Risk of Suicide and Suicidality in Patients with Moderate to Severe Psoriasis: results from the British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR)

Running head: Suicide risk in patients with psoriasis: results from BADBIR

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What is already known about this topic?

- Psoriasis is associated with poor mental health, depression and reduced quality of life.
- Results of existing meta-analyses regarding risk of suicidality, including suicidal thoughts, attempts and suicide, in patients with psoriasis are conflicting.
- Findings regarding suicide risk in patients with clinically-confirmed moderate to severe disease are lacking.

What does this study add?

- Incidence rate of suicide was 12.5 per 100,000 person-years (95% CI 6.53, 24.11) in patients with moderate to severe psoriasis. This was not significantly elevated compared with the general population.
- Psychiatric comorbidity or past suicidality significantly increased the risk for any death, self-injurious behaviours, suicidal ideation and suicide attempts among patients.
- Mental health monitoring is important in psoriasis, in particular exploring past and present suicidal thoughts/behaviour in at risk patients.

Abstract

Background. Psoriasis is associated with poor mental health and reduced quality of life. Although the high risk for depression in patients with psoriasis is well-established, their suicidality risk is uncertain. Previous studies provide contrasting results and have not included patients with clinically-confirmed severe disease.

Objectives. Our aim was to determine risk of suicide among patients with moderate to severe psoriasis compared with the general population, and investigate if psychiatric comorbidity or history of suicidality increases future suicidality risk in psoriasis. We further estimated the incidence of suicidal and self-injurious behaviours in patients.

Methods. Analysis was performed using the British Association of Dermatologists Biologics and Immunomodulators Register (BADBIR). As controls, general population mortality and suicide data were used.

Results. There were 9 suicides in BADBIR. The incidence rate of suicide was 12.5 per 100,000 person-years (95% CI 6.53, 24.11) in BADBIR versus 11.0 per 100,000 person-years (95% CI 10.7, 11.3) in the general population in England and Wales. Among patients, psychiatric comorbidity or past suicidality was associated with higher risk for suicidal ideation, suicide attempts and self-injurious behaviours.

Conclusions. Suicide rates among patients with moderate to severe psoriasis were not significantly higher compared with the general population. Suicide is a rare event and our results are limited by the uncertainty in the estimate reliability. However, considering the high depression prevalence in psoriasis, our findings support the need for prompt assessment of patients for psychiatric comorbidities and suicidality history. Further research is required on suicidal behaviours and the role of psoriasis severity.

Introduction

Psoriasis can have a major impact on all areas of life and one in four patients feel depressed [1,2]. Although there is significant evidence for a high risk of depression and poor mental health in psoriasis, data are lacking as to whether patients are at an increased risk of suicide and other suicidal phenomena [3]. Four systematic reviews report conflicting results. Pompili *et al.* [4] and Singh *et al.* [5], who did not exclude cross-sectional research, report an increased risk of suicidality outcomes (including suicidal ideation, suicide attempts and suicides), whereas two reviews by the group of Chi and colleagues [6,7] found no increased risk, using cohort studies only. Interestingly, a well-controlled pan-European study of 626 adult patients reported that not only is anxiety and depression overrepresented, but that there is a significant (at least 2.5 times greater than controls) risk of suicidal ideation in people with psoriasis [8]. Among tertiary patients with moderate to severe disease, up to 47% of patients may have lifetime suicidal thoughts [9].

There are even fewer studies looking at suicidality risk in children and adolescent patients with psoriasis; the prevalence of suicidal ideation and suicide attempts are approximately 0.45% and 0.08% respectively in younger patients [10]. A systematic review by Hung *et al.* [7] found that psoriasis increases the risk for suicidal ideation (HR 1.50, 95% CI 1.12–2.03) among children, but not adults.

Knowing that both psoriasis and suicide are associated with mental disorders, (e.g., depression and alcohol abuse) [11], we investigated whether patients with moderate to severe psoriasis have a higher rate of suicide than the general population. Furthermore, our secondary aim was to investigate effects of psychiatric comorbidity or past suicidality on risk for suicidal outcomes in this population.

Materials and methods

We performed an analysis using the British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR), a prospective, observational cohort study which assesses the long-term safety of biologic and small molecule therapies in moderate to severe

psoriasis [12]. BADBIR has expanded to include over 160 sites in the United Kingdom (UK) and the Republic of Ireland since 2007; the National Institute for Health and Clinical Excellence (NICE) advises that all UK patients with psoriasis meeting the eligibility criteria should register in BADBIR.

Being a pharmacovigilance register, BADBIR uses the International Council for Harmonisation's (ICH) Medical Dictionary for Regulatory Activities (MedDRA) to record comorbidities and report all potential adverse outcomes, including suicidal phenomena [13].

