Patient and health professional views on risk-stratified monitoring of immune-suppressing treatment in adults with inflammatory diseases

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ABSTRACT

Objective To explore the acceptability of an individualised risk-stratified approach to monitoring for target-organ toxicity in adult patients with immune-mediated inflammatory diseases established on immune-suppressing treatment(s).

Methods Adults (≥18 years) taking immune-suppressing treatment(s) for at-least six months, and healthcare professionals (HCPs) with experience of either prescribing and/or monitoring immune-suppressing drugs were invited to participate in a single, remote, one-to-one, semi-structured interview. Interviews were conducted by a trained qualitative researcher and explored their views and experiences of current monitoring and acceptability of a proposed risk-stratified monitoring plan. Interviews were transcribed verbatim and inductively analysed using thematic analysis in NVivo.

Results Eighteen patients and 13 HCPs were interviewed. While participants found monitoring of immune-suppressing drugs with frequent blood-tests reassuring, the current frequency of these was considered burdensome by patients and HCPs alike, and to be a superfluous use of healthcare resources. Given abnormalities rarely arose during long-term treatment, most felt that monitoring blood-tests were not needed as often. Patients and HCPs found it acceptable to increase the interval between monitoring blood-tests from three-monthly to six-monthly or annually depending on the patients' risk profiles. Conditions of accepting such a change included: allowing for clinician and patient autonomy in determining an individuals' frequency of monitoring blood-tests, the flexibility to change monitoring frequency if someone's risk profile changed, and endorsement from specialist societies and healthcare providers such as the National Health Service.

Conclusion A risk-stratified approach to monitoring was acceptable to patients and HCPs. Guideline groups should consider these findings when recommending blood-test monitoring intervals.

KEYWORDS

Immune mediated inflammatory disease, steroid sparing drugs, blood monitoring, qualitative.

KEY MESSAGES

- Risk-stratifying monitoring blood-tests during established immune-suppressing drug treatment is cost-effective, but its acceptability unknown.
- Patients and health professionals found it acceptable to extend monitoring blood-test intervals based on individualised risk profiles.
- Monitoring guidelines could change, reducing the burden of monitoring on patients' and healthcare systems.

INTRODUCTION

Immune-mediated inflammatory diseases (IMIDs) such as rheumatoid arthritis (RA), inflammatory bowel disease (IBD), psoriasis (PsO) +/- arthritis (PsA), ankylosing spondylitis (AS) and systematic lupus erythematosus (SLE) together affect over 4% of adults (1-6). They are treated with long-term steroid sparing disease-modifying anti-rheumatic drugs (DMARDs), which can cause hepatotoxicity, myelotoxicity, and nephrotoxicity. Those prescribed these medicines undergo regular blood-tests to check for such side-effects, typically fortnightly-to-monthly when treatment is commenced and three-monthly once treatment becomes stable (7-10). These side-effects seldom occur during stable long-term treatment (11-16). The practice of undertaking three-monthly monitoring blood-tests for all patients is based on expert opinion from guideline writing groups, often underpinned by the summary of product characteristics. Performing these tests at fixed intervals regardless of individuals' risk is an unjustifiable use of resources and goes against the tenets of personalised medicine.

We have developed risk-stratified monitoring strategies for methotrexate, leflunomide, thiopurine, sulfasalazine, and 5-aminosalicylate toxicity (12, 15-18). These consider individuals' risk of developing clinically significant side-effects to determine their individualised frequency of monitoring blood-tests, rather than having a standard approach for all. A health economic analysis based upon these risk predictions revealed that this approach was more cost-effective than current practice (12, 19). For anti-TNF-alpha (α) drugs, we evaluated the cost-effectiveness of different blood-test monitoring strategies to ascertain the most cost-effective strategy due to low outcome event rate and availability of a single dataset that precluded prognostic model development (19).

Before this new evidence is used to change guidelines and clinical practice, it is vital to explore whether such changes would be acceptable to patients and healthcare professionals (HCPs). Therefore, this study explored the views and experiences of people with IMIDs and HCPs managing their treatment, about current monitoring practice and the acceptability of a risk-stratified monitoring strategy.

