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ABSTRACT

Objectives. The overall aim of the current study was to quantify physical activity levels in inflammatory rheumatic diseases (IRDs) and to explore its role in fatigue.

Methods. Secondary analysis of data from the Lessening the Impact of Fatigue in IRDs (LIFT) trial of the personalized exercise programme (PEP) intervention for fatigue. Participants with IRDs were recruited from 2017-2019 and the current analysis used the fatigue, measured by the chalder fatigue scale (CFS) and the fatigue severity scale (FSS), and accelerometer measured physical activity data collected at baseline and at 6 months follow up. Physical activity levels were quantified, associations with fatigue and effects of PEP investigated.

Results. Of the 337 included participants, 195 (68.4%) did not meet the current recommendations for moderate-vigorous physical activity (MVPA). In baseline cross-sectional analysis, many dimensions of physical activity were associated with fatigue. After mutual adjustment, overall physical activity (vector magnitude) was associated with CFS (-0.88(-0.12, -1.64)) and distribution of time spent at different activity intensity was associated with FSS (-1.16 (-2.01, -0.31)). Relative to usual care, PEP resulted in an increase in upright time, with trends for increases in step count and overall physical activity. People who increased overall physical activity (vector magnitude) more had greater improvements in CFS and FSS, whilst those that increased step count and MVPA more had greater improvements in FSS.

Conclusion. Increasing physical activity is important for fatigue management in people with IRDs and further work is needed to optimize PEP to target the symptoms and impact of fatigue.

Trial registration: ClinicalTrials.Gov, NCT03248518

Keywords: Physical activity, fatigue, inflammatory rheumatic disease

Key Messages

- Fatigue remains a common and highly deleterious symptom in people with inflammatory rheumatic diseases.
- This study has shown that objectively measured physical activity levels are associated with fatigue.
- Our personalized exercise programme resulted in modest improvements, with increases in physical activity related to improvements in fatigue.

Lay Summary

What does this mean for patients?

This study aimed to measure how much physical activity people with inflammatory rheumatic diseases (IRDs) engage in and how it affects their fatigue. Data from a trial called Lessening the Impact of Fatigue in IRDs (LIFT), which tested a personalized exercise program for reducing fatigue, was analysed. The results showed that a large portion of participants did not meet the recommended levels of moderate to vigorous physical activity. The analysis revealed that both the amount and the distribution of physical activity were linked to fatigue levels. Those who increased their overall physical activity experienced improvements in their fatigue levels. The personalized exercise program, therefore, showed promise in increasing physical activity and reducing fatigue. Overall, the study suggests that increasing physical activity is important for managing fatigue in people with IRDs. Further research is needed to refine personalized exercise programs to better address fatigue symptoms and their impact.

INTRODUCTION

Inflammatory rheumatic diseases (IRDs) (e.g., rheumatoid arthritis (RA), axial spondyloarthritis and systemic lupus erythematosus) are common and make a major contribution to the global disability burden [1]. Despite recent transformations in IRDS treatment, the symptom of fatigue remains highly prevalent. Approximately 80% of people with IRDs report significant fatigue [2] and more than 70% consider the symptom to be as great a burden as pain [3]. Additionally, fatigue is a major contributor to low quality of life and work disability [4].

There are no effective pharmacological treatments for fatigue related to IRDs [5]. Cross-sectional data indicates that higher levels of physical activity are associated with lower fatigue levels, in the general population and in people with RA[6–11], but this data cannot demonstrate causation or directionality. We recently conducted the LIFT trial which included an investigation of whether a personal exercise programme (PEP) was effective in reducing fatigue in people with IRDS [12]. This programme was designed to gradually increase the level and intensity of participants' exercise and/or physical activity to, at least, the levels recommended by national guidelines (150 min of moderate intensity physical activity per week) [13]. After 6 months of PEP, the severity and impact of fatigue was reduced, and these changes were sustained after a 6-month follow up[14]. This finding highlighted the importance of exercise and physical activity in the management of fatigue in IRDS.

In the LIFT trial, PEP was tailored to each participant's needs with the general goal of meeting physical activity recommendations, whilst avoiding boom and bust patterns of activity. However, we did not investigate the factors (i.e., intensity, time, distribution) of physical activity that were most effective for improving fatigue in this population. Importantly, "physical activity" is a broad term that encompasses numerous modalities and intensities. Recent advancements in physical activity measurement have moved beyond simple and older measures of step count or light/moderate/vigorous intensity activity, so new metrics like distribution of physical activity intensity across the activity profile can be assessed. One such metric, the intensity gradient, is a measure of how much time people spend at different intensities of physical activity [15, 16]. A negative intensity gradient reflects more time performing lower intensity exercise compared to high intensity, whereas a less negative gradient reflects an even distribution between the

intensities. In the general population, people spend more time performing lower intensity exercise and therefore have a more negative intensity gradient [15]. In previous research on both adolescent girls and in people with type 2 diabetes the intensity gradient was associated with cardiometabolic risk factors independent of overall physical activity levels [15]. Given this independent association, intensity gradient may also be an important health metric beyond total physical activity. Intensity gradient may provide complementary information to measures of overall physical activity levels. Additionally, intensity gradient can allow us to more fully describe the activity profile of various populations and how activity may be related to health outcomes [15].

