational data pull in a third direction: in psoriasis, biologic therapy of any class is associated with a lower incidence of depression than conventional systemic therapy [5], and the excess of suicidality is concentrated in patients with preexisting psychiatric comorbidity rather than emerging with treatment [6]. Four disproportionality analyses of bimekizumab in the FDA Adverse Event Reporting System (FAERS) have been published, none with psychiatric safety as a primary objective. Three identified depression or suicidal ideation among their signals [7-9]; one did not [10]. Because these analyses draw on the same reporting system over overlapping periods, their agreement reflects reproducibility within one data source, not independent replication, and none tested whether the signal survives a change of comparator.

We therefore conducted a disproportionality analysis of FAERS, reported according to the READUS-PV guideline [11]. The single primary objective was to estimate the reporting odds ratio (ROR) and proportional reporting ratio (PRR) for 10 psychiatric preferred terms associated with bimekizumab. The terms were chosen to span the two domains named in the warning, suicidal ideation and suicidal behaviour, together with depression, which the warning invokes as a risk modifier, and anxiety and insomnia, which it does not mention and which therefore serve as adjacent psychiatric events against which any excess confined to the labeled domain can be read.

We hypothesized that depression and suicidality would show disproportionate reporting, and we tested whether any such signal persisted when both groups were restricted to reports from physicians and pharmacists, when the comparator was restricted to other biologic agents used for the same indications [12], and when both groups were restricted to spontaneous reports. Two secondary objectives, neither bearing on the primary estimate, were to describe the severity of psychiatric reports and to determine whether any signal was confined to a single approved indication. The comparator analyses were designed to test the robustness of the disproportionality estimates, not to establish drug-specific risk or causality.

Materials And Methods

Data source and design

We performed a retrospective case/non-case disproportionality analysis [13] of FAERS, accessed through the openFDA application programming interface (/drug/event.json), which mirrors the FAERS quarterly files and returns only the most recent version of each case safety report, thereby resolving duplicate and amended submissions at the source [14]. Adverse events were coded as preferred terms using the Medical Dictionary for Regulatory Activities (MedDRA) [15]. The study was conducted and reported in accordance with the READUS-PV guideline [11]. The study used publicly available, de-identified data and did not require ethics review.

Study population

The study period began on October 18, 2023, the date of first FDA approval, and ended on June 30, 2026, the receipt date of the most recent report included in the dataset. The data were obtained from the openFDA release with a last-updated date of July 30, 2026. Reports were extracted on September 3 and September 8, 2026, from the same release using an identical query structure; the two dates reflect the order in which the analyses were conducted rather than different data versions. openFDA replaces its release in place and does not archive earlier versions, so the last-updated date, rather than the extraction date, identifies the data. Exposure was defined by the normalized substance name BIMEKIZUMAB, with drug characterization coded as suspect.

Because openFDA nests drug entries within each report, a query combining these two filters can be satisfied by different entries within the same report; every candidate was therefore reparsed to ensure that a single drug entry met both criteria. This removed 185 of 21,124 reports (0.9%), leaving a locked cohort of 20,939 reports. The removed reports, in which another drug was the suspect agent, were retained in the comparator. One report identified during manual audit as a probable true case recorded under a free-text trade name was not reinstated, preserving a fixed and auditable denominator. The openFDA schema does not distinguish primary from secondary suspect drugs; our case definition is therefore broader than those used in prior analyses restricted to primary-suspect reports.

Outcomes

Ten MedDRA preferred terms were examined: depression, depressed mood, depression suicidal, suicidal ideation, suicidal behaviour, suicide attempt, completed suicide, intentional self-injury, anxiety, and insomnia. Every string was verified against the preferred-term spelling indexed by openFDA, including British spellings, using an exact-match query that was required to return a non-zero count across FAERS; a string returning no reports was treated as a spelling failure rather than evidence of an absent term. Counts are not mutually exclusive, since a report may contain more than one term. Standardized MedDRA Queries cannot be retrieved through openFDA; the eight depression- and suicidality-related terms approximate the narrow scope of the corresponding queries but are not equivalent to them. Accordingly, the findings reported here are confined to the 10 terms named above rather than representing psychiatric safety in general. openFDA does not expose the MedDRA version under which each report was coded.

Comparators

For each outcome, we constructed a two-by-two table (a, exposed reports with the term; b, exposed reports without the term; c, comparator reports with the term; d, comparator reports without the term) under the disjoint convention, whereby the comparator excludes the exposed cohort [12,13]. The principal comparator comprised all other FAERS reports meeting the same suspect-drug and period criteria (3,535,150 reports, from a pool of 3,556,089). Sensitivity analysis A restricted both groups to reports from physicians or pharmacists (2,398 exposed reports and 921,733 comparator reports). Sensitivity analysis B restricted the comparator to reports for 11 other biologic agents approved for psoriasis or hidradenitis suppurativa (secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, ustekinumab, adalimumab, infliximab, certolizumab pegol, and etanercept), excluding 892 reports naming both bimekizumab and a comparator agent (204,029 reports).

Sensitivity analysis C restricted both groups to spontaneous reports (17,007 exposed reports and 2,859,093 comparator reports). openFDA records a report type that distinguishes spontaneous reports from reports arising within a study. Under ICH E2D, a solicited report from a patient support programme is classified as a study report. The nested-array artifact arises only when a cohort is defined by a substance name combined with a drug characterization, because the two filters may then be satisfied by separate drug entries within the same report. It therefore affects the exposed cohort and the sensitivity analysis B comparator, but not the comparators defined by the presence of any suspect drug. The correction was applied to the exposed cohort, and its effect on the sensitivity analysis B comparator was established by applying the same correction there, as reported in the Appendices.

Statistical analysis

The ROR with a Woolf 95% confidence interval (CI) [16] was the primary measure, while the PRR with its chi-square statistic (1 degree of freedom) was used as a supportive measure. A continuity correction of 0.5 was added to all cells of any table containing a zero [17]. A signal was defined as a lower 95% confidence limit above 1, with at least three exposed reports [11,13,17]. As a stricter supplementary criterion, we also applied the criteria of Evans et al. (at least three reports, a PRR of at least 2, and a chi-square statistic of at least 4) [12]; the two criteria may yield different conclusions for associations of modest magnitude. Forty comparisons were made (10 terms across four analyses). Although multiplicity adjustment is not conventional in signal detection, we report Bonferroni-adjusted intervals (two-sided alpha of 0.05/40) so that the conclusions do not depend on that convention. openFDA returns the most recent version of each case safety report but does not merge separate reports of the same event. Accordingly, a further sensitivity analysis repeated the within-class comparison using cohorts deduplicated by age, sex, country, receipt date, suspect drug set, and reaction set, as reported in the Appendices.