METHODS

Study design

Multi-centre, qualitative interview study.

Participants

Patients

Adults aged ≥18 years self-reporting physician diagnosed RA, IBD, PsO and/or PsA, AS or SLE, and treated with conventional DMARDs or anti-TNF-αs for six months or longer comprised the patient participants. They were recruited from dermatology, gastroenterology, and rheumatology clinics in National Health Service (NHS) hospitals or via advertisements promoted by patient organisations (see acknowledgements) in their online newsletters, webpages, and social media platforms. Patients answered a questionnaire (Supplementary Data S1, available at *Rheumatology* online) to assess eligibility for interview and to recruit people representing the broad range of conditions, treatments, and engagement with monitoring. A combination of purposive stratified and maximum variation sampling was employed to recruit participants with different IMIDs, treatments, risk factors for drug toxicity, and levels of adherence to monitoring recommendations.

HCPs

HCP participants comprised of doctors (consultants and general practitioners (GP)); and allied health professionals (specialist nurses and pharmacists) with experience of prescribing and/or monitoring DMARDs. The latter group was included because specialist nurses and pharmacists prescribe immune-suppressing drugs and participate in their monitoring in the UK. HCPs were recruited using a snowballing technique (20) and through national associations' mailing lists. Purposive sampling was employed to recruit a mix of HCPs working in rheumatology, dermatology, gastroenterology, or primary care. They completed a brief questionnaire to assess their eligibility for interview.

Data collection

Single, one-to-one, semi-structured interviews were conducted remotely by AF, an experienced qualitative research fellow, who made the initial email contact and recruited participants. At the start of interviews, it was explained to participants that AF was not involved in patient care and would remain impartial to their views. Interviews were digitally audio-recorded and transcribed verbatim.

Separate interview guides were developed for patients and HCPs (Supplementary Data S2-3, available at *Rheumatology* online). Two Patient and Public Involvement (PPI) volunteers with IMIDs treated with immune-suppressing medications advised on the patient questionnaire, interview guide and interview format.

The interview guides were in two parts. Part 1 for patients explored their experience of current monitoring blood-tests, reasons for adherence or non-adherence, perceived risks and benefits, and view on the importance of continuing with current monitoring. Part 1 for HCPs explored the practicalities and perceived risks and benefits of current monitoring.

In part 2, for both patients and HCPs, the risk-stratified monitoring strategy was introduced. This covered the development and deployment of a risk calculator that resulted from the prior work and determined a persons' individual risk of developing side-effects from their IMID treatment, presented as a score.

With patient participants taking conventional DMARDs, AF computed and presented their risk score using the calculator and discussed the different potential frequencies of monitoring that the health economic analysis demonstrated would be cost-effective - six-monthly, annually, and biennially. Patient participants taking anti-TNF-αs were informed of the overall rate of side-effects and presented with the potential frequencies of monitoring.

HCPs were presented with four-to-five anonymised descriptive scenarios representing a range of risk profiles (Supplementary Data S4, available at *Rheumatology* online). Participant

acceptability, concerns, and perceived risks and benefits of changing to the different frequencies of monitoring blood-tests were then explored.

Risk calculator and score

The risk calculator, developed in prior work (12, 15-18), considers different prognostic factors to give an overall risk score. The risk score is expressed as the percentage of people with the same characteristics that would have to stop treatment due to an abnormal blood-test result over12 months.

Although broadly similar, the exact prognostic factors and how much they influence the risk score are unique to each DMARD (12, 15-18).

Data analysis

Anonymised transcripts were analysed thematically using an inductive approach (21). Analysis was managed using NVivo (version 12), taking place in parallel with data collection so initial results informed subsequent sampling and data collection. Analysis of the first four patient and six HCP interviews was performed independently by AF and JH, noting initial meanings, patterns, and codes. They came together repeatedly to discuss and generate an initial coding framework of data-driven themes and identify areas for further exploration. With good agreement in coding, AF analysed the remaining interviews and further developed the coding framework using the principles of constant comparison to refine and ensure preliminary themes were consistent with the rest of the interviews. AF, JH, and AA (rheumatology and medicine expertise) also came together to discuss the preliminary themes, and clarify clinical concepts which supported coding and theme development. Following analysis of the eighteenth patient and thirteenth HCP interview, no further changes were made to the coding framework. Thus, it was concluded sufficient saturation of the data had been achieved and data collection ended.