With this in mind, we nested an accelerometery sub-study into the LIFT trial where we measured physical activity using activPAL thigh-worn accelerometers (PAL Technologies Ltd., Glasgow, UK). Our original plan (although this was not pre-specified in the study protocol) was to focus on more standard metrics, such as step counts, but with developments in physical activity measurement we were able to add novel metrics, such as the intensity gradient. This sub-study provides an opportunity to further explore objectively-measured habitual physical activity levels and patterns. These devices have previously been validated in people with RA for the measurement of physical activity and sedentary behaviour [17]. Current data, which are primarily based on self-reported data, indicated that sedentary time is high and physical activity low in people with IRDs [18–20], which is supported by a small study demonstrating that activPAL-measured sedentary time was higher and physical activity lower in people with RA compared to sex, age and body mass index (BMI) matched control participants [21]. How established objective measures of overall physical activity (e.g. step count), along with complementary dimensional metrics (e.g. intensity gradient), are associated with fatigue in people with IRDS remains to be established.

Therefore, the aims of the current study were to 1) quantify physical activity levels and patterns in IRDs with stratification based on age, disease and sex, 2) investigate associations between IRDS fatigue and comprehensive physical activity metrics, including the novel intensity gradient, 3) determine the effects of the PEP on physical activity metrics and 4) explore how changes in physical activity associate with changes in fatigue following PEP in people with IRDS.

METHODS

The LIFT trial methods are briefly described here, with full details published separately[12, 14].

Study design and participants

The LIFT trial was a multicentre randomised controlled open-label parallel-group trial which recruited participants with stable IRDS who reported fatigue to be persistent (>3 months) and clinically significant (≥6/10 based on the question: "please circle the number that shows your average level of fatigue during the past 7 days on a numerical rating scale of 0 (no fatigue) to 10 (totally exhausted)"). Participants were randomised to either PEP, cognitive behavioural approaches (CBA) or usual care (1:1:1 ratio). The current analysis will focus on the effects of PEP, rather than CBA, in comparison to usual care although in baseline analysis all participants were included. Ethical approval was granted by Wales REC 7 (17/WA/0065) and informed consent provided by all participants.

Procedures

PEP was delivered by physiotherapists working within the National Health Service (NHS). Participants were invited to seven one-to-one sessions (up to 45 min per session) over a 14-week period, with a follow-up booster session at 22 weeks. Apart from the first session which was delivered in person, all other sessions were delivered remotely by telephone. The therapist and participant agreed on goals and developed a personalised exercise programme with the aim to meet the physical activity guidelines, by increasing duration and intensity of physical activity whilst avoiding boom and bust patterns [13].

Outcomes were assessed at baseline, 10 weeks, 28 weeks and 56 weeks. Outcomes included in the current study were the co-primary outcomes from the LIFT trial. These were Chalder Fatigue Scale (CFS; 0 [low] to 33 [high]) [22], which assesses the physical and mental symptoms of fatigue, and the Fatigue Severity Scale (FSS; 1 [low] to 9 [high]) [23], which measures the impact of fatigue. These distinct measures of fatigue, covering both symptoms and impact, may be influenced to varying degrees by physical activity. Physical activity was measured with an activPAL accelerometer worn in a mid-anterior position on either thigh, attached via a waterproof dressing, continuously for a 7-day period at each time point. Age, body mass and sex were recorded. Disease

activity was self-reported using a numeric rating scale (0 (not active) -10 (extremely active)) and presence of comorbidities recorded via the Charlson Comorbidity Index [24]