Seriousness, death, and hospitalization were compared between reports with and without a target term. The frequency of each term was also compared between the psoriasis-spectrum and hidradenitis suppurativa indication subgroups. These comparisons used Pearson's chi-square test with Yates continuity correction (1 degree of freedom) and the phi coefficient (ϕ) as the effect size. When any expected cell count was below 5, Fisher's exact test was used, with the odds ratio as the effect size. A planned time-to-onset analysis was not performed because the treatment-start date was available in only 25.8% of depression reports and 43.0% of suicidal ideation reports, suggesting a pattern of missingness that was unlikely to be random. Case-level causality assessment was not attempted because openFDA provides structured fields rather than case narratives.

Analyses were performed in Python 3.11 using pandas and SciPy. Reports were retrieved using the query patient.drug.openfda.substance_name: "BIMEKIZUMAB" AND patient.drug.drugcharacterization: "1" for the exposed cohort and patient.drug.drugcharacterization: "1" for the principal comparator. Sensitivity analysis A added primarysource.qualification: ("1" "2") to both sides, sensitivity analysis B replaced the substance name with the 11 comparator agents, and sensitivity analysis C added reporttype: "1" to both sides. Each query was intersected with receivedate:[20231018 TO 20261231] and issued month by month to ensure that no single request exceeded the openFDA pagination limit. The extraction and analysis code, the derived two-by-two cells, and a traceability record specifying the receipt date and report-identifier range of every arm are deposited in a public repository [18].

Results

Characteristics of the reports

Of the 21,124 reports retrieved, 20,939 (99.1%) met the case definition and formed the analytic cohort (Table *1*). Sex was recorded as female in 3,031 reports (14.5%) and male in 1,898 (9.1%), and was not recorded in 16,010 (76.5%); age was recorded in 12,413 reports (59.3%), with a mean of 48.9 ± 14.4 years, after conversion of the 64 reports (0.31%) recorded in decades and the 1 (< 0.01%) recorded in months to years. Reports came predominantly from the United States, which accounted for 18,375 reports (87.8%). They were submitted by health professionals who were neither physicians nor pharmacists in 14,017 reports (66.9%), by consumers in 4,516 (21.6%), and by physicians or pharmacists in 2,398 (11.5%), as compared with 924,131 of 3,556,089 reports (26.0%) from physicians or pharmacists across FAERS as a whole. Spontaneous reports numbered 17,007 (81.2%) and reports arising within a study, 3,924 (18.7%). The recorded indication was psoriasis-spectrum disease in 12,820 reports (61.2%), hidradenitis suppurativa in 4,419 (21.1%), and another or unclassified indication in 3,658 (17.5%). Seriousness was recorded in 18,742 reports (89.5%), of which 7,045 (37.6%) were coded serious; death was recorded in 142 reports (0.68%), hospitalization in 1,859 (8.88%), a life-threatening designation in 81 (0.39%), and disability in 61 (0.29%). At least one target psychiatric preferred term appeared in 702 reports (3.4%), with a mean of 1.22 such terms per affected report.

Characteristic	Value	Percentage
Sex		
Female	3,031	14.5
Male	1,898	9.1
Sex not recorded	16,010	76.5
Age		
Age recorded	12,413	59.3
Age recorded in years	12,348	59
Age recorded in decades and converted to years	64	0.3
Age recorded in months and converted to years	1	< 0.1
Mean age, years	49	Not applicable
Standard deviation of age, years	14	Not applicable
Median age, years	49	Not applicable
Minimum age, years	0	Not applicable
Maximum age, years	95	Not applicable
Younger than 18 years	25	0.1
18 to 39 years	3,341	16
40 to 64 years	7,294	34.8
65 years or older	1,753	8.4
Reporter qualification		
Other health professional	14,017	66.9
Consumer or non-health professional	4,516	21.6
Physician	2,207	10.5
Pharmacist	191	0.9
Reporter qualification not recorded	8	< 0.1
Report type		
Spontaneous	17,007	81.2
Report from study	3,924	18.7

Other report type	8	< 0.1
Recorded indication		
Psoriasis-spectrum disease	12,820	61.2
Hidradenitis suppurativa	4,419	21.1
Other or unclassified indication	3,658	17.5
Indication not recorded	42	0.2
Outcome		
Serious, of 18,742 reports with seriousness recorded	7,045	37.6
Death	142	0.68
Hospitalization	1,859	8.88
Life-threatening	81	0.39
Disability	61	0.29
Target psychiatric preferred term		
At least one target term	702	3.4

TABLE 1: Characteristics of the 20,939 bimekizumab-associated reports

Reports naming bimekizumab as a suspect drug in the FDA Adverse Event Reporting System (FAERS) between October 18, 2023, and June 30, 2026, the receipt date of the most recent report in the openFDA release analyzed. Percentages are of all 20,939 reports unless another denominator is shown; summary statistics of age carry none. Ages recorded in decades or in months were converted to years. Other health professional denotes a reporter who is a health professional but neither a physician nor a pharmacist. Entries are as supplied by the reporter and are unverified, and spontaneous reports carry no denominator of treated patients; no incidence can be derived from this table

Disproportionality

Table *2* presents the RORs for the eight terms under the three comparator definitions. In the principal analysis, depression (349 reports (1.67%); ROR: 2.38; 95% CI: 2.14 to 2.65; PRR, 2.36), suicidal ideation (142 reports (0.68%); ROR: 1.93; 95% CI: 1.63 to 2.28; PRR, 1.92) and suicidal behaviour (six reports (0.03%); ROR: 2.32; 95% CI: 1.04 to 5.20) met the signal criterion. Depressed mood (65 reports (0.31%); ROR: 1.27; 95% CI: 1.00 to 1.63) and depression suicidal (5 reports (0.02%); ROR: 2.29; 95% CI: 0.95 to 5.53) approached it without reaching it, and anxiety (186 reports (0.89%); ROR: 0.89; 95% CI: 0.77 to 1.02) did not. Insomnia, suicide attempt, completed suicide, and intentional self-injury had confidence intervals entirely below 1. Under the stricter Evans criterion, only depression qualified; suicidal ideation fell short on the PRR threshold.

Psychiatric preferred term	Bimekizumab reports listing this term, No.	Bimekizumab reports listing this term, %	Reporting odds ratio	95% confidence interval, lower limit	95% confidence interval, upper limit	Meets signal criterion
Principal analysis (comparator, all other FAERS reports; exposed cohort, 20,939 reports)						
Depression	349	1.67	2.38	2.14	2.65	Yes
Depressed mood	65	0.31	1.27	1	1.63	No
Depression suicidal	5	0.02	2.29	0.95	5.53	No
Suicidal ideation	142	0.68	1.93	1.63	2.28	Yes
Suicidal behaviour	6	0.03	2.32	1.04	5.2	Yes
Suicide attempt	8	0.04	0.16	0.08	0.32	No