Ethical approval

West Midlands-Black Country Research Ethics Committee (Ref: 21/WM/0285). Participants gave their informed consent via an online consent form prior to the interview.

RESULTS

Eighteen patient and 13 HCPs were interviewed (Table 1). Patients were predominantly female, white ethnicity and had a range of IMIDs and treatments. Their risk scores ranged between 1% and 3%. The HCPs included consultants, GPs, nurses, and pharmacists from four specialisms. Patient and HCP interviews lasted for 50 (range 38–57) and 44 (range 20–61) minutes on average, respectively. Four themes with eight subthemes were generated in the data. These are presented in Table 2 with accompanying illustrative quotes, which are denoted in the text with a letter.

Benefits and challenges to current monitoring

Reassurance and continuity of care

Both patients and HCPs regular monitoring reassuring, to know that the treatment was not causing side-effects and could be stopped early should abnormal results arise (a). This was a key reason for patients adhering to monitoring blood-tests. Conversely, some patients viewed monitoring as a tick-box exercise to continue receiving their prescription (b). Patients and HCPs alike said the regularity of monitoring provided a feeling of continuity of care through regular contact between patients and prescribers (c).

Incidental findings leading to the diagnosis of another condition

HCPs said that frequent blood-tests meant other conditions including comorbidities were occasionally detected early and could be investigated or treated promptly, however, acknowledged this was uncommon (d).

Practical challenges of frequent monitoring

Organising and attending their monitoring blood-tests was time consuming and inconvenient for many patients because of work commitments, difficulties securing an appointment, or having to chase results to receive their prescription (e). HCPs noted that monitoring was resource intensive, taking up a large proportion of their workload. Capacity issues were highlighted within busy NHS settings to provide and review tests at the current frequency (f).

Remembering to book a test and consequences of non-compliance

While many participants ensured they had timely blood-tests so that their prescription would be renewed, others often forgot to do so because they lost track of time, were busy, prioritised other health issues or didn't receive a prompt before the test was due. These were common reasons for non-compliance (g). HCPs reported that when patients missed a blood-test, they were unable to issue a prescription risking the patients' flaring or having a poorly controlled IMID (h).

Clinicians' interpretation and actioning of monitoring results

HCPs discussed how abnormal test results were often false positives or transient abnormalities not caused by treatment e.g., raised liver markers due to excessive alcohol consumption before a blood-test, but still required investigation or repeat testing. This resulted in unnecessary concern for patients, and risked an IMID flaring if medication was paused.

Some HCPs highlighted how clinicians had different thresholds for investigating abnormalities, with the perception that some blood-tests are repeated unnecessarily (i).

Questioning the need for the current frequency of monitoring

Most patients questioned why they should continue with such frequent monitoring given their IMID, medication dosage and test results had remained stable, and felt it could be reduced (j). Many HCPs viewed the current approach to monitoring as outdated and overly cautious. Based on their clinical experience, abnormalities arising from DMARDs were uncommon once a patient was established on a stable dose, and thus a reduction in frequency would be

plausible (k). Some HCPs were already working to reduced monitoring schedules for medications considered to be low risk of causing side effects, such as anti-TNF-αs and sulfasalazine. A few also reported that there were no observable increases in the rate of abnormal results during the COVID-19 pandemic lockdown when they had to implement reduced monitoring schedules. This made them question the need to return to three-monthly monitoring (l).