Accelerometer data processing

Data were downloaded using the PALbatch software (PAL Technologies Ltd., Glasgow, UK), using the default setting of the 24-hour protocol, which considers days valid if there are <4 hours of non-wear. Standard metrics of step count, activity score, sedentary time, upright time, stepping time, cycling time, lying time, seated transport time, breaks in sedentary time (time transitioning from sedentary behaviours to non-sedentary behaviours), and vector magnitude ($vector\ magnitude = \sqrt{(x^2 + y^2 + z^2)}$ where x, y, and z are the accelerometer axes) were obtained using the enhanced PAL analysis algorithm (CREA) available within the software. Additionally, the raw accelerometery data were exported to calculate the following physical activity metrics. Moderate to vigorous physical activity (MVPA), the target of most government physical activity guidelines, was calculated as time spent at an intensity of >80 steps/min, and participants were defined as having insufficient physical activity if they performed less than 150 min/week of MVPA [25]. More detailed analyses of the data were also conducted in order to understand the movement patterns of participants. Specifically, the vector magnitude data were used to calculate the intensity gradient, a measure of the intensity distribution of physical activity, as described previously [15]. Additionally, the MX metrics, which describe the acceleration (vector magnitude) above which the most active X minutes are accumulated, as described previously [16] were calculated. The M5 (acceleration in the most active 5 minutes) and M60 (acceleration in the most active 60 minutes) were calculated in the current study. MX metrics give insight into a wearer's most active portion of the day and provide an alternative way to assess adherence to physical activity recommendations (e.g., if the M60 is above a given MVPA threshold, it is clear that the individual engaged in at least 60 minutes of MVPA that day) but also to allow researchers to understand distribution of activity intensity in a more continuous way than the more traditional, cut-point thresholds used to categorize activity intensities as sedentary light, or MVPA.

Statistical analysis

Variables were compared between participants with RA vs. those with other IRDs (non-RA), between males and females, and between younger (<60 years) and older (≥60 years) participants, by independent t-tests. Data were split in these categories as we considered these the main variables which might influence participants' physical activity data. Associations of physical activity metrics (exposures) with FSS and CFS (outcomes) were tested using multivariable linear regression in all participants (PEP, CBA and usual care) at baseline. Due to the high number of potential exposures we selected the following variables to represent physical activity volume, patterns and sedentary behaviours (step count, vector magnitude, intensity gradient, M5, M60, lying time, sedentary time, upright time and MVPA). The following models were employed: Model 1 = unadjusted; Model 2 = adjusted for age, sex, body mass, disease activity score and Charlson index score; and Model 3 = adjusted for model 2 + vector magnitude when intensity gradient is the exposure and model 2 + intensity gradient when vector magnitude was the exposure. Vector magnitude was chosen as a marker of overall physical activity and the intensity gradient as a marker of activity intensity distribution. Changes in physical activity metrics in PEP at 6 months were compared to usual care via ANCOVA, with baseline values of the physical activity metric included as a covariate. The CBA group were not included in this analysis as our focus was on the PEP group. The 6-month time point was chosen as the end of the active intervention, as at 12 months the number of participants with valid accelerometer data had decreased to 30 in PEP and 42 in usual care, compared to 45 in PEP and 48 in usual care at 6 months. In exploratory analysis the change in CFS and FSS was explored within PEP by stratifying the sample by change in physical activity metrics at the median (low and high change). We then compared CFS and FSS at 6 months between low and high changes groups with baselines CFS and FSS scores as a covariate.

RESULTS

Study population and basic demographics

Three hundred and thirty-seven participants (225 female and 82 male) were included in the current study, with 191 having RA and 146 non-RA IRDs (including connective tissue disease, axial spondyloarthritis, systemic vasculitis; juvenile inflammatory arthritis, and undifferentiated inflammatory arthritis), with the latter grouped together due to low numbers for each condition. Basic baseline demographics are presented in table 1, with demographics by condition, sex and

age (<60 years and ≥ 60 years) presented in Supplementary Tables S1-3, respectively (available at *Rheumatology Advances in Practice* online).

Physical activity metrics

Baseline overall physical activity metrics are presented in table 1 with novel physical activity metrics presented in table 2. Summarizing briefly, in the whole sample participants took an average of 6959 steps/day, participated in 17.8 min/day of MVPA with 68.4% of participants being classed as having insufficient physical activity. The same data presented stratified by RA vs non-RA, males vs females and <60 years vs ≥60 years are presented in supplementary material (Supplementary Tables S1-6, available at *Rheumatology Advances in Practice* online). To visualize the time spent in each activity across the day we present stacked plots for the overall cohort in figure 1 and stratified by RA status, sex and age in supplementary figures S1-3. No major differences were seen between RA and non-RA groups but some sex and age differences were noted. Women spent less time cycling, although cycling time was low regardless of sex, less time in seated transport, lower overall physical activity (vector magnitude) and lower M60 value. Younger people were more sedentary, spent more time in seated transport, had higher overall physical activity (vector magnitude) and higher M5 and M60 values.