Psychiatric comorbidities at baseline were used to define two patient groups within BADBIR, an "At Risk" group and a "Not At Risk" group. The At Risk group included all patients with a recorded baseline entry of depression, anxiety or any other psychiatric disorder and/or previous suicidal or self-injurious behaviour. All the MedDRA terms used for classification can be found in Tables S1 and S2, Supporting Information. The Not At Risk group were those with no history of the above.

For all patients, we extracted serious adverse events coded to MedDRA Preferred Term (PT) "Death" and "Completed suicide" to investigate deaths of any cause and suicides respectively. We also extracted adverse events coded to any of the MedDRA PTs in the High-Level Group Terms (HLGT) of "Suicidal and self-injurious behaviours NEC" (NEC=not elsewhere classified).

In BADBIR, suicidal ideation was coded for all events where the patient expressed suicidal thoughts, regardless of whether the patient acted on these thoughts. Where they acted on the thoughts, an additional code was added as appropriate. Suicide attempt included events where the patient attempted suicide but the outcome was not death. An additional code regarding method (for example, overdose) could accompany this coding. Completed suicide is a MedDRA code used where the patient attempted suicide and died as a result. The method of suicide is also coded alongside this code as well as a code for death.

Self-injurious ideation was coded when the patient has had self-harm thoughts or hallucinations but not acting on them at the time. Self-injurious behaviour was coded for all behaviour of an individual which results to harm oneself, either as a direct or indirect result of

this individual's actions, independently of intent. Intentional self-injury was coded for events of intentional self-harm, including both suicidal and non-suicidal intent. As BADBIR enables narrative description of events, there can be enough information to determine whether the self-injury was suicidal in which case there would also be a suicide attempt code for that event. Where there is no mention of suicidal intent, there would be no additional code.

We calculated incidence rates per 100,000 person-years with confidence intervals (CI) for death, suicide, suicide attempt, suicidal ideation, intentional self-injury, self-injurious ideation, self-injurious behaviour, suicidal behaviour, intentional overdose and poisoning deliberate (plus the incidence rate for all events in HLGT of "Suicidal and self-injurious behaviours NEC" combined) for the total BADBIR population and for the two groups.

Incidence rates of death and suicide in BADBIR were compared with age-standardised general population data from England and Wales derived from the Office of National Statistics (ONS) Mortality Data 2020 [14] and ONS Suicide Data 2020[15] .

Person-years were calculated from the start date of a patient's registration drug until their adverse event or death or their last follow-up in BADBIR. The BADBIR incidence rates are given per 100,000 person-years to enable comparison with the general population rates available from ONS. ONS deaths registered in 2019 were used to avoid any potential impact of COVID-19 on death rates, and were a close match to the BADBIR dataset cut off of February 2020 (ONS Mortality Data, 2020 and ONS Suicide Data, 2020).

Proportional mortality due to suicide (%) was also estimated and the difference between proportions was compared using a z-test at significance level 0.05.

Due to the sample size, hypothesis testing for differences in baseline characteristics between the patient groups were not performed as small yet statistically significant differences would not be clinically important. General population sex data were derived from ONS [16,17].

All analyses were performed in Stata version 14.0 (StataCorp, USA).

Results

We analysed data from 19,052 patients with moderate to severe psoriasis in BADBIR; 4,656 patients (24.4%) were classified as At Risk and 14,396 patients (75.6%) as Not At Risk.

Baseline characteristics for BADBIR are presented in Table 1. General population characteristics corresponding to the period of the ONS death data are not available. Men were ~49.4% of the general population during this period. In BADBIR, 57.9% of patients were men.

There were 9 suicides in total in BADBIR. The suicide incidence rate for patients was 12.5 per 100,000 person-years (95% CI 6.5, 24.1). This rate is slightly higher when compared to the incidence rate in the general population which was 11.0 (95% CI 10.7, 11.3) per 100,000 persons in a year; however, the difference does not appear to be statistically significant as the confidence intervals largely overlap.

The proportional mortality due to suicide in BABDIR was 1.65% (9 suicides in 545 deaths) versus 1.07% (5,691 suicides in 530,841 deaths) in the general population. We found no significant difference in these proportions (p=0.19).

Table 2 presents all suicidality outcomes among patients, including a combined outcome for adverse events except death ("HLGT Combined").

Out of 9 patient suicides, 4 were in the At Risk group and 5 in the Not At Risk group. Suicide attempt was the most commonly reported outcome (88 events reported by 73 patients), followed by self-injurious behaviour (52 events for 21 patients) and suicidal ideation (43 events for 36 patients). Event counts higher than the respective patient counts indicated multiple events in some patients. Twenty seven out of 42 self-injurious incidents in the At Risk group occurred in a single patient.

Incidence rates per 100,000 person-years with CIs for all outcomes are shown in Table 3.

The incidence rate for the combined event of suicidal or self-injurious behaviour was 186.37 per 100,000 person years for all patients with moderate to severe psoriasis (95% CI (157.24, 220.89)).