Completed suicide	2	0.01	0.04	0.01	0.14	No
Intentional self-injury	2	0.01	0.12	0.03	0.49	No
Anxiety	186	0.89	0.89	0.77	1.02	No
Insomnia	93	0.44	0.45	0.37	0.55	No
Sensitivity analysis A (comparator, physician and pharmacist reports); exposed cohort, 2,398 reports						
Depression	63	2.63	5.44	4.23	7	Yes
Depressed mood	8	0.33	1.68	0.84	3.36	No
Depression suicidal	0	0	2.54	0.16	41.07	No
Suicidal ideation	31	1.29	3.84	2.69	5.49	Yes
Suicidal behaviour	4	0.17	12.42	4.58	33.64	Yes
Suicide attempt	2	0.08	0.16	0.04	0.64	No
Completed suicide	1	0.04	0.05	0.01	0.37	No
Intentional self-injury	0	0	0.19	0.01	2.99	No
Anxiety	24	1	1.83	1.22	2.74	Yes
Insomnia	5	0.21	0.41	0.17	0.99	No
Sensitivity analysis B (comparator, 11 other biologic agents); exposed cohort, 20,939 reports						
Depression	349	1.67	1.24	1.1	1.38	Yes
Depressed mood	65	0.31	2.29	1.75	3	Yes
Depression suicidal	5	0.02	4.06	1.43	11.53	Yes
Suicidal ideation	142	0.68	3.81	3.14	4.63	Yes
Suicidal behaviour	6	0.03	5.32	1.97	14.38	Yes
Suicide attempt	8	0.04	0.95	0.46	1.96	No
Completed suicide	2	0.01	0.43	0.11	1.79	No
Intentional self-injury	2	0.01	0.75	0.18	3.16	No
Anxiety	186	0.89	0.74	0.64	0.87	No
Insomnia	93	0.44	0.28	0.23	0.34	No
Sensitivity analysis C (comparator, spontaneous reports only); exposed cohort, 17,007 reports						
Depression	258	1.52	2.23	1.97	2.53	Yes
Depressed mood	46	0.27	1.18	0.88	1.57	No
Depression						

suicidal	3	0.02	1.58	0.51	4.91	No
Suicidal ideation	75	0.44	1.27	1.01	1.59	Yes
Suicidal behaviour	6	0.04	2.66	1.19	5.96	Yes
Suicide attempt	4	0.02	0.09	0.03	0.23	No
Completed suicide	2	0.01	0.05	0.01	0.18	No
Intentional self-injury	0	0	0.04	0	0.56	No
Anxiety	118	0.69	0.71	0.59	0.85	No
Insomnia	50	0.29	0.32	0.24	0.42	No

TABLE 2: Reporting odds ratios for 10 psychiatric preferred terms associated with bimekizumab, according to comparator

The reporting odds ratio compares the odds that a report lists the term among bimekizumab reports with the odds among comparator reports; confidence intervals are those of Woolf. Every comparator excludes the bimekizumab cohort. The principal comparator comprises all other FAERS reports of the study period naming any suspect drug; sensitivity analysis A restricts both groups to physician and pharmacist reports, analysis B restricts the comparator to eleven other biologic agents approved for psoriasis or hidradenitis suppurativa, and analysis C restricts both groups to spontaneous reports. A signal required a lower confidence limit above 1 with at least three bimekizumab reports; a continuity correction of 0.5 was added to every cell of any table containing a zero. A reporting odds ratio describes the composition of a reporting stream, not risk or incidence

Restricting both groups to physician and pharmacist reports raised the ROR for depression (63 of 2,398 reports (2.63%)) to 5.44 (95% CI: 4.23 to 7.00), for suicidal ideation (31 of 2,398 (1.29%)) to 3.84 (95% CI: 2.69 to 5.49) and for suicidal behaviour (4 of 2,398 (0.17%)) to 12.42 (95% CI: 4.58 to 33.64); all three met the Evans criterion. Anxiety (24 of 2,398 (1.00%)) also met the primary criterion here (ROR: 1.83; 95% CI: 1.22 to 2.74) but neither the Evans criterion nor the Bonferroni adjustment. The restriction raised the estimate for eight of the 10 terms, with a median ratio to the principal estimate of 1.45, and shifted the composition of both groups: the 10 target terms were denser among physician- and pharmacist-reported bimekizumab reports than in the full cohort (138 of 2,398 term occurrences (5.75%) versus 858 of 20,939 (4.10%)), whereas in the comparator the proportion of reports listing depression fell (4,550 of 921,733 (0.49%) versus 24,995 of 3,535,150 (0.71%)).

Against the comparator of other biologic agents, depression attenuated to an ROR of 1.24 (95% CI: 1.10 to 1.38), whereas suicidal ideation rose to 3.81 (95% CI: 3.14 to 4.63), suicidal behaviour to 5.32 (95% CI: 1.97 to 14.38), depression suicidal to 4.06 (95% CI: 1.43 to 11.53) and depressed mood to 2.29 (95% CI: 1.75 to 3.00), the last four meeting the Evans criterion. Anxiety and insomnia had intervals below 1; suicide attempt, completed suicide, and intentional self-injury had intervals spanning 1.

Restricting both groups to spontaneous reports moved the estimates in the opposite direction, lowering the ROR for eight of the 10 terms, with a median ratio to the principal estimate of 0.75. Depression attenuated least, to 2.23 (258 of 17,007 reports (1.52%); 95% CI: 1.97 to 2.53), and remained a signal; suicidal ideation attenuated most among the signalling terms, to 1.27 (75 of 17,007 (0.44%); 95% CI: 1.01 to 1.59), retaining the lower limit above 1 but losing the Evans criterion and the Bonferroni adjustment. Suicidal behaviour rose to 2.66 (6 of 17,007 (0.04%); 95% CI: 1.19 to 5.96).

Depression was the only term that met the signal criterion in all four analyses and survived Bonferroni correction for 40 comparisons in all four (adjusted lower limits, 2.00, 3.59, 1.03 and 1.82). Suicidal ideation met the criterion in all four and survived adjustment in three, failing only under restriction to spontaneous reports. Suicidal behaviour survived adjustment against the physician and pharmacist comparator and against the biologic comparator. No term met the Evans criterion in all four.

Severity and indication

Reports containing a target term were more often coded serious than the remainder of the cohort (372 of 651 (57.14%) versus 6,673 of 18,091 (36.89%); $\chi^2(1, N = 18,742) = 109.1$; $p < 0.001$; $\phi = 0.076$), a difference that is partly definitional, since suicidal ideation and related terms are coded serious by regulatory convention, and small in effect size. Death (3 of 702 (0.43%) versus 139 of 20,237 (0.69%); Fisher's exact $p = 0.64$; odds ratio, 0.62) and hospitalization (63 of 702 (8.97%) versus 1,796 of 20,237 (8.87%); $\chi^2(1, N = 20,939) = 0.00$; $p = 0.98$;

ϕ < 0.001) did not differ (Table 3). The frequency of depression (196 of 12,820 (1.53%) versus 66 of 4,419 (1.49%); $\chi^2(1, N = 17,239) = 0.01$; p = 0.92; ϕ < 0.001) and of suicidal ideation (74 of 12,820 (0.58%) versus 30 of 4,419 (0.68%); $\chi^2(1, N = 17,239) = 0.41$; p = 0.52; ϕ = 0.005) did not differ between the psoriasis-spectrum and hidradenitis suppurativa subgroups; in the comparison for all 10 terms, insomnia alone differed nominally (72 of 12,820 (0.56%) versus 8 of 4,419 (0.18%); $\chi^2(1, N = 17,239) = 9.50$; p = 0.002; ϕ = 0.023) in an unplanned comparison.

