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# Overcoming provider barriers to therapeutic drug monitoring of tumour necrosis factor inhibitors for rheumatoid arthritis: a qualitative analysis

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## Abstract

**Objective:** Therapeutic drug monitoring (TDM) of tumour necrosis factor-α inhibitors (TNFi), by measuring drug levels and/or anti-drug antibodies, is being considered by various international bodies to improve patient health outcomes and the value of care for people with rheumatoid arthritis. Rheumatology care providers may perceive barriers to adopting TNFi TDM within their own clinical practice, limiting the potential for patients and health care systems to benefit. This study aimed to explore the barriers perceived by rheumatologists that may reduce their uptake of TNFi TDM for rheumatoid arthritis.

**Method:** Semi-structured one-to-one telephone interviews were performed with a convenience sample of senior rheumatologists with experience of managing people with rheumatoid arthritis. The interviews explored the rheumatologists' understanding of TDM and their beliefs about how it can be integrated into their own routine practice. Interviews were audio recorded, transcribed verbatim and anonymized. Transcripts were coded inductively and barriers to using TNFi TDM were identified by thematic framework analysis.

**Result:** A sample of eleven senior rheumatologists were interviewed. The rheumatologists described five barriers to adopting TNFi TDM in routine practice: (i) observing clinical need; (ii) understanding how testing can improve practice; (iii) insufficient clinical evidence; (iv) insufficient resources to pay for testing; and (v) insufficient capability to deliver testing.

**Conclusion:** Barriers to adopting TNFi TDM in routine care settings will restrict the ability for patients to benefit from effective monitoring strategies as they begin to emerge. Strategies to overcome these barriers are suggested which will require a coordinated response from stakeholders across health care systems.

## Lay Summary

**What does this mean for patients?**

Treatments called tumour necrosis factor inhibitors are used for people with rheumatoid arthritis. Rheumatologists can perform tests (called therapeutic drug monitoring) to improve how these treatments are prescribed. Better prescribing decisions can improve health outcomes, but there might be barriers stopping rheumatologists from using therapeutic drug monitoring in routine care. This study explored what these barriers might be. Eleven experienced rheumatologists in the United Kingdom were interviewed by telephone. The rheumatologists were asked to talk about how therapeutic drug monitoring could help their own clinical practice. The interviews found five important reasons for why routine therapeutic drug monitoring might not be possible. These reasons were: (1) not seeing a need for monitoring in their own practice; (2) not understanding how monitoring can improve prescribing decisions; (3) being dissatisfied about the evidence supporting monitoring; (4) not having enough money to pay for monitoring from their hospital's budget; and (5) not having the ability to perform monitoring in their own hospital. These findings are important because they show what needs to change to bring therapeutic drug monitoring into routine practice. Different people in the healthcare system can now work together to overcome these barriers so that people with rheumatoid arthritis can benefit.

**Keywords:** anti-drug antibody, drug level, qualitative, rheumatoid arthritis, therapeutic drug monitoring.

**Key messages**

- Effective therapeutic drug monitoring of tumour necrosis factor-α inhibitors can improve prescribing for rheumatoid arthritis.
- Rheumatologists perceive practical barriers to therapeutic drug monitoring which may reduce uptake in routine care.
- Stakeholders should implement strategies to overcome these barriers so patients benefit from therapeutic drug monitoring.

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## Introduction

Therapeutic drug monitoring (TDM) of biologic tumour necrosis factor-α inhibitors (TNFi) for rheumatoid arthritis is gaining interest internationally to improve disease control and the value of care amongst rheumatology care providers and professional organizations such as the European Alliance of Associations for Rheumatology (EULAR) [1, 2]. TNFi drug levels and anti-drug antibodies (ADAb) are associated with treatment response for people with RA [3, 4]. TNFi TDM strategies comprise regular measurement of TNFi ADAb and/or drug levels to inform prescribing decisions [1]. In 2023, the EULAR taskforce on TDM found that whilst the clinical evidence supporting TDM was maturing, there was little understanding of the practical barriers faced by rheumatologists when considering whether to measure TNFi drug levels and ADAb routinely [1, 5].