Suicide incidence was higher in the At Risk compared with the Not At Risk group, although the difference was not statistically significant (22.96 per 100,000 person-years (95% CI 8.62, 61.17) versus 9.20 per 100,000 person-years (95% CI 3.83, 22.11)). However, we note that the incidence of death of any cause was significantly higher in the At Risk vs Not At Risk group (IR 958.45 (95% CI 823.57, 1115.42) vs 695.80 (95% CI 629.08, 769.60) per 100,000 person-years).

For all other suicidality outcomes except suicide, and including the HLGT combined outcome, incidence was significantly higher in the At Risk group vs Not At Risk group (Table 3).

Discussion

Using a real-world, prospective, multi-centre cohort of a well-defined clinical population with moderate to severe psoriasis, we did not find significantly increased suicide rates compared to the general population. However, we found higher rates of suicide attempts and suicidal ideation as well as a higher rate of self-harm behaviours in patients with psoriasis and a psychiatric comorbidity or past suicidality compared to those without.

Although our data show a slightly higher suicide incidence in patients with psoriasis compared to the general population, our results reassuringly point towards the null hypothesis. This result aligns with a recent systematic review of Hung *et al.*, who used cohort studies only and found no association between psoriasis and suicide [7]. Supporting our incident suicide findings, the proportional mortality due to suicide in BADBIR showed a similar trend; although it was 0.58% higher compared to the general population proportion, it did not differ significantly.

The incidence rate for suicide attempts was 102 (95% CI 81, 129) per 100,000 person years across the total BADBIR cohort. Comparable general population incidence rates were not available for outcomes other than suicide and there is high methodological heterogeneity

across studies reporting these rates in existing literature [18]. For example, using primary care databases but different outcome definitions, the reported incidence rate for suicide attempts in the U.K. general population ranges from 82 (79, 85) during the years 2000-2007 [19] to 124 (121, 127) between 1998 and 2014 [11]. We note that a quarter of patients in BADBIR had a diagnosed psychiatric comorbidity and/or history of suicidality, with depression being the most common comorbidity. We found higher incident rates in the At Risk compared to the Not At Risk group for the combined and all individual self-harm and suicidality outcomes except suicide; for suicide, we found no difference between the groups.

Taken together with previous results of Parisi *et al*., who found no increase -and possible reduction- in suicide risk in psoriasis, despite an increased rate of mental disorders and self-harm [11], our results may reflect a true discrepancy between suicide and other mental health and suicidality outcomes in psoriasis, in particular for patients with pre-existing vulnerability to poor mental health. One explanation may be due to increased medical attention and monitoring of this cohort receiving systemic treatments, which may act preventatively against progression of suicidal thoughts to suicide in at risk patients. It is also plausible that immunomodulating drugs may have some additional protective impact due to reducing systemic inflammation, which has been linked to suicidality even among depressed individuals [20,21].

Nevertheless, our results do not fully align with data from other populations, which suggest that history of past suicidality and psychiatric comorbidity increase not only future suicidal ideation and suicide attempts, but also future suicide risk [22]. Given our findings for all other suicidality outcomes and the relative rarity of suicides, our results may also reflect insufficient power of the BADBIR sample size to detect a truly higher risk in the group with previous mental health history.

Interestingly, little difference in baseline disease severity was observed between the At Risk and Not At Risk groups for PASI, yet DLQI was almost two points higher in the At Risk group. This may indicate that disease severity in isolation may not be a co-factor for psychiatric co-

morbidities or disability in patients and those with co-existing mental disorders might find psoriasis more difficult to cope with.

Overall, our findings support the directive for holistic care in psoriasis, which includes addressing comorbidities and psychological needs of patients with this complex chronic disease [23,24]. Routine mental health assessments are increasingly advocated for in psoriasis, given the extent of poor mental health, high rates of undiagnosed depression and associated impact on dermatology-related quality of life in this population [9,25-28]. The regular appointments offered for patients on systemic therapy should be an opportunity to explore suicidality and self-harm, in particular among the significant number of patients with mental health history. Suicide is a major global public health issue [29]; interventions targeting medical professionals other than psychiatrists have shown promising results in reducing patient suicide rates [22,30]. But even when not dying by suicide, the burden of suicidality should be appropriately recognised to improve patient outcomes. Suicidal ideation and self-harm reduce quality of life, which may improve with intervention [31-33]. As many patients may not ask for help when struggling, dermatology appointments may be the only contact patients have with healthcare professionals.

A distinct need to train dermatologists on mental health has been identified [27]. A tendency of normalising depression among patients with long-term illness can hinder depression recognition and management [34]. Although some clinicians fear that asking about suicidal thoughts may cause a suicide attempt, this is not the case and can instead enable disclosure of negative feelings [35]. DLQI scores that seem at odds with PASI should be addressed to ascertain other factors influencing quality of life. Referral to specialised services is paramount for patients who are at high risk or experiencing suicidality. Furthermore, comprehensive dedicated multidisciplinary psychodermatology services need to be available across the UK and globally [23].