Adopting a risk-stratified monitoring plan

Views on risk scores and acceptability of proposed frequencies

Most patients perceived their risk of stopping treatment to be low. A small number of patients with scores of 1% and 2% per year interpreted their risk as a little high, but despite this had similar views on the potential monitoring frequencies as other patients (m). All patients felt six-monthly testing was a suitable monitoring frequency, either as a comfortable stepdown or reflective of how often they currently had a blood-test. Some were happy to reduce to annual monitoring and felt it could tie in with their annual consultations, although several stipulated monitoring should be tapered down rather than suddenly move to yearly. But a few patients were uncomfortable with annual monitoring, considering it too long for side effects to be left undetected (n).

HCPs were in favour of adopting a risk-stratified approach to monitoring blood-tests. All were happy for anti-TNF-αs to be monitored annually, were viewed as rarely or never causing the blood-test abnormalities that can arise from conventional DMARDs (o).

For conventional DMARD scenarios, HCPs viewed risk scores of 1-2% per year as low risk with acceptable frequencies being either six-monthly or annually. Risk scores of 3% or 4% per year were generally viewed by HCPs as higher risk, acceptable frequencies included staying at three-monthly, six-monthly, or annually. Several also suggested tapering as a reassuring approach if annual monitoring was implemented, enabling them to see results are stable at a slightly lower frequency i.e. six-monthly testing, before further increasing the gap between blood-tests (p). Most patients and HCPs were uncomfortable with biennial monitoring given

the potential toxicity of the medications. While some HCPs used the risk scores to determine which monitoring frequency they found acceptable, several factored in their clinical experience and opinion of individual risk factors presented in the scenarios, which sometimes changed their viewpoint (q). GPs were less resolute than the other HCPs about the frequency of monitoring, happy to follow whatever was recommended by national guidance.

Provisos to accepting a reduced monitoring schedule

All participants had conditions or requests related to accepting a reduction in monitoring frequency.

While most patients welcomed NHS cost-savings, many stressed that they would expect assurance this would not come at a cost to their care and safety. Some also wanted to receive feedback on their results, rather than having to assume everything was stable as they did currently (r).

For HCPs, consensus and endorsement from national level organisations and clinical specialty bodies was deemed necessary before any change in practice would be implemented (s). Some HCPs wanted guidance on how to interpret the risk score and select a suitable frequency, but also flexibility for them to override a recommended frequency e.g., for patients considered particularly high-risk, and to accommodate patients' preferences. Being involved in the decision was also important to some patients. Both participant groups felt there should be regular review of individuals' risk score and the ability to change monitoring frequency where a person's risk changed, although there were concerns that completing individual risk calculators would be a time-consuming exercise for clinicians.

Perceived impact of proposed strategy

Participants noted that reducing the frequency of monitoring blood-tests would reduce the burden of IMIDs on patients' lives, as they would spend less time organising, attending, and for some, anxiously awaiting the results of blood-tests (t).

HCPs said not only would it reduce costs associated with providing monitoring blood-tests, but also free up time to see patients earlier in their disease trajectory and provide more medication counselling and advice on managing their IMID (u).

While some HCPs felt reducing the frequency of monitoring may reassure patients about the safety of their medication, they too highlighted some may become more complacent or forgetful towards monitoring. Some patients said they would need to be prompted with the larger gap between blood-tests.

Communicating a change in practice

HCPs felt that any changes should be communicated through various channels (direct to clinicians, through specialist societies and/or articles in medical publications and magazines). Furthermore, they felt while a risk-stratified approach would be well received by most clinicians, some would need persuading beyond an update to national guidance (v). Additional detail about the research evidence behind the proposed changes was wanted by some HCP participants before they could say they would fully accept it, including an explanation of the prognostic factors included and excluded from the risk calculator and the weight each factor contributes towards the risk score. Given that they have been emphasising the importance of three-monthly testing to their patients, HCPs felt that information leaflets and disseminating changes in practice through patient organisations would be necessary to support any verbal explanation they could provide (w).