Barriers to adopting new testing or monitoring strategies are a phenomenon faced by care providers across many clinical areas [6]. Complementary testing strategies, such as TNFi TDM, are not mandatory when making prescribing decisions within current regulatory or reimbursement frameworks [7]. The proposed benefits of TNFi TDM can only be realized if care providers choose to integrate and follow tests measuring TNFi ADAb and/or drug levels within their routine care settings [8]. Therefore, failing to understand and address rheumatologists' perceived barriers to TNFi TDM will threaten the adoption of these strategies and the ability for patients to benefit. Exploring and resolving rheumatologists' perceived barriers to TDM will help to improve health outcomes for people with RA through the uptake of effective TNFi drug level and ADAb monitoring strategies [5]. The aim of this study was to explore the barriers perceived by rheumatologists that may reduce their uptake of TNFi TDM for RA.

## Method

Semi-structured qualitative interviews were undertaken with practicing rheumatologists to explore their perceived barriers to TNFi TDM for RA. The study was reported according to the standards for reporting qualitative research [9].

### Sample

The target population was senior rheumatologists who had experience of using biologic agents to manage people with RA. A convenience sample of interviewees was recruited from the sampling frame of principal investigators belonging to the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate [10]. These individuals were rheumatologists in the United Kingdom with experience of managing RA, knowledge of the pathway for prescribing TNFi treatments, and a research interest in using biomarkers to inform treatment decisions for RA. Recruitment emails were sent to all rheumatologists in the sampling frame during December 2014 and March 2015.

### Data collection

Data were collected using one-to-one telephone interviews with rheumatologists who consented to participate. The interviews were part of a wider project to understand TNFi prescribing behaviour for RA. Telephone interviews facilitated the data collection from rheumatologists distributed across the country [11]. Interviews occurred at a time most convenient for the rheumatologist and the interviewer. The rheumatologists discussed their current knowledge of TNFi TDM for RA and how they would use this strategy to inform their clinical decision-making in a routine care setting. Questions were adapted after each interview to explore whether future participants shared similar experiences [12]. Interviews were recorded digitally and transcribed verbatim. All interviews and transcriptions were undertaken by one author (SPG) who had received training in qualitative data collection.

### Data analysis

The transcripts were analysed by thematic framework analysis [13]. Descriptive codes were applied to each line of the transcripts inductively by SPG. Supplementary coding was completed independently by two other researchers (GDW and KP) [14]. Codes labelled excerpts of each transcript that described potential barriers to testing. Themes were formed by grouping codes that had a similar interpretation to characterize a pattern of responses between rheumatologists. Coding and theme formation were undertaken during data collection. A matrix was produced for each theme (row: participant; column: code) and populated with data from each transcript. Data collection continued until interviewees no longer volunteered from the sampling frame. As a result, the analysis was designed to identify an initial plausible set of barriers to adopting TNFi TDM for RA rather than achieve thematic saturation. Themes are described in the text with supporting quotations. To ensure anonymity, the rheumatologists were provided an identification number and quotations were not attributed to specific individuals.

### Ethics

Ethical approval for this study was obtained from The University of Manchester Research Ethics Committee 2 (reference number: 14147). All participants contributed voluntarily with no financial compensation and provided written informed consent for the publication of anonymized quotations.

## Results

Figure 1 illustrates the process to obtain the final sample. Recruitment emails were sent to 45 rheumatologists and 24% of the sampling frame ($n = 11$) consented to be interviewed. The rheumatologists were distributed evenly across the country (north: 36%; midlands: 36%; south: 27%).

### Awareness of TNFi therapeutic drug monitoring

All rheumatologists were aware of the tests to perform TNFi TDM, and some had been approached by representatives of commercial manufacturers. Only one rheumatologist described using TNFi TDM within their current practice.

> *'People are trying to sell us a little kit to check drug levels and antibody levels'* [**Rheumatologist 1**].

> *'To be honest, we don't … routinely measure any antibodies here. So, I mean, I know it's a kind of interesting area … but it doesn't really alter our clinical practice here as of yet'*. [**Rheumatologist 9**].

> *'… we have already worked with our immunologist who have got some antibody assays to use … our plan is to change our guidelines at some point in the near future. So, we'll include screening for antibodies'*. [**Rheumatologist 3**].