Outcome	Reports listing a psychiatric term, No.	Reports listing a psychiatric term, total No.	Reports listing a psychiatric term, %	Reports listing no psychiatric term, No.	Reports listing no psychiatric term, total No.	Reports listing no psychiatric term, %	Statistical test	Test statistic	Degrees of freedom	P-value	Effect size measure	Effect size value
Serious, of reports with seriousness recorded	372	651	57.14	6,673	18,091	36.89	Chi-square	109.1	1	< 0.001	Phi coefficient	0.076
Death	3	702	0.43	139	20,237	0.69	Fisher's exact	Not applicable	Not applicable	0.64	Odds ratio	0.621
Hospitalization	63	702	8.97	1,796	20,237	8.87	Chi-square	0.0	1	0.98	Phi coefficient	0.000

TABLE 3: Seriousness, death, and hospitalization among reports with and without a target psychiatric preferred term

The 702 bimekizumab reports listing at least one of the 10 target preferred terms are compared with the remaining 20,237. Chi-square is Pearson's with the Yates correction, and phi is its effect size, for which 0.1 is small, 0.3 moderate, and 0.5 large; Fisher's exact test replaced it where an expected count fell below 5, with the odds ratio as the effect size. Percentages for seriousness are of reports in which seriousness was recorded. Suicidal ideation, suicidal behaviour, suicide attempt, completed suicide, and intentional self-injury are coded as serious by regulatory convention, so the excess of serious reports is partly definitional and does not indicate greater clinical severity

Supporting analyses

The two-by-two contingency cells underlying Table 2 are given in Tables 4-7; PRRs, chi-square statistics, effect sizes, Evans-criterion status, and Bonferroni-adjusted intervals for all 40 comparisons are presented in Table 8; the ratio of each sensitivity-analysis estimate to the principal estimate is reported in Table 9; the indication comparison for all 10 terms is presented in Table 10; the country of origin of the reports is reported in Table 11; the effect of applying the nested-array correction to the sensitivity analysis B comparator is presented in Table 12; and the within-class comparison repeated on deduplicated cohorts is presented in Table 13. The correction removed 10,723 of 204,029 comparator reports (5.26%) and raised eight of the 10 estimates by at most 26%. Deduplication removed 1,939 of 20,939 bimekizumab reports (9.26%) and 5,187 of 204,029 comparator reports (2.54%). Under both analyses, depression lay between 1.22 and 1.27, and suicidal ideation between 3.98 and 4.02, and no term changed signal status.

Psychiatric preferred term	Bimekizumab reports listing this term (a)	Bimekizumab reports not listing this term (b)	Comparator reports listing this term (c)	Comparator reports not listing this term (d)
Depression	349	20,590	24,995	3,510,155
Depressed mood	65	20,874	8,618	3,526,532
Depression suicidal	5	20,934	369	3,534,781
Suicidal ideation	142	20,797	12,470	3,522,680
Suicidal behaviour	6	20,933	436	3,534,714
Suicide attempt	8	20,931	8,474	3,526,676
Completed suicide	2	20,937	9,468	3,525,682
Intentional self-injury	2	20,937	2,773	3,532,377
Anxiety	186	20,753	35,380	3,499,770
Insomnia	93	20,846	34,531	3,500,619

TABLE 4: Two-by-two contingency cells underlying the principal analysis

Cells of the two-by-two table for each of the 10 preferred terms: a, bimekizumab reports listing the term; b, bimekizumab reports not listing it; c, comparator reports listing it; d, comparator reports not listing it. The reporting odds ratio is (a x d) / (b x c), and the proportional reporting ratio is [a / (a + b)] / [c / (c + d)]. A report may list more than one term, so counts are not mutually exclusive. Here, a + b is 20,939 and c + d is 3,535,150, all other FAERS reports of the study period naming any suspect drug

Psychiatric preferred term	Bimekizumab reports listing this term (a)	Bimekizumab reports not listing this term (b)	Comparator reports listing this term (c)	Comparator reports not listing this term (d)
Depression	63	2,335	4,550	917,183
Depressed mood	8	2,390	1,837	919,896
Depression suicidal	0	2,398	75	921,658
Suicidal ideation	31	2,367	3,130	918,603
Suicidal behaviour	4	2,394	124	921,609
Suicide attempt	2	2,396	4,804	916,929
Completed suicide	1	2,397	7,305	914,428
Intentional self-injury	0	2,398	1,026	920,707
Anxiety	24	2,374	5,070	916,663
Insomnia	5	2,393	4,649	917,084

TABLE 5: Two-by-two contingency cells underlying sensitivity analysis A (physician and pharmacist reporters)

Cells of the two-by-two table for each of the 10 preferred terms: a, bimekizumab reports listing the term; b, bimekizumab reports not listing it; c, comparator reports listing it; d, comparator reports not listing it. The reporting odds ratio is (a x d) / (b x c), and the proportional reporting ratio is [a / (a + b)] / [c / (c + d)]. A report may list more than one term, so counts are not mutually exclusive. Here, a + b is 2,398 and c + d is 921,733, both groups being restricted to reports whose primary source was a physician or a pharmacist

Psychiatric preferred term	Bimekizumab reports listing this term (a)	Bimekizumab reports not listing this term (b)	Comparator reports listing this term (c)	Comparator reports not listing this term (d)
Depression	349	20,590	2,762	201,267
Depressed mood	65	20,874	277	203,752
Depression suicidal	5	20,934	12	204,017
Suicidal ideation	142	20,797	365	203,664
Suicidal behaviour	6	20,933	11	204,018
Suicide attempt	8	20,931	82	203,947
Completed suicide	2	20,937	45	203,984
Intentional self-injury	2	20,937	26	204,003
Anxiety	186	20,753	2,426	201,603
Insomnia	93	20,846	3,216	200,813

TABLE 6: Two-by-two contingency cells underlying sensitivity analysis B (other biologic agents for psoriasis or hidradenitis suppurativa)

Cells of the two-by-two table for each of the 10 preferred terms: a, bimekizumab reports listing the term; b, bimekizumab reports not listing it; c, comparator reports listing it; d, comparator reports not listing it. The reporting odds ratio is (a x d) / (b x c), and the proportional reporting ratio is [a / (a + b)] / [c / (c + d)]. A report may list more than one term, so counts are not mutually exclusive. Here a + b is 20,939 and c + d is 204,029, comprising reports for secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, ustekinumab, adalimumab, infliximab, certolizumab pegol, or etanercept, after exclusion of reports naming both bimekizumab and one of these agents. Sharing the psychiatric burden of the underlying diseases, this is the most conservative comparator used in this study