DISCUSSION

This study explored patient and HCP views on monitoring for toxicity due to DMARDs using periodic blood-tests during established treatment. It demonstrated the burden placed on patients and HCPs from such testing and their appetite to reduce it, with monitoring considered reassuring but the current recommended frequency unnecessary. A risk-stratified approach to increasing the interval between monitoring blood-tests was acceptable although acceptability reduced with increasing gap between tests. Adoption of this strategy into practice was dependent upon endorsement from specialist societies and healthcare organisations, and flexibility in being responsive to clinical need and patient preference, in keeping with principles of shared decision-making.

There is a need to manage the burden of treatment on patients with long-term conditions (22) and move away from a one-size-fits-all approach. Our study demonstrates that risk-stratified monitoring is acceptable to both patients and HCPs with potential for positive impacts to individuals and health systems by reducing the burden of monitoring, and minimising pauses in continuous treatment due to missed blood tests and/or insignificant abnormalities. The views of different types of HCPs were similar.

For it to be adopted a change in guidelines is required; this was an important condition of HCP acceptability. Given DMARDs are used across different specialities, efforts should be targeted towards changing the overarching monitoring recommendations e.g., those issued by the National Institute of Health and Care Excellence, the Medicines and Healthcare products Regulatory Agency and manufacturing authorisation holders.

The health economic exercise we previously carried out suggested that six-monthly, annual, or biennial monitoring frequencies would all be more cost-effective than three-monthly monitoring (12, 19). All patients were comfortable with reducing the frequency of their testing to every six months; however, some HCPs were hesitant to reduce monitoring beyond three-monthly for those with a risk score of ≥3% per year. It was unusual for patients to have such high risk; however, as patients occasionally do so, care must be taken when implementing

risk-stratified monitoring (12-16, 19). With variability in accepted frequencies amongst HCPs, and the preference by some to have autonomy in their decision-making, monitoring recommendations may need to be given for risk score ranges. For example, six-monthly to annual monitoring for risk scores up to 2% per year, and three- to six-monthly for risk scores over 2% per year. All HCPs were happy to move to annual monitoring for anti-TNF-αs, suggesting a different recommendation could be made for such medications. The recommended monitoring frequency may change over time, e.g., as the patient accrues comorbidities. The most feasible way to implement risk-stratified monitoring is to integrate the calculator as an application in GP electronic health records. Such an application will automatically produce a risk score and recommend any changes in monitoring frequency each time a prescription is issued. Alternatively, this can be decided by the GP and/or the specialist during patients' annual reviews.

Should annual monitoring be considered for national guidance, tapering may increase the likelihood it is accepted by patients and prescribers given many participants were more comfortable with this over moving straight to annual monitoring.

Some HCPs put more emphasis on individual prognostic factors such as age, lifestyle factors, other medications, and comorbidities rather than on the overall risk score. The acceptance of moving to annual monitoring for anti-TNF-αs appeared to be facilitated by this chiming with HCPs clinical experience of rarely seeing side-effects in those treated with these drugs. To minimise such preconceptions from impeding the interpretation of the risk score, it would be essential to communicate that HCPs should not focus on individual factors but the total score given it is based on the most recent evidence and takes all prognostic factors into account.

Furthermore, some HCPs wanted more information about how the risk-stratified approach was created to feel comfortable adopting it. To ensure HCP support and trust in adopting a risk-stratified approach to monitoring, a clear explanation of how the calculators producing risk scores were developed should also be included. This should also be considered when explaining changes to monitoring with patients given that participants had the risk score

calculated with and explained to them, which may have provided important reassurance that facilitated their view that less frequent monitoring would be acceptable.

Strengths of this study include nationwide recruitment with findings reflecting the experiences of those receiving and providing medical care from different hospitals. There was a broad eligibility criterion for patients with different IMIDs, on different medications, and different HCP roles representing each disease area, enhancing transferability of the findings. Monitoring of long-term immune-suppressing treatments is done by GPs and a strategy that includes all conditions allows for ease of implementation across different conditions. Participants were informed that the interviewer was not involved in the care of patients to encourage honest sharing of opinion, minimise response bias and convey equipoise in whether a monitoring frequency reduction was acceptable or not. Data collection and analysis were conducted concurrently, which allowed for identification of areas requiring further exploration in the following interviews. With no changes to the codebook upon analysis of the final patient and HCP interviews, we can be confident that we reached a sufficient level of data saturation for the findings to be clinically meaningful and transferable (23). Involvement of a second coder and clinical investigator enhanced the rigour of analysis. Our use of purposive sampling ensured a mix of patients with different levels of adherence to their recommended monitoring frequency were interviewed, and less adherent patients were forthcoming in discussing reasons for non-compliance.