Association of physical activity metrics with fatigue

Results from our multiple linear regression analysis, on baseline data, are presented in table 3. In unadjusted analysis (model 1) step count ($p<0.001$), vector magnitude ($p<0.001$), intensity gradient ($p=0.002$), M5 ($p=0.008$), M60 ($p=0.001$), upright time ($p=0.012$) and MVPA ($p<0.001$) were negatively associated with CFS. Lying time was positively associated ($p=0.005$) with CFS. The associations remained, apart from for lying time ($p=0.056$), in model 2. In model 3 vector magnitude remained associated with CFS ($p=0.025$) but intensity gradient ($p=0.111$) did not.

In unadjusted analysis (model 1) step count ($p<0.001$), vector magnitude ($p<0.001$), intensity gradient ($p<0.001$), M5 ($p<0.001$), M60 ($p<0.001$), upright time ($p=0.029$) and MVPA ($p<0.001$) were negatively associated with FSS. Lying time was positively associated ($p=0.003$) with FFS. The associations remained, apart from for lying time ($p=0.124$) and upright time ($p=0.625$), in

model 2. In model 3 intensity gradient remained associated with FSS (p=0.008) but vector magnitude (p=0.407) did not.

Effects of PEP on physical activity metrics

Accelerometer data were available for 48 participants in usual care and 45 participants in PEP at baseline and at the end of the intervention at 6 months, and physical activity data at these time points are presented in table 4. At 6 months there was, relative to usual care, numerically higher values for step count (p=0.071), vector magnitude (p=0.062) and M5 (p=0.087), and upright time was significantly higher in PEP (p=0.043).

Association of changes in physical activity metrics with changes in fatigue

After stratifying those in the PEP group into high and low change groups, the change in physical activity metrics and CFS and FSS, from baseline to 6 months, are presented in table 5. There was a greater decrease in CFS in the high change group for vector magnitude (p=0.046) and M5 (p=0.009). There was a greater decrease in FSS in the high change group for step count (p=0.003), vector magnitude (p<0.001) and MVPA (p=0.038). No other significant differences between groups were seen.

DISCUSSION

Overall, physical activity levels were generally low in our sample of people with IRDs, with almost 70% of people being classified as not meeting the physical activity MVPA recommendations. Our baseline cross-sectional analysis found that several physical activity metrics were associated with fatigue, with some differences comparing CFS and FSS as outcomes. The PEP intervention increased upright time and numerically higher measures of total physical activity, relative to usual care, which was associated with a greater decreases in both CFS and FSS.

Importantly in the current study the use of accelerometers, as opposed to self-reported measures, is a strength as previous work has shown that self-reported methods can underestimate sedentary time and overestimate physical activity [26–28] and that the association of physical activity with health data can be underestimated when self-report measures of physical activity are used [29]. Physical activity levels in the current participants were lower than the general population (Yates

et al., 2017). The current physical activity data is similar to previous small studies measuring physical activity by activPAL in people with RA and axial spondyloarthritis [7, 21] and, as expected, lower than where physical activity was measured by questionnaire [18, 19, 31]. With 68% of our population not meeting the current MVPA recommendations, this highlights that interventions to increase physical activity levels in people with IRDs are needed.

The current study also investigated the distribution of physical activity and its intensity using novel metrics such as the intensity gradient [15]. There is little data to allow a comparison in people with IRDs, but compared to adults from the UK Biobank the intensity gradient is considerably higher (less negative) in the current study [32]. This may be due to the current study being the first, to our knowledge, to measure the intensity gradient using thigh worn accelerometers, with previous studies using wrist-worn accelerometers. Alternatively, it could indicate a more even distribution of physical activity across the intensities in our population, i.e. less time spent at higher relative to lower intensities. Further work is clearly needed to investigate this possibility.

In the original LIFT trial we demonstrated that our PEP intervention, designed to increase physical activity levels, resulted in modest reductions in fatigue severity and impact [14]. These findings are strengthened by our current findings of association of physical activity levels with fatigue. This is in agreement with previous work which has shown, in a broad range of populations, that higher physical activity levels are associated with lower fatigue [6–11]. We extended these findings by showing that overall physical activity is associated with fatigue impact (CFS), whereas the intensity gradient, a measure of the intensity distribution of physical activity, is associated with fatigue severity (FSS). This indicates that tailoring of the physical activity intervention depending on the clinical presentation of fatigue in the patient may enhance its benefits. For example, some populations may benefit simply from more physical activity regardless of intensity, whereas others may experience the most benefit to fatigue symptoms by increasing time spent in higher-intensity activities. However, this data cannot demonstrate causality and so we further explored the follow up trial data to extend and potentially strengthen these assertions.