Psychiatric preferred term	Bimekizumab reports listing this term (a)	Bimekizumab reports not listing this term (b)	Comparator reports listing this term (c)	Comparator reports not listing this term (d)
Depression	258	16,749	19,573	2,839,520
Depressed mood	46	16,961	6,573	2,852,520
Depression suicidal	3	17,004	320	2,858,773
Suicidal ideation	75	16,932	9,956	2,849,137
Suicidal behaviour	6	17,001	379	2,858,714
Suicide attempt	4	17,003	7,647	2,851,446
Completed suicide	2	17,005	7,376	2,851,717
Intentional self-injury	0	17,007	2,383	2,856,710
Anxiety	118	16,889	27,818	2,831,275
Insomnia	50	16,957	26,142	2,832,951

TABLE 7: Two-by-two contingency cells underlying sensitivity analysis C (spontaneous reports only)

Cells of the two-by-two table for each of the 10 preferred terms: a, bimekizumab reports listing the term; b, bimekizumab reports not listing it; c, comparator reports listing it; d, comparator reports not listing it. The reporting odds ratio is (a x d) / (b x c), and the proportional reporting ratio is [a / (a + b)] / [c / (c + d)]. A report may list more than one term, so counts are not mutually exclusive. Here, a + b is 17,007 and c + d is 2,859,093, both groups being restricted to spontaneous reports; under ICH E2D, a solicited report from a patient support program is classified as arising within a study and is excluded

Psychiatric preferred term	Proportional reporting ratio	Chi-square statistic	Degrees of freedom	Phi coefficient	Meets Evans criterion	Bonferroni-adjusted confidence interval, lower limit	Bonferroni-adjusted confidence interval, upper limit	Survives Bonferroni adjustment
Principal analysis								
Depression	2.36	269.6	1	0.0087	Yes	2.00	2.84	Yes
Depressed mood	1.27	3.5	1	0.0010	No	0.85	1.91	No
Depression suicidal	2.29	2.4	1	0.0008	No	0.53	9.78	No
Suicidal ideation	1.92	61.5	1	0.0042	No	1.47	2.54	Yes
Suicidal behaviour	2.32	3.2	1	0.0010	No	0.62	8.76	No
Suicide attempt	0.16	34.7	1	0.0031	No	0.05	0.50	No
Completed suicide	0.04	51.3	1	0.0038	No	0.00	0.35	No
Intentional self-injury	0.12	11.8	1	0.0018	No	0.01	1.19	No
Anxiety	0.89	2.5	1	0.0008	No	0.70	1.13	No
Insomnia	0.45	60.7	1	0.0041	No	0.32	0.63	No
Sensitivity analysis A								

Depression	5.32	214.9	1	0.0153	Yes	3.59	8.23	Yes
Depressed mood	1.67	1.5	1	0.0013	No	0.53	5.27	No
Depression suicidal	0.00	0.0	1	0.0000	No	0.03	248.04	No
Suicidal ideation	3.81	61.0	1	0.0081	Yes	2.14	6.91	Yes
Suicidal behaviour	12.40	30.3	1	0.0057	Yes	2.41	64.07	Yes
Suicide attempt	0.16	8.0	1	0.0029	No	0.02	1.56	No
Completed suicide	0.05	16.2	1	0.0042	No	0.00	1.32	No
Intentional self-injury	0.00	1.8	1	0.0014	No	0.00	17.97	No
Anxiety	1.82	8.1	1	0.0030	No	0.94	3.55	No
Insomnia	0.41	3.6	1	0.0020	No	0.10	1.75	No
Sensitivity analysis B								
Depression	1.23	13.4	1	0.0077	No	1.03	1.49	Yes
Depressed mood	2.29	37.0	1	0.0128	Yes	1.47	3.58	Yes
Depression suicidal	4.06	5.9	1	0.0051	Yes	0.73	22.63	No
Suicidal ideation	3.79	208.3	1	0.0304	Yes	2.77	5.25	Yes
Suicidal behaviour	5.31	10.7	1	0.0069	Yes	1.03	27.35	Yes
Suicide attempt	0.95	0.0	1	0.0000	No	0.29	3.14	No
Completed suicide	0.43	0.9	1	0.0020	No	0.04	4.46	No
Intentional self-injury	0.75	0.0	1	0.0001	No	0.07	8.00	No
Anxiety	0.75	14.7	1	0.0081	No	0.58	0.95	No
Insomnia	0.28	167.2	1	0.0273	No	0.20	0.39	No
Sensitivity analysis C								
Depression	2.22	169.9	1	0.0077	Yes	1.82	2.74	Yes
Depressed mood	1.18	1.0	1	0.0006	No	0.73	1.90	No
Depression suicidal	1.58	0.2	1	0.0003	No	0.24	10.25	No
Suicidal ideation	1.27	3.9	1	0.0012	No	0.87	1.84	No
Suicidal behaviour	2.66	4.6	1	0.0013	Yes	0.71	10.05	No
Suicide attempt	0.09	37.0	1	0.0036	No	0.02	0.44	No

Completed suicide	0.05	39.1	1	0.0037	No	0.00	0.45	No
Intentional self-injury	0.00	13.2	1	0.0021	No	0.00	3.38	No
Anxiety	0.71	13.4	1	0.0022	No	0.53	0.96	No
Insomnia	0.32	71.4	1	0.0050	No	0.20	0.50	No

TABLE 8: Proportional reporting ratios, chi-square statistics, effect sizes, Evans criterion status, and Bonferroni-adjusted confidence intervals for all 40 comparisons

Each row is one preferred term under one of the four analyses. The proportional reporting ratio is the proportion of bimekizumab reports listing the term divided by the same proportion among comparator reports; chi-square is Pearson's with the Yates correction, and phi is its effect size, necessarily small for a single term in a database of this size. The criterion of Evans et al. requires at least three bimekizumab reports, a proportional reporting ratio of at least 2, and a chi-square of at least 4, and is stricter than the signal criterion used here, which asks only that the lower confidence limit of the reporting odds ratio exceed 1. Bonferroni-adjusted intervals use a two-sided alpha of 0.05 divided by 40, the number of comparisons

Psychiatric preferred term	Ratio of reporting odds ratios, sensitivity analysis A to principal analysis	Ratio of reporting odds ratios, sensitivity analysis B to principal analysis	Ratio of reporting odds ratios, sensitivity analysis C to principal analysis
Depression	2.29	0.52	0.94
Depressed mood	1.32	1.80	0.93
Depression suicidal	1.11	1.77	0.69
Suicidal ideation	1.99	1.97	0.66
Suicidal behaviour	5.35	2.29	1.15
Suicide attempt	1.00	5.94	0.56
Completed suicide	1.25	10.75	1.25
Intentional self-injury	1.58	6.25	0.33
Anxiety	2.06	0.83	0.80
Insomnia	0.91	0.62	0.71
Median of the 10 terms	1.45	1.89	0.75

TABLE 9: Ratio of each sensitivity-analysis reporting odds ratio to the principal-analysis estimate

Each entry is the reporting odds ratio obtained under a sensitivity analysis divided by the principal-analysis estimate for the same term; values above 1 denote a higher estimate under that analysis. A shift that moves most terms in one direction indicates a compositional effect on the reporting stream rather than anything specific to a single term