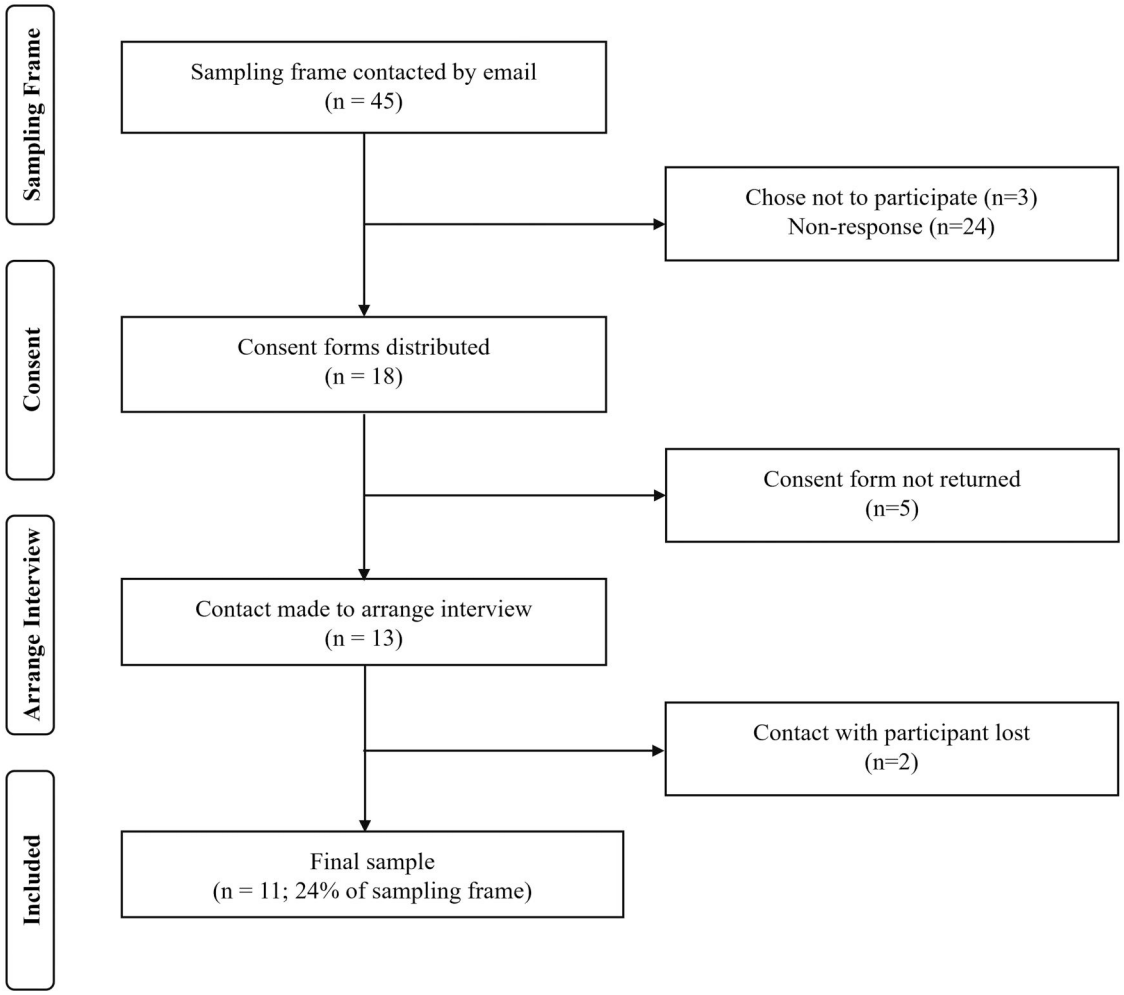


**Figure 1.** Recruitment and inclusion

Five barriers to adopting TNFi TDM reported by the rheumatologists are now described.

## Barrier: Observing clinical need

The rheumatologists explained that their preference for using TNFi TDM would reduce if they did not experience a clinical need in their routine practice. The clinical impact of immunogenicity to TNFi described in the literature [15] was not observed by the rheumatologists with their own patients.

> *'Put it this way, I know it's described [immunogenicity against TNFi therapies], but we don't see it particularly'.* [**Rheumatologist 5**].