In the subgroup of participants with baseline and 6 month accelerometer data, we found a trend for a modest increase in overall physical activity (step count and vector magnitude) with PEP. Interestingly, in our exploratory analysis, we found associations of improvements in step count,

MVPA, M60 and intensity gradient (i.e., more time spent doing activities of higher intensity) (trend) with reductions in FSS and improvements in M5 associated with changes in CFS. These data further support, also in partial agreement with our cross-sectional data, the assertion that different aspects of physical activity are associated with differential changes in fatigue impact and severity. However, it was interesting that changes in the intensity gradient tended to be only associated with changes in FSS, as also shown in our cross-sectional analysis, and so interventions which specifically target a more even distribution of time spent at different physical activity intensities may be of particular benefit for the impact of fatigue. Further work is needed to test this assertion and to investigate the mechanism underlying these observations and how to optimize physical activity interventions to incorporate these findings. To add in this it may be prudent to consider a qualitative evaluation of PEP to supplement/support these findings based on the questionnaires. Overall, this indicates interventions should probably focus on encouraging overall activity, i.e. moving more regardless of intensity, but it may be worth considering distribution of activity primarily to target improvements in FSS. Whilst increases in overall physical activity are relatively intuitive this is not necessarily the case for the intensity gradient. In the current data a high change in the intensity gradient reflects an increase (less negative) in values. This reflects a more even distribution of time spread across the intensity range which our data would indicate is better for lowering fatigue and fits with previous concepts around the negatives of "boom and bust" patterns of physical activity, e.g. [33]

The current study is not without limitations. This analysis was not pre-specified in our initial statistical analysis plan and should be interpreted with caution as exploratory data. Due to COVID-19 and other technical issues, accelerometer data collection was partial and so this analysis is based on a small number of participants which results in a level of uncertainty in our conclusions. On top of this it is likely that the changes in physical activity (as we have measured) induced by PEP do not fully explain the observed improvements in fatigue, suggesting that PEP may also have had other benefits. It is possible that PEP also, independently of changes in physical activity, improved sleep, cognition and mood which may influence fatigue.

In conclusion, the current data highlight the importance of physical activity for management of fatigue in people with IRDS and that different aspects of physical activity may have differentially influenced fatigue severity and impact. With physical activity levels generally low, the current

study shows that PEP is an important strategy for managing fatigue in people with IRDs. Yet, further work is needed to develop and optimize the components of PEP to target the symptoms and impact of fatigue.

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Conflict of interest statement: The authors have declared no conflicts of interest.

Data availability statement: Anonymised individual patient data will be made available following any reasonable request made to the corresponding author, subject to a data sharing agreement and UK research governance regulations. The intervention manuals can be found on https://www.abdn.ac.uk/iahs/research/epidemiology/lift-1286.php.

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Table 1 Basic demographic and physical activity variables in participants from the LIFT trial

	Overall (n=337)
Age (years)	57.9 (12.6)
Body Mass (kg)	78.5 (16.4)
Sex (number male (%))	82 (24.3)
Step Count (steps/day)	6959 (3259)
Activity Score (MET.s^{-1})	83.3 (3.5)
Sedentary Time (min/day)	549.4 (110.7)
Upright Time (min/day)	325.8 (112.6)
Stepping Time (min/day)	91.3 (38.3)
Cycling Time (min/day)	0.83 (2.86)
Lying Time (min/day)	565.8 (82.2)
Seated Transport (min/day)	51.3 (39.9)

Data are mean (SD).

Table 2 Novel physical activity metrics in participants from the LIFT trial overall

	Overall (n=337)
Vector Magnitude (cpm)	2799 (1185)
MVPA (min/day)	17.8 (16.4)
MVPA recommendations (insufficient PA (%))	195 (68.4)
M5 (cpm)	40835 (14590)
M60 (cpm)	17023 (7126)
Intensity Gradient	-1.80 (0.20)

Data are mean (SD). Insufficient PA refers to those not meeting the guidelines of 150 min/week MVPA

Table 3 Associations of physical activity metrics with CFS and FSS scores in people with inflammatory rheumatic diseases