The main strength of the present study is the quality of the BADBIR data source. In contrast to previous UK-based studies investigating suicide risk in psoriasis, which used codes from non-specific databases such as hospital episode statistics and primary care [11,36,37], BADBIR includes a

clinically well-defined psoriasis population and uses descriptive adverse events entries, processed by trained staff, with robust cross-referencing and linkage to external sources. The inclusion criteria of recent clinically-assessed PASI and DLQI ensure all patients have moderate to severe psoriasis. To our knowledge, no other UK cohort studies investigating suicidality used clinical disease severity measures. For example, Parisi *et al.* [11] carried out a large, high-quality study using the Clinical Practice Research Datalink, however without access to hospital prescription data to enhance primary care records.

Even though we used a national patient sample, suicide is a rare event and there is uncertainty regarding the reliability of the estimate with our sample size. A further limitation is that we were unable to adjust for confounders for the incidence rates, as mentioned above; however, the patients have been stratified by psychiatric comorbidities or history of suicidality. Although it is estimated that the amount of missing data is limited (8% of cohort), we can't exclude missingness for some to be related to a mental disorder. We note that ethnicity is reported in two combined wider groups, which should be considered when interpreting our descriptive results. Finally, suicidality under-reporting and under-coding is common in large cohorts, in particular for suicidal thoughts [38]. In our data, this likely explains the lower frequency of suicidal and self-injurious ideation compared to suicidal and self-injurious behaviours in BADBIR, as well as compared to respective general population rates in Ireland and parts of the UK, estimated using emergency department statistics before Covid-19 [39,40]. Contributing to this may be the fact that questions are not directly asked by the dermatology teams, patients' reluctance to disclose, and recall bias.

Conclusion

We could not detect an increased risk of suicide among patients with moderate to severe psoriasis. However, patients with psychiatric comorbidities or previous suicidality history are at increased risk of overall suicidal burden in the form of suicidal ideation, suicide attempts and self-harm behaviours. As there were few suicide events in BADBIR, further research is required on a population level to confirm these findings, taking into account the severity of psoriasis. It will also be important to examine temporal relationships among the onset of mental disorders,

onset of psoriasis and suicidal phenomena. The implications for clinical practice include greater focus on addressing mental health comorbidities in patients with psoriasis to reduce suicidality-related morbidity in patients. To facilitate this, it is critical to expand clinical training to improve dermatologists' understanding and attitudes surrounding patients' mental health needs.

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The BADBIR Study Group comprises the BADBIR Steering Committee and the BADBIR Data Monitoring Committee (DCM). BADBIR Steering Committee members are http://www.badbir.org/Clinicians/Information/SteeringCommittee [badbir.org]. Members of the DMC are: Prof Anja Strangfeld (Chair), Dr Girish Gupta, Imke Redeker and Dr Rick Woolf.

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Table 1. Baseline Characteristics of the population in BADBIR

Characteristic	Total	At Risk	Not At Risk
Total, n (%)	19,052 (100)	4,656 (24.4)	14,396 (75.6)
Age, mean years (SD)	44.7 (13.8)	45.6 (13.0)	44.4 (14.0)
Disease Duration, mean years (SD)	20.7 (13.0)	21.6 (13.3)	20.4 (12.9)
Age of Onset, mean years (SD)	24.1 (14.2)	24.1 (14.2)	24.1 (14.2)
Males, n (%)	11,027 (57.9)	2,129 (45.7)	8,898 (61.8)
Psoriasis Area and Severity Index, mean score (SD)	14.9 (8.2)	15.2 (8.3)	14.8 (8.1)
Missing, n (%)	1,477 (7.8)	361 (7.8)	1,116 (7.8)
Dermatology Life Quality Index, mean score (SD)	15.4 (8.3)	16.8 (8.4)	14.9 (8.2)
Missing, n (%)	5,378 (28.2)	1,631 (35.0)	3,747 (26.0)
Work Status, n (%)			
Full Time	9,623 (50.5)	1,653 (35.5)	7,970 (55.4)
Part Time	2,151 (11.3)	579 (12.4)	1,572 (10.9)
Homemaker	735 (3.9)	228 (4.9)	507 (3.5)
Unemployed	744 (3.9)	242 (5.2)	502 (3.5)
Not Working due to ill-health/disability	1,849 (9.7)	997 (21.4)	852 (5.9)
Student	575 (3.0)	102 (2.2)	473 (3.3)
Retired	1,894 (9.9)	510 (11.0)	1,384 (9.6)
Missing	1,481 (7.8)	345 (7.4)	1,136 (7.9)
Ethnicity, n (%)			
Non-White	1,976 (10.4)	274 (5.9)	1,702 (11.8)
White	17,076 (89.6)	4,382 (94.1)	12,694 (88.2)
BMI, n (%)			
Not Obese (BMI <30)	9,238 (48.5)	1,992 (42.8)	7,246 (50.3)
Obese (BMI ≥30.0)	8,473 (44.5)	2,342 (50.3)	6,131 (42.6)
Missing	1,341 (7.0)	322 (6.9)	1,019 (7.1)
Alcohol Status, n (%)			
Does not drink alcohol	6,395 (33.6)	1,795 (38.6)	4,600 (32.0)
Currently drinks alcohol	11,317 (59.4)	2,564 (55.1)	8,753 (60.8)
Missing	1,340 (7.0)	297 (6.4)	1,043 (7.3)
Smoking Status, n (%)			
Never Smoked	6,357 (33.4)	1,228 (26.4)	5,129 (35.6)
Previous Smoker	6,231 (32.7)	1,546 (33.2)	4,685 (32.5)
Current Smoker	5,085 (26.7)	1,566 (33.6)	3,519 (24.4)
Missing	1,379 (7.2)	316 (6.8)	1,063 (7.4)
Psoriatic Arthritis, n (%)	3,736 (19.6)	1,071 (23.0)	2,665 (18.5)