> *'… we've not really seen a lot of problems with immunogenicity'.* [**Rheumatologist 2**].

## Barrier: Understanding how testing can improve practice

The rheumatologists varied in their understanding of how the information revealed by measuring TNFi ADAb and drug levels can improve practice to inform management decisions for patients. Some rheumatologists were optimistic about the use cases of TNFi TDM whereas others were more sceptical.

> *'One algorithm would be all patients have drug levels checked automatically at, maybe two or three times a year … whether or not they're doing well … I think drug levels are gonna' allow us to reduce doses of drugs as well, which is the other reason to use them'.* [**Rheumatologist 10**].

> *'… we've known about immunogenicity for twenty years. So why hasn't it, you know, taken off?'* [**Rheumatologist 8**].

> *'It [TNFi TDM] appeals to us. We don't know why it appeals to us. We think it's just, you know, a shiny little gizmo … it's interesting'.* [**Rheumatologist 1**].

## Barrier: Insufficient clinical evidence

The rheumatologists explained how a lack of robust clinical evidence was perceived as a considerable barrier to using TNFi TDM.

> *'I think those … things like drug antibody kits and drug levels should be evaluated in proper controlled studies, really … The danger is that the market will be flooded with kits and everybody will think, "that's great, I'll have a go," and … no one will know, in the end, what's actually happening'.* [**Rheumatologist 1**].

*'I think that if … we have robust, you know, reliable methods … to measure antibodies and relate them to clinical response, then possibly they could go in the therapeutic algorithm. But I really think that we are a long way away'.* [**Rheumatologist 8**].

### Barrier: Insufficient resources to pay for testing

A lack of financial resources to pay for ADAb and drug level testing was highlighted as a barrier to routine TNFi TDM. If there is uncertainty about how resources to pay for testing will be acquired, then rheumatologists will have little incentive to integrate TDM within their clinical practice.

*'It's [testing] a bit of a faff, and again it's more time, more money, more thought around it … I'm still not convinced that for the majority of patients it really changes management'.* [**Rheumatologist 4**].

### Barrier: Insufficient capability to deliver testing

Rheumatologists in the sample also highlighted that the technical capability to perform ADAb and drug level tests routinely may not be available in all health care settings. This raises a practical barrier to adopting TNFi TDM if there is variation in the facilities to perform testing between rheumatology providers.

*'I don't think we've got the capability [to perform testing]. There's only a couple of places in the country that'll do it, so it's not something that we are getting too concerned about'.* [**Rheumatologist 2**].

## Discussion

This study found that rheumatologists were generally aware of the potential use of TNFi TDM but perceived five different barriers to adopting testing within their routine clinical practice. The presence of these barriers will restrict the ability for effective TDM strategies to be used by health care providers. Patient health outcomes will, ultimately, be inhibited if barriers to TNFi TDM remain present as effective monitoring strategies emerge.

The responsibility to resolve these barriers will fall to different stakeholders across health care systems including guideline developers, care providers, assay manufacturers, service commissioners and payers. International organizations such as EULAR can help to align this activity through regular engagement with different stakeholders and proposing roadmaps for change [1]. At a national level, system readiness exercises can be undertaken to pre-empt and mitigate barriers to adopting TDM within different health care jurisdictions [16].

Possible actions to overcome the identified barriers are now described. Clinical need for TNFi TDM can be established with jurisdiction-specific data about the prevalence of ADAb and average drug levels in routine practice for disease activity subgroups [17]. Clear guidance on how TNFi TDM can inform clinical prescribing decisions (reflecting dosing or treatment-switching policies in different countries) will improve rheumatologists' understanding about the purpose of measuring ADAb and drug levels [18]. Overcoming insufficient clinical evidence is central to the wider adoption of TDM. In 2019, the National Institute for Health and Care Excellence, who are responsible for producing recommendations for care providers in England, assessed the effectiveness and cost-effectiveness of assays for TNFi TDM [19]. To demonstrate the importance of clinical evidence, the assessment concluded that there was insufficient evidence to support the national adoption of TDM for RA and recommended that additional clinical effectiveness research should be undertaken [18]. Whilst conventional measures of effectiveness in RA (such as the Disease Activity Score-28 [20]) provide a good reflection of overall disease activity, they may fail to measure the extent of joint inflammation objectively [21]. More objective measures of joint inflammation may help to demonstrate the effectiveness of TNFi TDM within research and clinical settings. Budget holders will need to evaluate how best to release resources elsewhere to pay for routine TNFi ADAb and drug level monitoring [22]. TNFi TDM will incur additional resources upfront including assay costs, time to analyse samples and time to communicate test results with patients before receiving treatment [22]. These costs can be optimized by integrating TDM reactively at the most valuable clinical decision points. Evidence from cost-effectiveness analyses can help to establish the most valuable clinical scenarios for TNFi TDM within different health care systems and are likely to be an essential source of evidence to support wider adoption in the future [23–25]. Finally, service planners will need to determine the infrastructure requirements to scale ADAb and drug level monitoring whilst ensuring that existing testing services remain unaffected.