	CFS					
	Model 1		**Model 2**		**Model 3**	
	Coefficient (95% CI)	**P value**	**Coefficient (95% CI)**	**P value**	**Coefficient (95% CI)**	**P value**
Step Count	-0.40(-0.21, -0.59)	**<0.001**	-0.44(-0.2, -0.69)	**<0.001**		
Vector Magnitude	-0.99(-0.45, -1.53)	**<0.001**	-1.18(-0.51, -1.85)	**<0.001**	-0.88(-0.12, -1.64)	**0.025**
Intensity Gradient	-5.00(-1.86, -8.14)	**0.002**	-6.27(-2.19, -10.35)	**0.003**	-3.75(0.84, -8.34)	0.111
M5	-0.06(-0.02, -0.10)	**0.008**	-0.09(-0.04, -0.14)	**0.0012**		
M60	-0.15(-0.06, -0.24)	**0.001**	-0.16(-0.05, -0.27)	**0.003**		
Lying time	1.30(8.07, -5.47)	**0.005**	8.90(17.97, -0.17)	0.056		
Sedentary time	0.23(6.16, -5.70)	0.938	3.82(12.15, -4.51)	0.370		
Upright time	-7.35(-1.62, -13.08)	**0.012**	-9.70(-2.11, -17.29)	**0.013**		
MVPA	-72.09(-33.14, -111.04)	**<0.001**	-90.75(-43.00, -138.50)	**<0.001**		
	FSS					
	Model 1		**Model 2**		**Model 3**	
	Coefficient (95% CI)		**Coefficient (95% CI)**		**Coefficient (95% CI)**	
Step Count	-0.07(-0.03, -0.11)	**<0.001**	-0.05(0.00, -0.10)	**0.027**		
Vector Magnitude	-0.20(-0.10, -0.30)	**<0.001**	-0.15(-0.02, -0.28)	**0.018**	-0.06(0.08, -0.20)	0.407
Intensity Gradient	-1.21(-0.64, -1.78)	**<0.001**	-1.33(-0.59, -2.07)	**<0.001**	-1.16-(2.01, -0.31)	**0.008**
M5	-0.02(-0.01, -0.03)	**<0.001**	-0.02(-0.01, -0.03)	**0.003**		
M60	-0.03(-0.01, -0.05)	**<0.001**	-0.03(-0.01, -0.05)	**0.008**		
Lying time	1.89(3.14, 0.64)	**0.003**	1.32(2.99, -0.35)	0.124		
Sedentary time	-0.19(0.90, -1.28)	0.738	-0.68(0.84, -2.20)	0.381		
Upright time	-1.19(-0.13, -2.25)	**0.029**	-0.35(1.07, -1.77)	0.625		
MVPA	-16.50(-9.42, -23.58)	**<0.001**	-14.94(-6.18, -23.70)	**0.001**		

Data are mean (95%CI).B-coefficients (95%CI) are present as x10^4 for all variables except intensity gradient. Bold text indicates significant P values.

Table 4 Changes in physical activity metrics after 6 months of PEP in people with inflammatory rheumatic diseases

	UC (n=48)			PEP (n=45)			
	Baseline	**6 months**	**Change**	**Baseline**	**6 months**	**Change**	**P value ANCOVA**
Step Count (steps/day)	6973 (411)	6763 (3959)	-209 (-678 to 259)	7455 (2477)	8208 (3831)	772 (-463 to 2008)	0.071
Vector Magnitude (cpm)	2815 (1420)	2725 (1452)	-90 (-282 to 101)	2950 (1026)	3255 (1528)	303 (-168 to 774)	0.062
Intensity Gradient	-1.82 (0.23)	-1.82 (0.24)	0.00 (-0.03 to 0.05)	-1.74 (0.19)	-1.72 (0.22)	0.02 (-0.04 to 0.09)	0.275
M5 (cpm)	39443(15875)	39470 (15140)	27.0 (-2307 to 2360)	44373 (12579)	46834(15036)	2501 (-884 to 5886)	0.087
M60 (cpm)	17247(9111)	16653 (9483)	-594 (-1485 to 297)	17983 (6746)	19450 (9593)	1429 (-1598 to 4456)	0.115
Lying time (min/day)	564.8 (99.6)	577.2 (104.1)	12.4 (-13.3 to 38.1)	556.5 (75.7)	547.5 (75.8)	-10 (-31 to 10)	0.103
Sedentary time (min/day)	551.7 (108.3)	549.4 (111.9)	-2.2 (27.4 to 22.9)	538.8 (109.9)	529.5 (117.1)	-8.1 (-35.5 to 19.2)	0.556
Upright time (min/day)	323.5 (123.4)	312.9 (120.1)	-10.6 (-25.9 to 4.7)	344.8 (102.6)	360.8 (103.6)	16.5 (-7.3 to 40.4)	**0.043**
MVPA (min/day)	18.1 (22.4)	18.3 (23.3)	0.22 (-2.1 to 2.6)	20.9 (14.5)	24.8 (25.8)	4.4 (-3.2 to 12.1)	0.237

Data are mean (SD). p values from comparison to usual care at 6 months after adjustment for baseline values (ANCOVA). Bold text indicates significant P values.