Baseline Psychiatric Disorder, n (%)			
None	14,396 (75.6)	-	14,396 (100)
Depression	4,226 (22.2)	4,226 (90.8)	-
Depression only	3,574 (18.8)	3,574 (76.8)	-
Anxiety	905 (4.8)	905 (19.4)	-
Anxiety only	336 (1.8)	336 (7.2)	-
Other Psychiatric Disorder	219 (1.1)	219 (4.7)	-
Other Psychiatric Disorder only	80 (0.4)	80 (1.7)	-
Previous Suicide Attempt/Non-Fatal Self-Harm	11 (0.1)	11 (0.1)	-
Previous Suicide Attempt/Non-Fatal Self-Harm only	0	0	-
2 or more Psychiatric Disorders	666 (3.5)	666 (14.3)	-
Alcohol Misuse, n (%)	130 (0.7)	113 (2.4)	17 (0.1)

Table 2. Patient and Event Count for All Outcomes: Total and by At Risk Groups

Outcome	Total	At Risk Group	Not at Risk Group
Total, n (%)	19,052 (100)	4,656 (24.4)	14,396 (75.6)
Death: Event Count, n (%)	**545 (2.9)**	**167 (3.59)**	**378 (2.63)**
Suicide: Event Count, n	9	4	5
HLGT combined: Patients (Events), n (%)	**133 (199)**	**81 (138)**	**52 (61)**
Suicide Attempt	73 (88)	43 (54)	30 (34)
Suicidal ideation	36 (43)	23 (29)	13 (14)
Intentional Self-Injury	11 (14)	8 (11)	3 (3)
Self-injurious ideation	2 (2)	2 (2)	0
Self-Injurious Behaviour	21 (52)	13 (42)	8 (10)
Suicidal Behaviour	0	0	0
Intentional Overdose	0	0	0
Poisoning Deliberate	0	0	0

Abbreviations: Higher Level Group Term (HLGT). The counts for suicide are included in the total death counts.

Table 3. Incidence Rates for All Outcomes: Total and by At Risk Groups

Outcome	Person Time (Years)	Incidence Rate per 100,000 Person Years (95% CI)
Death Total	71,749.72	759.58 (698.42, 826.11)
At Risk	17,423.91	958.45 (823.57, 1115.42)
Not At Risk	54,325.81	695.80 (629.08, 769.60)
Suicide	As above	12.54 (6.53, 24.11)
At Risk		22.96 (8.62, 61.17)
Not At Risk		9.20 (3.83, 22.11)
HLGT Combined	71,364.48	186.37 (157.24, 220.89)
At Risk	17,156.78	472.12 (379.73, 586.99)
Not At Risk	54,207.70	95.93 (73.10, 125.89)
Suicide Attempt	As above	102.29 (81.32, 128.67)
At Risk		250.63 (185.88, 337.94)
Not At Risk		55.34 (38.69, 79.15)
Suicidal Ideation	As above	50.45 (36.39, 69.93)
At Risk		134.06 (89.08, 201.73)
Not At Risk		23.98 (13.93, 41.30)
Intentional Self-Injury	As above	15.41 (8.54, 27.83)
At Risk		46.63 (23.32, 93.24)
Not At Risk		5.53 (1.78, 17.16)
Self-injurious ideation	As above	2.80 (0.70, 11.21)
At Risk		11.66 (2.92, 46.61)
Not At Risk		-
Self-Injurious Behaviour	As above	29.43 (19.19, 45.13)
At Risk		75.77 (44.00, 130.49)
Not At Risk		14.76 (7.38, 29.51)