Psychiatric preferred term	Psoriasis-spectrum reports listing this term, No.	Psoriasis-spectrum reports, total No.	Psoriasis-spectrum reports listing this term, %	Hidradenitis suppurativa reports listing this term, No.	Hidradenitis suppurativa reports, total No.	Hidradenitis suppurativa reports listing this term, %	Statistical test	Test statistic	Degrees of freedom	P-value	Effect size measure	Effect size value
Depression	196	12,820	1.53	66	4,419	1.49	Chi-square	0.01	1	0.93	Phi coefficient	0.001
Depressed mood	39	12,820	0.30	15	4,419	0.34	Chi-square	0.04	1	0.84	Phi coefficient	0.002
Depression suicidal	5	12,820	0.04	0	4,419	0.00	Fisher's exact	Not applicable	Not applicable	0.34	Odds ratio	Not applicable
Suicidal ideation	74	12,820	0.58	30	4,419	0.68	Chi-square	0.41	1	0.52	Phi coefficient	0.005
Suicidal behaviour	4	12,820	0.03	2	4,419	0.05	Fisher's exact	Not applicable	Not applicable	0.65	Odds ratio	0.689
Suicide attempt	6	12,820	0.05	1	4,419	0.02	Fisher's exact	Not applicable	Not applicable	0.69	Odds ratio	2.069
Completed suicide	0	12,820	0.00	0	4,419	0.00	Fisher's exact	Not applicable	Not applicable	1.00	Odds ratio	Not applicable
Intentional self-injury	1	12,820	0.01	1	4,419	0.02	Fisher's exact	Not applicable	Not applicable	0.45	Odds ratio	0.345
Anxiety	118	12,820	0.92	35	4,419	0.79	Chi-square	0.48	1	0.49	Phi coefficient	0.005
Insomnia	72	12,820	0.56	8	4,419	0.18	Chi-square	9.50	1	0.00	Phi coefficient	0.023

TABLE 10: Frequency of the 10 target preferred terms according to recorded indication

Each row compares how often bimekizumab reports list the term in the two recorded indications. Denominators are the reports assigned to psoriasis-spectrum disease or to hidradenitis suppurativa; reports with another, unclassified, or absent indication are not shown. Chi-square is Pearson's with the Yates correction, and phi is its effect size; Fisher's exact test replaced it where an expected count fell below

Country	No. of reports	Percentage of reports
United States	18,375	87.8
Canada	958	4.6
European Union (regulatory aggregate)	447	2.1
United Kingdom	406	1.9
Germany	160	0.8
Japan	156	0.7
Australia	123	0.6
France	49	0.2
Italy	30	0.1
Spain	27	0.1
Brazil	24	0.1
Sweden	21	0.1
Belgium	19	< 0.1
All other countries	144	0.7

TABLE 11: Country of origin of the 20,939 bimekizumab-associated reports

Country is the country of occurrence recorded in FAERS, or the reporter country where that field is absent. European Union denotes reports filed under a regulatory aggregate rather than an individual member state; the countries contributing the fewest reports are combined in the final row

Psychiatric preferred term	Reporting odds ratio, uncorrected comparator	Reporting odds ratio, corrected comparator	95% confidence interval, lower limit, corrected comparator	95% confidence interval, upper limit, corrected comparator	Ratio of corrected to uncorrected estimate
Depression	1.24	1.27	1.14	1.42	1.02
Depressed mood	2.29	2.31	1.76	3.04	1.01
Depression suicidal	4.06	5.13	1.72	15.31	1.26
Suicidal ideation	3.81	3.98	3.27	4.85	1.04
Suicidal behaviour	5.32	5.04	1.86	13.62	0.95
Suicide attempt	0.95	1.00	0.48	2.07	1.05
Completed suicide	0.43	0.43	0.10	1.77	1.00
Intentional self-injury	0.75	0.77	0.18	3.26	1.03
Anxiety	0.74	0.77	0.67	0.90	1.04
Insomnia	0.28	0.29	0.23	0.35	1.04

TABLE 12: Effect of applying the nested-array correction to the comparator of sensitivity analysis B

openFDA nests drug entries within each report, so a query combining a substance name with a drug characterization can be satisfied by different entries of the same report; the correction retains a report only when a single entry satisfies both. The artifact arises only where a cohort is defined by that conjunction, as the bimekizumab cohort and this comparator are, and not where a cohort is defined by the presence of any suspect drug. Applying the correction here removed 10,723 of 204,029 comparator reports (5.26%). The final column is the corrected estimate divided by the uncorrected one, so 1 denotes no change. Confidence intervals are those of Woolf

Psychiatric preferred term	Bimekizumab reports listing this term, No.	Reporting odds ratio	95% confidence interval, lower limit	95% confidence interval, upper limit	Meets signal criterion
Depression	320	1.22	1.09	1.37	Yes
Depressed mood	64	2.43	1.85	3.19	Yes
Depression suicidal	5	4.36	1.54	12.38	Yes
Suicidal ideation	138	4.02	3.30	4.90	Yes
Suicidal behaviour	6	6.28	2.28	17.28	Yes
Suicide attempt	7	0.89	0.41	1.93	No
Completed suicide	2	0.48	0.12	1.96	No
Intentional self-injury	2	0.81	0.19	3.39	No
Anxiety	184	0.79	0.68	0.92	No
Insomnia	92	0.30	0.24	0.37	No

TABLE 13: Reporting odds ratios against the within-class comparator after deduplication of both cohorts

openFDA returns the most recent version of each individual case safety report but does not merge separate reports of the same event, such as one filed by the manufacturer and another by the treating clinician. Reports were therefore grouped by age, sex, country, receipt date, suspect drug set, and reaction set, and one report was retained from each group, leaving 19,000 bimekizumab and 198,842

Discussion

In 20,939 bimekizumab-associated reports in FAERS, depression was the only psychiatric term reported disproportionately under all four analyses and the only one to survive Bonferroni correction across all 40 comparisons. Suicidal ideation met the signal criterion under all four and survived correction under three, failing when both sides were restricted to spontaneous reports. The findings are modest in magnitude and, as with any disproportionality result, describe the composition of a reporting stream rather than a risk. The association survived the removal of every consumer report, and it persisted when the drug was compared with other agents used for the same diseases. The pattern also maps onto what the label already says. Suicidality is the domain the warning names, and the terms whose estimates strengthened against the within-class comparator were suicidal ideation and suicidal behaviour; depression, which the warning invokes only as a risk modifier, is the one that attenuated there, in the direction expected if much of it belongs to the disease. Anxiety and insomnia, which the label does not mention, were not reported disproportionately under any comparator.

The four analyses answer different questions. The whole-database comparison is the conventional one but pits a dermatologic biologic against a denominator dominated by oncologic and psychotropic drugs. The comparison against other psoriasis and hidradenitis suppurativa biologics controls for the psychiatric burden of the underlying diseases, whose pooled prevalence of depression in psoriasis across 56 studies is estimated at 20% [19], and is the most conservative; that the depression estimate halved against this comparator while suicidal ideation doubled suggests that much of the apparent depression excess reflects the disease rather than the drug, and that whatever drives the suicidal ideation reporting is not shared with the rest of the class, a pattern that the drug and the monitoring it attracts explain equally well. The physician-and-pharmacist restriction raised the estimate for nearly every term, and a shift that general is the signature of a compositional effect rather than of anything specific to one term; it acts asymmetrically on the two sides of the ratio, raising the numerator and lowering the denominator at once. It establishes one thing precisely: that removing every consumer report leaves the association intact.

