Brodalumab: 4-Year US Pharmacovigilance Report

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OBJECTIVE

- **To review the US pharmacovigilance data over a 4-year reporting period to provide insight into the safety of brodalumab for the treatment of moderate-to-severe plaque psoriasis in adults**

CONCLUSIONS

- **These US pharmacovigilance data are consistent with the established safety profile of brodalumab reported in long-term clinical trials and 3-year pharmacovigilance data**
- **No completed suicides occurred throughout the 4-year reporting period, and no new cases of suicide attempts were reported since the 3-year report**

SYNOPSIS

- Brodalumab is an interleukin-17 receptor A antagonist indicated for moderate-to-severe plaque psoriasis in adult patients with loss of or no response to alternative systemic therapies[1]
  - Brodalumab has a boxed warning for suicidal ideation and behavior in the United States, even though pivotal clinical trials and recent pharmacovigilance data do not confirm a causal relationship[1-3]
  - No completed suicides and 1 suicide attempt by a patient with a history of depression occurred during the initial 3-year pharmacovigilance reporting period[3]
  - Arthralgia was the most common treatment-specific adverse event (AE) in the 2- and 3-year pharmacovigilance reports[3,4]

METHODS

- Pharmacovigilance data reported to Ortho Dermatologics by US patients and healthcare providers were compiled from August 15, 2017, through August 14, 2021
- The most common AEs listed in the brodalumab package insert (incidence ≥1%; arthralgia, headache, myalgia, influenza, diarrhea, oropharyngeal pain, nausea, injection-site reactions, fatigue, neutropenia, and *Tinea* infections) and AEs of special interest were assessed as exposure-adjusted rates per 100 patient-years (PYs)
- Brodalumab exposure was estimated as the time between the first and last prescription-dispensing authorization dates. Patients with the same initial and last prescription-dispensing authorization date were excluded

RESULTS

Commonly reported AEs from package insert

- Data were collected from 4019 US patients and exposure was estimated as 4563 PYs
- Of 2118 unique AE cases, 22% were reported by healthcare providers and 78% by patients
- Common AEs are listed in the Table; similar to previous reports,[3,4] arthralgia was the most commonly reported AE within the 4-year reporting period (115 cases; 2.52 events/100 PYs)
  - Of arthralgia cases, 53 and 25 patients continued and discontinued treatment, respectively, whereas treatment status was unknown for 37 patients
  - Of the 4 new cases of arthralgia since the 3-year report, 3 patients were temporarily off brodalumab when their joint pain recurred
- There were no new reports of injection-site reactions, fatigue, or neutropenia since the 3-year report

Table. US Pharmacovigilance Monitoring of Brodalumab Through 4 Years (August 15, 2017–August 14, 2021)

AE	Event, n (r)[a]	Event drug related, n[b]	Discontinued, n (%)[c]	Maintained, n (%)[c]	Action unknown/NA, n (%)[c]
Arthralgia	115 (2.52)	1	25 (22)	53 (46)	37 (32)
Headache	45 (0.99)	0	6 (13)	25 (56)	14 (31)
Fatigue	44 (0.96)	1	6 (14)	20 (45)	18 (41)
Injection-site reaction	35 (0.77)	3	1 (3)	18 (51)	16 (46)
Diarrhea	33 (0.72)	0	6 (18)	19 (58)	8 (24)
Myalgia	31 (0.68)	0	6 (19)	18 (58)[d]	7 (23)
Nausea	29 (0.64)	0	5 (17)	17 (59)	7 (24)
Influenza	23 (0.50)	1	9 (39)	7 (30)	7 (30)
Oropharyngeal pain	21 (0.46)	0	2 (10)	11 (52)[e]	8 (38)
Neutropenia	1 (0.02)	0	0	1 (100)	0
Tinea infection	0	—	—	—	—

AE, adverse event; NA, not applicable; r, exposure-adjusted event rate per 100 patient-years. [a]Number of patients experiencing AE, not total number of AEs. [b]Relatedness to brodalumab was based on company-determined causality. [c]Treatment action taken upon AE occurrence. Percentage is event divided by total number of patients experiencing event. [d]One patient increased brodalumab dose. [e]One patient temporarily stopped taking the drug but planned to resume brodalumab treatment.

Clinical events of special interest

- Exposure-adjusted event rates are reported in the Figure

Infections

- Of 102 serious infections reported, only 3 were considered related to brodalumab
- Although no serious fungal infections were reported, 1 new fungal infection (onychomycosis) led to the patient discontinuing brodalumab; there were no new reports of oral candidiasis
- One case of tuberculosis, 24 cases of confirmed COVID-19, and 2 cases of suspected COVID-19 were reported

Inflammatory bowel disease

- No new cases of Crohn's disease were reported (1 case was previously reported in a patient who had symptomatic history before brodalumab initiation)
- One case of ulcerative colitis, which was not suspected to be related to brodalumab, was reported

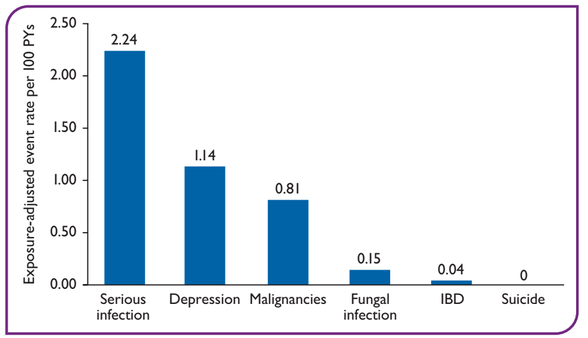
Malignancies

- 37 malignancies were reported in 32 patients (0.81 events/100 PYs); none were considered related to brodalumab

Depression and suicide

- There were 4 new depression cases reported during year 4; no causality assessments were provided
- There were no completed suicides throughout the 4-year report and no new suicide attempts reported (there was 1 previously reported suicide attempt, with no indicated causal relationship between brodalumab and the patient's attempted self-harm)

Figure. Exposure-adjusted clinical events of special interest, as deemed by the reporter or company, within the 4-year reporting period.



Exposure-adjusted event rate per 100 PYs is the number of events per 45.63 PYs of exposure. IBD, inflammatory bowel disease; PY, patient-year.

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References: 1. Siliq [package insert]. Bausch Health US, LLC; 2017. **2.** Lebwohl et al. *J Am Acad Dermatol*. 2018;78:81-89. **3.** Lebwohl et al. *Dermatol Ther*. 2021;34:e15105. Erratum in *Dermatol Ther*. 2022;35:e15664. **4.** Lebwohl et al. *Dermatol Ther (Heidelb)*. 2021;11:173-180.

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