Table 5. Changes in CFS and FSS at 6 months in the PEP group by change in physical activity variables

	Physical Activity Variable		CFS			FSS		
	Low Change	**High Change**	**Low Change**	**High Change**	**P value**	**Low Change**	**High Change**	**P value**
Step Count (steps/day)	-1770 (2069)	3314 (4004)	-6.7 (6.9)	-8.8 (8.2)	0.122	-0.50 (0.93)	-1.49 (1.59)	**0.003**
Vector Magnitude (cpm)	-693 (746)	1300 (1509)	-6.6 (7.2)	-8.9 (8.0)	**0.046**	-0.44 (0.96)	-1.55 (1.53)	**<0.001**
Intensity Gradient	-0.14 (0.14)	0.18 (0.14)	-6.5 (6.7)	-8.9 (8.4)	0.150	-0.60 (1.09)	-1.39 (1.55)	0.059
M5 (cpm)	-5934 (6369)	10937 (8017)	-5.2 (6.0)	-10.2 (8.3)	**0.009**	-0.71 (1.30)	-1.28 (1.43)	0.157
M60 (cpm)	-5176 (5529)	8033 (9006)	-7.4 (7.1)	-8.0 (8.2)	0.367	-0.62 (1.23)	-1.37 (1.45)	**0.028**
Lying time (min/day)	-61.1 (34.9)	39.8 (56.6)	-10.1 (8.7)	-5.6 (5.9)	0.062	-1.43 (1.55)	-0.60 (1.10)	0.154
Sedentary time (min/day)	-79.8 (64.0)	63.5 (42.2)	-7.5 (7.1)	-7.9 (8.3)	0.966	-0.92 (1.19)	-1.07 (1.57)	0.675
Upright time (min/day)	-41.3 (47.6)	74.5 (57.4)	-6.1 (7.1)	-9.3 (7.9)	0.150	-0.75 (1.48)	-1.24 (1.26)	0.129
MVPA (min/day)	-8.2 (10.3)	17.0 (29.2)	-6.6 (6.3)	-8.9 (8.7)	0.102	-0.63 (1.18)	-1.36 (1.49)	**0.038**

Data are mean (SD). P value from comparison between low and high change groups via ANCOVA. Bold text indicates significant P values.

Figure Legends

Figure 1. Variation in accelerometer measured time by activity type in all participants in the LIFT trial

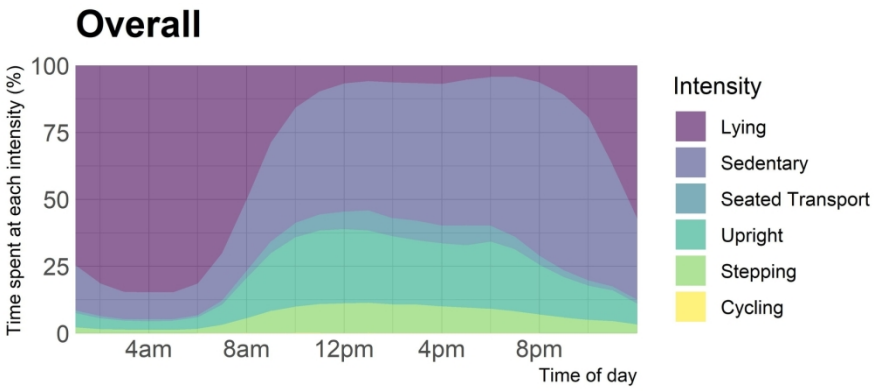

Figure 1

169x84mm (300 x 300 DPI)

Are you using a treatment that addresses all 6 key manifestations of PsA?

The key clinical manifestations of PsA are joints, axial, skin, enthesitis, dactylitis and nails.[1]

Joint relief in PsA:

68% of patients achieved **ACR50** with Cosentyx® (secukinumab) at **Year 1** (observed data)[2]

Results from ULTIMATE (N=166). The primary endpoint of GLOESS mean change from baseline vs placebo at Week 12 was met (−9 vs −6, p=0.004)[2,3]

Click here to visit our HCP portal and learn more

Skin clearance in PsO:

55% of patients achieved **PASI100** at **Week 52** with Cosentyx 300 mg AI (secondary endpoint, observed data, N=41)[4]

Results from MATURE. The co-primary endpoints PASI 75 and IGA mod 2011 0/1 at Week 12 were met for Cosentyx 300 mg (N=41) vs placebo (N=40), (95% vs 10% and 76% vs 8% respectively, p<0.0001)[4]

Axial joint relief in PsA:

69% of patients achieved **ASAS40** at **Week 52** with Cosentyx 300 mg (secondary endpoint, observed data, N=139)[1]

Results from MAXIMISE. The primary endpoint of ASAS20 with Cosentyx 300 mg (N=164) vs placebo (N=164) at Week 12 was met (63% vs 31% respectively, p<0.0001)[1]