Concordance with the label admits a second reading. The warning directs prescribers to monitor for suicidal ideation and behavior, and the development program screened for it prospectively with a structured instrument, so clinicians caring for these patients are prompted to ask about, and to report, precisely the events counted here. The mechanism is the one invoked below for brodalumab. A disproportionality measure cannot separate a true excess of events from an excess of ascertainment, and an association

concentrated in the domain the label names fits stimulated reporting as readily as a drug effect. The within-class comparison leaves this open, since no comparator agent other than brodalumab carries an equivalent warning: the contrast is between a monitored drug and largely unmonitored ones.

Our result is consistent with three of four prior FAERS screens of bimekizumab [7-10], but that consistency is reproducibility within one database, not replication; the reports analyzed by those studies are largely a subset of ours, and our cohort is larger because the period extends further and because openFDA does not permit restriction to primary-suspect reports, which makes our case definition more sensitive and less specific, so our estimates are comparable to theirs in direction but not in magnitude. The reporting channel is the most important unresolved threat to interpretation, and it is now partly measured. A cohort of this size accumulated in under three years, two-thirds of it from non-physician health professionals, is characteristic of manufacturer-sponsored patient-support programmes, whose structured follow-up generates solicited reports.

Under ICH E2D, such reports are classified as arising within a study, and openFDA records that distinction. Restricting both sides to spontaneous reports lowered most of the 10 estimates, which is itself the signature of a compositional shift rather than of anything specific to one term. Within that general movement, the two signalling terms behaved differently: depression moved least of all and remained a signal under multiplicity correction, whereas suicidal ideation fell further than the median and lost that protection. The field marks study origin rather than solicitation by a support programme, so the analysis bounds the problem rather than resolving it; what it establishes is that the suicidal ideation association is the more channel-dependent of the two.

The signal coexists with reassuring adjudicated data. Across 7,166 patient-years in nine phase 2/3 trials with prospective screening and independent adjudication, the rate of suicidal ideation and behavior with bimekizumab was 0.13 per 100 patient-years, within the ranges reported for the general psoriasis population and for anti-interleukin-17A and anti-interleukin-23 therapies [20]. The two designs observe different populations, answer different questions, and cannot be compared directly. Trials excluded patients with significant psychiatric history and adjudicated events under close follow-up, whereas FAERS captures the unselected population that includes exactly those patients, without denominators or verification; a low adjudicated rate in a trial-eligible population does not exclude a signal in a broader one.

The class precedent is instructive in the same way: brodalumab carries a boxed warning based on trial events yet has recorded no completed suicide in seven years of surveillance [3], while FAERS analyses continue to detect suicidal ideation and, more recently, depression as signals for it [21], under conditions of heightened awareness that would be expected to inflate reporting. Pooled trial data for secukinumab, which inhibits interleukin-17A alone, show no elevated rate of depression, anxiety, or suicidality [22], and an aggregate scoping review offers no psychiatric-specific comparison across the class [23]. Suicidality was not stringently monitored in the brodalumab trials, whereas the bimekizumab programme monitored it prospectively [20], so direct comparison between agents is not possible from existing data.

A cohort study has since addressed the same question with denominators. In the TriNetX United States network, adults with psoriasis who started bimekizumab were matched to adults who started an interleukin-23 inhibitor; patients with psychiatric history or prior psychotropic use were excluded, and over two years bimekizumab was not associated with an increased risk of the composite of new-onset depression, suicidal ideation, or initiation of an antidepressant or antipsychotic [24]. With an active comparator and a defined period of risk, that design speaks to a prescribing decision as a reporting ratio cannot. Two features bound its reach. Its outcome is a composite in which depression and medication initiation predominate, so it does not estimate suicidal ideation on its own, and suicidal ideation is the term carrying the largest disproportionality here. Its comparator is the interleukin-23 class rather than the interleukin-17 pathway inhibitors to which bimekizumab is mechanistically closest. Together, the two lines of evidence support the monitoring the label already recommends, which is in any case consistent with good clinical practice, and give no reason to withhold an effective therapy from patients with a psychiatric history.

The secondary findings should be interpreted conservatively. Anxiety met the criterion only under reporter restriction, where nearly every estimate rose, and did not survive multiplicity correction; we do not regard it as a signal. Insomnia, suicide attempt, completed suicide, and intentional self-injury had estimates below 1 against the whole database that rose toward unity against the biologic comparator, a pattern characteristic of competition bias in a compositional measure rather than of protection. The last three rest on two to eight reports, as do the two terms recovered during revision, and estimates built on so few reports carry almost no information: their intervals are wide, they move substantially when a single report is added or removed, and a point estimate below 1 among them must not be read as absence of increased risk for those outcomes. Two reported completed suicides should not be presented as reassurance. Neither recovered term is therefore treated here as more than consistent with the pattern the better-populated terms describe. The absence of a difference between the psoriasis and hidradenitis suppurativa subgroups suggests the association is not confined to one indication, though both subgroups share the same reporting channel.

Beyond the limitations already stated, most reports originated in the United States (Table *11*), which limits

generalization to other reporting cultures; demographic fields were substantially incomplete, sex unrecorded in more than three-quarters of reports and age in two-fifths, so no subgroup description here can be regarded as representative; coding was not harmonized across MedDRA versions; latency could not be characterized; and no case was individually adjudicated. The analysis plan, including the term list, was not registered in a public forum before the data were examined, so its timing cannot be verified by a reader. Ages are as entered by the reporter and are not verified, which is the most plausible reading of the small number of reports carrying an age below the approved range for a drug not licensed in children.

Each of these constrains the precision of the estimates, and none of them plausibly produces an excess confined to the labeled psychiatric domain while leaving the remaining terms unaffected. Applying the nested-array correction to the within-class comparator raised rather than lowered almost every estimate, and deduplicating both cohorts left every signal standing, so neither omission inflated the findings reported here. None of this makes the pattern an effect of the drug: differential ascertainment under a labeled warning remains a sufficient explanation for the whole of it.