One limitation of this study was that data were not collected to achieve saturation. However, the goal was to explore an initial series of barriers to TNFi TDM rather than a definitive taxonomy. The findings should be interpreted as a lower-bound on the plausible barriers to TDM as perceived by rheumatologists. A second limitation was that these data were collected in 2015 which may raise concerns about whether the findings are relevant for current clinical practice. As the clinical evidence supporting TNFi TDM is starting to mature, recent trial and observational evidence has shown how measuring ADAb and/or drug levels may benefit clinically [5, 26, 27]. The availability of these empirical data may change the extent that rheumatologists perceive barriers due to insufficient clinical evidence. However, routine TNFi TDM is still not performed in the United Kingdom which reflects the clinical environment at the time of data collection. A third limitation was that the interview schedule did not distinguish between proactive TDM (regular monitoring irrespective of the clinical scenario) and reactive TDM (measuring ADAb and/or drug levels during specific clinical scenarios only) [1]. Since data collection, the EULAR task force on TDM of biopharmaceuticals for inflammatory rheumatic and musculoskeletal diseases recommended against proactive TDM [1]. The rationale for this recommendation was that an optimal blood concentration range for biologic treatment has not been defined for most indications [1]. By contrast, the EULAR task force recommended reactive TDM because of the potential to inform treatment-switching decisions following loss of response or tapering decisions for people experiencing low disease activity and remission [1]. The responses provided by the rheumatologists may have been different if this distinction was made during the interviews.

Future research could replicate this study to explore barriers to TNFi TDM with rheumatologists from

other countries. A global perspective will help to support international guideline developers when proposing recommendations for implementing TDM in rheumatic conditions. Future research should also investigate the barriers to TDM perceived by rheumatologists who are less experienced with strategies to personalize health care. Finally, a robust investigation into patients' beliefs around TDM will be essential to demonstrate acceptability and identify implementation challenges amongst those receiving care.

## Conclusion

TNFi TDM has the potential to improve health outcomes for RA. Yet rheumatologists perceive barriers to measuring drug levels and ADAb routinely which may limit the scope for TDM to become standard of care. If effective TNFi TDM strategies are being considered for adoption, early and active engagement with stakeholders across health care systems, including rheumatologists responsible for front-line care, will be vital to pre-empt and mitigate barriers to ensure that patients can benefit.

## Data availability

The data underlying this article cannot be shared publicly because consent to make anonymized transcripts available was not sought.

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|---|---|---|---|---|---|---|---|
| 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® (secukinumab) licensed indications in rheumatology:** Cosentyx, alone or in combination with methotrexate, is indicated for the treatment of active **psoriatic arthritis** in adult patients 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; 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.[1,2]

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

*Patients prescribed Cosentyx for any indication since launch.

†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; HCP, healthcare professional; IBD, inflammatory bowel disease; MACE, major adverse cardiac event; 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 February 2024]; **4.** Novartis Data on File. Secukinumab – Sec008. 2023; **5.** Novartis. Novartis Cosentyx® positive 16-week PREVENT results advance potential new indication for patients with axial spondyloarthritis. Available at: https://www.novartis.com/news/media-releases/novartis-cosentyx-positive-16-week-prevent-results-advance-potential-new-indication-patients-axial-spondyloarthritis [Accessed February 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.

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## Cosentyx® (secukinumab) Northern Ireland Prescribing Information.

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

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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. 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:**

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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