Abbreviations: confidence interval (CI); Higher Level Group Term (HLGT)

Consistent safety profile with over 8 years of real-world evidence, across licensed indications[1–3]

Cosentyx® secukinumab

1,000,000 patients treated globally, and counting across indications[4]

150+ clinical trials across indications[5]

8+ years of real-world evidence, worldwide across indications[1–3]

8 indications[1–3]

Click here to visit our HCP portal and learn more

Real-world evidence shows a consistent safety profile with long-term use of Cosentyx over 6 years[6,7]

No trend toward increased AE rates over time (pooled PsA, AS, PsO):*[6]

AEs of select interest (EAIR per 100 PY)	1 year	2 years	3 years	4 years	5 years	6 years	Cumulative rate
Serious infections Cases	2.0 n=149	1.7 n=475	0.7 n=649	1.3 n=1,841	1.3 n=2,285	1.1 n=2,226	1.3 n=8,719
Malignant or unspecified tumours Cases	0.2 n=15	0.2 n=50	0.2 n=225	0.3 n=422	0.3 n=520	0.3 n=573	0.3 n=1,896
MACE Cases	0.2 n=15	0.1 n=39	0.2 n=151	0.2 n=238	0.2 n=264	0.1 n=287	0.2 n=1,031
Total IBD Cases	0.2 n=12	0.2 n=46	0.2 n=185	0.3 n=340	0.2 n=312	0.1 n=261	0.2 n=1,291
Exposure (PY)	7450	28,549	93,744	137,325	182,024	212,636	680,470

No trend towards increased rates of malignancy, MACE or IBD over time[6]

The most frequently reported adverse reactions are upper respiratory tract infections (17.1%) (most frequently nasopharyngitis, rhinitis).[1,2] Refer to the prescribing information for a summary of adverse events.

Adapted from Novartis Data on File. 2021.[6]

Refer to the Cosentyx Summary of Product Characteristics for full details, dosing and administration, including special populations.

Cosentyx is indicated for the treatment of moderate to severe **PsO** in adults, children and adolescents from the age of 6 years who are candidates for systemic therapy; active **PsA** in adult patients (alone or in combination with methotrexate) when the response to previous disease-modifying anti-rheumatic drug therapy has been inadequate; active **AS** in adults who have responded inadequately to conventional therapy; active **nr-axSpA** with objective signs of inflammation as indicated by elevated C-reactive protein and/or magnetic resonance imaging evidence in adults who have responded inadequately to non-steroidal anti-inflammatory drugs; active moderate to severe **HS** (acne inversa) in adults with an inadequate response to conventional systemic HS therapy; active **ERA** in patients 6 years and older (alone or in combination with methotrexate) whose disease has responded inadequately to, or who cannot tolerate, conventional therapy; active **JPsA** in patients 6 years and older (alone or in combination with methotrexate) whose disease has responded inadequately to, or who cannot tolerate, conventional therapy.[1,2]

Prescribing information, adverse event reporting and full indication can be found on the next page.

*Successive time periods of PSUR shown with cumulative rate: 26 Dec 2014 to 25 Dec 2015; 26 Dec 2015 to 25 Dec 2016; 26 Dec 2016 to 25 Dec 2017; 26 Dec 2017 to 25 Dec 2018: 26 Dec 2018 to 25 Dec 2019; 26 Dec 2019 to 25 Dec 2020.[6]

Abbreviations: AE, adverse event; AS, ankylosing spondylitis; EIAR, exposure-adjusted incidence rate; ERA, enthesitis-related arthritis; HCP, healthcare professional; HS, hidradenitis suppurativa; IBD, inflammatory bowel disease; JPsA, juvenile psoriatic arthritis; MACE, major adverse cardiac event; nr-axSpA, non-radiographic axial spondyloarthritis; PsA, psoriatic arthritis; PsO, plaque psoriasis; PY, patient year.

References: 1. Cosentyx® (secukinumab) GB Summary of Product Characteristics; **2.** Cosentyx® (secukinumab) NI Summary of Product Characteristics; **3.** European Medicines Agency. European public assessment report. Available at: https://www.ema.europa.eu/en/documents/overview/cosentyx-epar-medicine-overview_en.pdf [Accessed August 2024]; **4.** Novartis Data on File. Secukinumab – Sec008. 2023; **5.** ClinicalTrials.gov. Search results for 'secukinumab', completed, terminated and active, not recruiting trials. Available at: https://clinicaltrials.gov/search?term=Secukinumab,&aggFilters=status:com [Accessed August 2024]; **6.** Novartis data on file. Cosentyx Periodic Safety Update Report (PSUR); 26 December 2019 – 25 December 2020. 22 February 2021; **7.** Deodhar A, et al. Arthritis Res Ther 2019;21(1):111.

NOVARTIS

UK | August 2024 | FA-11239622

Cosentyx® (secukinumab) Northern Ireland Prescribing Information.