Conclusions

Depression was reported disproportionately with bimekizumab under all four analyses and was the only term to survive correction for multiplicity in all of them; suicidal ideation met the signal criterion under all four but not after correction when both sides were restricted to spontaneous reports. The excess was confined to the psychiatric domain the US label already names. The magnitude was modest and depended on both the comparator and the reporting channel, and a measure of reporting establishes neither causation nor incidence: it cannot separate an excess of events from an excess of ascertainment under a warning that directs clinicians to look for them. These data describe how a labeled concern appears in postmarketing reporting; estimating the risk behind it requires cohort data with denominators.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Alana Leão

Acquisition, analysis, or interpretation of data: Alana Leão, Augusto A. Manfredi, Julia Bastos M. Dos Santos, Giovana G. Dantas, Beatriz C. De Souza, Verônica M. Franco, Letícia C. Lopes, Nicole L. Bergman, Victoria de Oliveira C. Borges, Pedro Paulo Stozek F. De Oliveira

Drafting of the manuscript: Alana Leão, Augusto A. Manfredi, Julia Bastos M. Dos Santos, Giovana G. Dantas, Beatriz C. De Souza, Letícia C. Lopes, Victoria de Oliveira C. Borges

Critical review of the manuscript for important intellectual content: Alana Leão, Augusto A. Manfredi, Beatriz C. De Souza, Verônica M. Franco, Nicole L. Bergman, Pedro Paulo Stozek F. De Oliveira

Supervision: Alana Leão

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Al Alshaikh SA, Almarhoon ZM, Momattin H, et al.: Bimekizumab: the first FDA-approved dual IL-17A/IL-17F inhibitor for plaque psoriasis - a comprehensive literature review. Psoriasis (Auckl). 2025, 15:351-60. 10.2147/PTT.S544166
2. US Food and Drug Administration: BIMZELX (bimekizumab-bkzx) injection, for subcutaneous use - highlights of prescribing information. BLA 761151, Supplement 10. (2024). Accessed: September 1, 2026: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761151s010lbl.pdf.
3. Lebwohl MG, Koo JY, Armstrong AW, et al.: Brodalumab: seven-year US pharmacovigilance report . Dermatol Ther (Heidelb). 2025, 15:3025-35. 10.1007/s13555-025-01497-w
4. Moulton CD, Malys M, Hopkins CW, Rokakis AS, Young AH, Powell N: Activation of the interleukin-23/Th17

axis in major depression: a systematic review and meta-analysis. Eur Arch Psychiatry Clin Neurosci. 2025, 275:1653-73. 10.1007/s00406-024-01864-2

5. Strober B, Soliman AM, Truong B, Patel MB, Barqawi YK, Gisondi P: Association between biologic exposure and the risk of depression in patients with psoriasis: a retrospective analysis of large US administrative claims data. Am J Clin Dermatol. 2024, 25:853-6. 10.1007/s40257-024-00877-w
6. Williams K, Lada G, Reynolds NJ, et al.: Risk of suicide and suicidality in patients with moderate to severe psoriasis: results from the British Association of Dermatologists Biologics and Immunomodulators Register (BADBIR). Clin Exp Dermatol. 2025, 50:804-11. 10.1093/ced/llae449
7. Lin Z, Yu X, Yang M, Xu J, Zhong J: A real-world pharmacovigilance study of FDA adverse event reporting system (FAERS) events for bimekizumab. Front Pharmacol. 2025, 16:1714173. 10.3389/fphar.2025.1714173
8. Cao J, Yang N: Signal detection and analysis of adverse events associated with bimekizumab postmarketing based on the FAERS database. Dermatol Ther. 2026, 4:8648980. 10.1155/dth/8648980
9. Tran TS, Le DV, Jacobs JC, Nguyen TM, Wetter DA, Nguyen GH: Post-marketing safety of bimekizumab in psoriasis patients: pharmacovigilance data from FDA Adverse Event Reporting System. Int J Dermatol. 2026, 65:825-7. 10.1111/ijd.70082
10. Lin X, Guo L, Lin T, Yan C, Huang X, Cheng Y, Chen M: Disproportionality analysis of adverse events associated with bimekizumab: a real-world study based on FDA Adverse Event Reporting System (FAERS) Database. Naunyn Schmiedebergs Arch Pharmacol. 2026, 399:7405-14. 10.1007/s00210-025-04894-2
11. Fusaroli M, Salvo F, Begaud B, et al.: The Reporting of a Disproportionality Analysis for Drug Safety Signal Detection Using Individual Case Safety Reports in PharmacoVigilance (READUS-PV): development and statement. Drug Saf. 2024, 47:575-84. 10.1007/s40264-024-01421-9
12. Evans SJ, Waller PC, Davis S: Use of proportional reporting ratios (PRRs) for signal generation from spontaneous adverse drug reaction reports. Pharmacoepidemiol Drug Saf. 2001, 10:483-6. 10.1002/pds.677
13. Faillie JL: Case-non-case studies: principle, methods, bias and interpretation . Therapie. 2019, 74:225-32. 10.1016/j.therap.2019.01.006
14. Kass-Hout TA, Xu Z, Mohebbi M, et al.: OpenFDA: an innovative platform providing access to a wealth of FDA's publicly available data. J Am Med Inform Assoc. 2016, 23:596-600. 10.1093/jamia/ocv153
15. Brown EG, Wood L, Wood S: The Medical Dictionary for Regulatory Activities (MedDRA) . Drug Saf. 1999, 20:109-17. 10.2165/00002018-199920020-00002
16. Woolf B: On estimating the relation between blood group and disease . Ann Hum Genet. 1955, 19:251-3. 10.1111/j.1469-1809.1955.tb01348.x
17. Bate A, Evans SJ: Quantitative signal detection using spontaneous ADR reporting. Pharmacoepidemiol Drug Saf. 2009, 18:427-36. 10.1002/pds.1742
18. De Souza BC, Leão A, Manfredi AA, et al.: Extraction Code, Contingency Data, and Traceability Record for a Disproportionality Analysis of Psychiatric Adverse Events Associated With Bimekizumab in the FDA Adverse Event Reporting System. Zenodo, Geneva, Switzerland; 2026. 10.5281/zenodo.23357366
19. Liu L, Lin NX, Yu YT, et al.: Epidemiology of mental health comorbidity in patients with psoriasis: an analysis of trends from 1986 to 2019. Psychiatry Res. 2023, 321:115078. 10.1016/j.psychres.2023.115078
20. Blauvelt A, Armstrong A, Merola JF, et al.: Mental health outcomes in patients with moderate to severe psoriasis treated with bimekizumab: analysis of phase 2/3 randomized trials. J Am Acad Dermatol. 2024, 91:72-81. 10.1016/j.jaad.2024.02.039
21. He K, Zhao K, Yin T, et al.: A real-world pharmacovigilance study of brodalumab based on the FDA adverse event reporting system. Sci Rep. 2025, 15:2346. 10.1038/s41598-025-86976-y
22. Strober BE, Langley RG, Menter A, et al.: No elevated risk for depression, anxiety or suicidality with secukinumab in a pooled analysis of data from 10 clinical studies in moderate-to-severe plaque psoriasis. Br J Dermatol. 2018, 178:e105-7. 10.1111/bjd.16051
23. Wang J, Wang C, Liu L, et al.: Adverse events associated with anti-IL-17 agents for psoriasis and psoriatic arthritis: a systematic scoping review. Front Immunol. 2023, 14:993057. 10.3389/fimmu.2023.993057
24. Tolete C, Friedman A, Calderon J, Tjahjono L: Psychiatric safety of bimekizumab versus interleukin-23 inhibitors in psoriasis: a real-world TriNetX cohort study. JAAD Int. 2026, 25:143-5. 10.1016/j.jdin.2026.02.006