Cosentyx is the first and only, fully human biologic that directly blocks IL-17A regardless of its source[5–10]

8 years

A **consistent safety profile** with **over 8 years** of real-world experience[5,6,11]

The most frequently reported adverse reactions are upper respiratory tract infections (17.1%) (most frequently nasopharyngitis, rhinitis).[5,6]

Cosentyx licensed indications in rheumatology: Cosentyx is indicated for the treatment of active psoriatic arthritis in adult patients (alone or in combination with methotrexate) when the response to previous disease-modifying anti-rheumatic drug therapy has been inadequate; active ankylosing spondylitis in adults who have responded inadequately to conventional therapy; active non-radiographic axial spondyloarthritis 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; moderate to severe plaque psoriasis in children and adolescents from the age of 6 years, and adults who are candidates for systemic therapy; active enthesitis-related 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 juvenile psoriatic arthritis in patients 6 years or older (alone or in combination with methotrexate) whose disease has responded inadequately to, or who cannot tolerate, conventional therapy.[5,6]

ULTIMATE (N=166), a multicentre, randomised, double-blind, placebo-controlled, 52-week Phase III trial in patients with PsA. Patients were randomly assigned to receive either weekly subcutaneous Cosentyx (300 mg or 150 mg according to the severity of psoriasis) or placebo followed by 4-weekly dosing thereafter. The primary outcome of mean change in the ultrasound GLOESS from baseline to Week 12 was met (−9 vs −6; p=0.004).[2,3]
MATURE (N=122), a 52-week, multicentre, double-blind, randomised, placebo-controlled, Phase III trial in patients with PsO. Eligible patients were randomised to Cosentyx 300 mg or placebo. The co-primary endpoints were PASI75 and IGA mod 2011 0/1 responses at Week 12. The study met the co-primary endpoints: PASI75 and IGA mod 2011 0/1 response at Week 12 were met for Cosentyx 300 mg vs placebo (95% vs 10% and 76% vs 8% respectively, p<0.0001).[4]
MAXIMISE (N=498) a double blind, placebo-controlled, multicentre, Phase IIIb study in patients with PsA. Patients were randomised in a 1:1:1 ratio to receive Cosentyx 300 mg, 150 mg or placebo. The primary endpoint of the proportion of patients achieving and ASAS20 response with Cosentyx 300 mg at Week 12 vs placebo was met (63% vs 31% respectively, p<0.0001).[1]

ACR, American College of Rheumatology; AI, auto-injector; ASAS, Assessment of SpondyloArthritis International Society; BASDAI, Bath; ankylosing spondylitis disease activity index; EULAR, European Alliance of Associations for Rheumatology; GLOESS, Global EULAR and OMERACT synovitis score; IGA mod 2011 0/1, investigator global assessment modified 2011 0/1; OMERACT, outcome measures in rheumatology; PASI, psoriasis area and severity index; PsA, psoriatic arthritis; PsO, plaque psoriasis.

References: 1. Baraliakos X, et al. *RMD open* 2019;5:e001005; **2.** Conaghan PG, et al. Poster 253. *Rheumatology* 2022;61(Suppl1). DOI:10.1093/rheumatology/keac133.252; **3.** D'Agostino MA, et al. *Rheumatology* 2022;61:1867–1876; **4.** Sigurgeirsson B, et al. *Dermatol Ther* 2022;35(3):e15285; **5.** Cosentyx® (secukinumab) GB Summary of Product Characteristics; **6.** Cosentyx® (secukinumab) NI Summary of Product Characteristics; **7.** Lynde CW, et al. *J Am Acad Dermatol* 2014;71(1):141–150; **8.** Fala L. *Am Health Drug Benefits* 2016;9(Special Feature):60–63; **9.** Schön M & Erpenbeck L. *Front Immunol* 2018;9:1323; **10.** Gorelick J, et al. *Practical Dermatol* 2016;12:35–50; **11.** European Medicines Agency. European public assessment report. Medicine overview. Cosentyx (secukinumab). Available at: https://www.ema.europa.eu/en/documents/overview/cosentyx-epar-medicine-overview_en.pdf [Accessed May 2024].

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

NOVARTIS

UK | May 2024 | 425034

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. 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. *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 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 75mg and 150 mg pre-filled syringe and 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:** PLGB 00101/1205 – 75 mg pre-filled syringe x 1 - £304.70; PLGB 00101/1029 - 150 mg pre-filled pen x2 £1,218.78; PLGB 00101/1030 - 150 mg pre-filled syringe x2 £1,218.78; PLGB 00101/1198 – 300 mg pre-filled pen x 1 £1218.78. **PI Last Revised:** June 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 | 290802 | June 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) 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. 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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.

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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