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Indications: Treatment of: moderate to severe plaque psoriasis in adults, children and adolescents from the age of 6 years who are candidates for systemic therapy; active psoriatic arthritis in adults (alone or in combination with methotrexate) who have responded inadequately to disease-modifying anti-rheumatic drug therapy; active ankylosing spondylitis in adults who have responded inadequately to conventional therapy; active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence in adults who have responded inadequately to non-steroidal anti-inflammatory drugs; active enthesitis-related arthritis and juvenile psoriatic arthritis in patients 6 years and older (alone or in combination with methotrexate) whose disease has responded inadequately to, or who cannot tolerate, conventional therapy; active moderate to severe hidradenitis suppurativa (acne inversa) in adults with an inadequate response to conventional systemic HS therapy. **Presentations:** Cosentyx 150 mg solution for injection in pre-filled pen; Cosentyx 300 mg solution for injection in pre-filled pen. **Dosage & Administration:** Administered by subcutaneous injection at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Consider discontinuation if no response after 16 weeks of treatment. Each 150 mg dose is given as one injection of 150 mg. Each 300 mg dose is given as two injections of 150 mg or one injection of 300 mg. If possible avoid areas of the skin showing psoriasis. *Plaque Psoriasis:* Adult recommended dose is 300 mg monthly. Based on clinical response, a maintenance dose of 300 mg every 2 weeks may provide additional benefit for patients with a body weight of 90 kg or higher. Adolescents and children from the age of 6 years: if weight ≥ 50 kg, recommended dose is 150 mg (may be increased to 300 mg as some patients may derive additional benefit from the higher dose). If weight < 50 kg, recommended dose is 75 mg. However, 150mg solution for injection in pre-filled pen is not indicated for administration of this dose and no suitable alternative formulation is available. *Psoriatic Arthritis:* For patients with concomitant moderate to severe plaque psoriasis see adult plaque psoriasis recommendation. For patients who are anti-TNFα inadequate responders, the recommended dose is 300 mg, 150 mg in other patients. Can be increased to 300 mg based on clinical response. *Ankylosing Spondylitis:* Recommended dose 150 mg. Can be increased to 300 mg based on clinical response. *nr-axSpA:* Recommended dose 150 mg. *Enthesitis-related arthritis and juvenile psoriatic arthritis:* From the age of 6 years, if weight ≥ 50 kg, recommended dose is 150 mg. If weight < 50 kg, recommended dose is 75 mg. However, 150mg solution for injection in pre-filled pen is not indicated for administration of this dose and no suitable alternative formulation is available. *Hidradenitis suppurativa:* Recommended dose is 300 mg monthly. Based on clinical response, the maintenance dose can be increased to 300 mg every 2 weeks. **Contraindications:** Hypersensitivity to the active substance or excipients. Clinically important, active infection. **Warnings & Precautions:** *Infections:* Potential to increase risk of infections; serious infections have been observed. Caution in patients with chronic infection or history of recurrent infection. Advise patients to seek medical advice if signs/symptoms of infection occur. Monitor patients with serious infection closely and do not administer Cosentyx until the infection resolves. Non-serious mucocutaneous candida infections were more frequently reported for secukinumab than placebo in the psoriasis clinical studies. Should not be given to patients with active tuberculosis (TB). Consider anti-tuberculosis therapy before starting Cosentyx in patients with latent TB. *Inflammatory bowel disease (including Crohn's disease and ulcerative colitis):* New cases or exacerbations of inflammatory bowel disease have been reported with secukinumab. Secukinumab, is not recommended in patients with inflammatory bowel disease. If a patient develops signs and symptoms of inflammatory bowel disease or experiences an exacerbation of pre-existing inflammatory bowel disease, secukinumab should be discontinued and appropriate medical management should be initiated. *Hypersensitivity reactions:* Rare cases of anaphylactic reactions have been observed. If an anaphylactic or serious allergic reactions occur, discontinue immediately and initiate appropriate therapy. *Vaccinations:* Do not give live vaccines concurrently with Cosentyx; inactivated or non-live vaccinations may be given. Paediatric patients should receive all age appropriate immunisations before treatment with Cosentyx. *Latex-Sensitive Individuals:* The removable needle cap of the 150mg pre-filled pen contains a derivative of natural rubber latex. *Concomitant immunosuppressive therapy:* Combination with immunosuppressants, including biologics, or phototherapy has not been evaluated in psoriasis studies. Cosentyx was given concomitantly with methotrexate, sulfasalazine and/or corticosteroids in arthritis studies. Caution when considering concomitant use of other immunosuppressants. **Interactions:** Live vaccines should not be given concurrently with secukinumab. No interaction between Cosentyx and midazolam (CYP3A4 substrate) seen in adult psoriasis study. No interaction between Cosentyx and methotrexate and/or corticosteroids seen in arthritis studies. **Fertility, pregnancy and lactation:** *Women of childbearing potential:* Use an effective method of contraception during and for at least 20 weeks after treatment. *Pregnancy:* Preferably avoid use of Cosentyx in pregnancy. *Breast feeding:* It is not known if secukinumab is excreted in human breast milk. A clinical decision should be made on continuation of breast feeding during Cosentyx treatment (and up to 20 weeks after discontinuation) based on benefit of breast feeding to the child and benefit of Cosentyx therapy to the woman. *Fertility:* Effect on human fertility not evaluated. **Adverse Reactions**: *Very Common* (≥1/10): Upper respiratory tract infection. *Common* (≥1/100 to <1/10): Oral herpes, headache, rhinorrhoea, diarrhoea, nausea, fatigue. *Uncommon (≥1/1,000 to <1/100):* Oral candidiasis, lower respiratory tract infections, neutropenia, inflammatory bowel disease. *Rare (≥1/10,000 to <1/1,000)*: anaphylactic reactions, exfoliative dermatitis (psoriasis patients), hypersensitivity vasculitis. *Not known:* Mucosal and cutaneous candidiasis (including oesophageal candidiasis). *Infections:* Most infections were non-serious and mild to moderate upper respiratory tract infections, e.g. nasopharyngitis, and did not necessitate treatment discontinuation. There was an increase in mucosal and cutaneous (including oesophageal) candidiasis, but cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in a small proportion of patients (0.015 serious infections reported per patient year of follow up). *Neutropenia:* Neutropenia was more frequent with secukinumab than placebo, but most cases were mild, transient and reversible. Rare cases of neutropenia CTCAE Grade 4 were reported. *Hypersensitivity reactions:* Urticaria and rare cases of anaphylactic reactions were seen. *Immunogenicity*: Less than 1% of patients treated with Cosentyx developed antibodies to secukinumab up to 52 weeks of treatment. *Other Adverse Effects:* The list of adverse events is not exhaustive, please consult the SmPC for a detailed listing of all adverse events before prescribing. **Legal Category:** POM. **MA Number & List Price:** EU/1/14/980/005 - 150 mg pre-filled pen x2 £1,218.78; EU/1/14/980/010 – 300 mg pre-filled pen x 1 £1218.78. **PI Last Revised:** May 2023. Full prescribing information, (SmPC) is available from: Novartis Pharmaceuticals UK Limited, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, W12 7FQ. Telephone: (01276) 692255.

UK | 284832 | May 2023

Adverse Event Reporting:

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis via uk.patientsafety@novartis.com or online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report

If you have a question about the product, please contact Medical Information on 01276 698370 or by email at medinfo.uk@novartis.com

Cosentyx® (secukinumab) Great Britain Prescribing Information.

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Indications: Treatment of: moderate to severe plaque psoriasis in adults, children and adolescents from the age of 6 years who are candidates for systemic therapy; active psoriatic arthritis in adults (alone or in combination with methotrexate) who have responded inadequately to disease-modifying anti-rheumatic drug therapy; active ankylosing spondylitis in adults who have responded inadequately to conventional therapy; active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence in adults who have responded inadequately to non-steroidal anti-inflammatory drugs; active enthesitis-related arthritis and juvenile psoriatic arthritis in patients 6 years and older (alone or in combination with methotrexate) whose disease has responded inadequately to, or who cannot tolerate, conventional therapy; active moderate to severe hidradenitis suppurativa (acne inversa) in adults with an inadequate response to conventional systemic HS therapy. **Presentations:** Cosentyx 75 mg solution for injection in pre-filled syringe; Cosentyx 150 mg solution for injection in pre-filled syringe; Cosentyx 150 mg solution for injection in pre-filled pen; Cosentyx 300 mg solution for injection in pre-filled pen. **Dosage & Administration:** Administered by subcutaneous injection at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Consider discontinuation if no response after 16 weeks of treatment. Each 75 mg dose is given as one injection of 75 mg. Each 150 mg dose is given as one injection of 150 mg. Each 300 mg dose is given as two injections of 150 mg or one injection of 300 mg. If possible avoid areas of the skin showing psoriasis. *Plaque Psoriasis:* Adult recommended dose is 300 mg. Based on clinical response, a maintenance dose of 300 mg every 2 weeks may provide additional benefit for patients with a body weight of 90 kg or higher. Adolescents and children from the age of 6 years: if weight ≥ 50 kg, recommended dose is 150 mg (may be increased to 300 mg as some patients may derive additional benefit from the higher dose). If weight < 50 kg, recommended dose is 75 mg. *Psoriatic Arthritis:* For patients with concomitant moderate to severe plaque psoriasis see adult plaque psoriasis recommendation. 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UK | 290802 | June 2023

Adverse Event Reporting:

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If you have a question about the product, please contact Medical Information on 01276 698370 or by email at medinfo.uk@novartis.com