Limitations include a lack of patient participants with an annual risk score >3% who may feel more cautious about adopting a reduced frequency of monitoring; however, most patients in the model development and validation populations had annual risk scores <3%. There were also no patient participants of non-white ethnicity whose views and experiences may differ. We were unable to engage with them despite inviting many patients. Adherence to current monitoring may have been overestimated as it was self-reported. Burden from excessive monitoring blood-tests is also an issue for paediatric patients but was not addressed in this study.

A risk-stratified approach to monitoring was acceptable to patients and HCPs. Recommendations towards adopting such a strategy in clinical practice should consider the preferred gaps in testing, tapering, clinician, and patient autonomy in deciding appropriate monitoring frequencies, and flexibility to change monitoring frequency according to need.

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COMPETING INTERESTS

HCW directed the NIHR Health Technology Assessment Programme from 2015-2020. He played no part in the funding decision for this study. GPA has received consulting fees contracted through Nottingham University Consultants from Pfizer, AstraZeneca, Merck, PureTech, Clinipace, Amryth, GSK, DNDi, Benevolent AI, and Agios. CF disclosures of interest are: consultancy/advisory boards with AbbVie, AstraZeneca, Atarabio, BMS, GenMab, Gilead/Kite, Incyte, Janssen, Lilly, Morphosys, Ono, Roche, SERB, SOBI, and Takeda; educational activities with AbbVie, Kite/Gilead, Incyte, Janssen, Roche, and Takeda; travel with Roche and Kite/Gilead; and, research funding with BeiGene. CM is the Director of the NIHR School for Primary Care Research, and declares Keele University have received funding from MRC, NIHR, and Versus Arthritis for their time. AA has received personal fees from Up ToDate and Springer (royalties), Cadilla pharmaceuticals (lecture fees), and NGM Bio and Limbic (consulting). The remaining authors have declared no conflicts of interest.

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DATA AVAILABILITY STATEMENT

Deidentified data are available upon reasonable request to the corresponding author.

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Table 1: Study participants

Patients	n=18
Age (years), range	21-67
Female gender, n (%)	13 (72)
White ethnicity, n (%)	18 (100)
Diagnosis, n (%)	
Rheumatoid arthritis	3 (17)
Ankylosing Spondylitis	3 (17)
Systemic Lupus Erythematosus	2 (11)
Ulcerative Colitis	2 (11)
Crohn's disease	4 (22)
Skin psoriasis	4 (22)
Adherence to monitoring, n (%)	
Good (>80% attendance)	12 (67)
Poor (<80% attendance)	6 (33)
Current immunosuppressant, n (%) [a]	
Methotrexate	7 (39)
Sulfasalazine	1 (6)
Leflunomide	1 (6)
Azathioprine	3 (17)
Mercaptopurine	1 (6)
Anti-TNF-alpha monotherapy	5 (28)
Duration on current immunosuppressant, n (%)	
1-2 years	3 (17)
2-3 years	3 (17)
3-4 years	5 (28)
5-10 years	4 (22)
>10 years	3 (17)
Recommended monitoring frequency, n (%)	
Fortnightly	1 (6)
Monthly or bi-monthly	3 (17)
Three-monthly	13 (72)
Six-monthly	1 (6)
Predicted risk (%) of stopping treatment due to abnormal blood test result in the next 12 months, n (%) [b].	
1%	5 (28)
2%	6 (33)
3%	2 (11)
Health professionals	n=13
Job role, n (%)	

Consultant	6 (46)
Specialist nurse or pharmacist	4 (31)
General practitioner	3 (23)
Speciality, n (%)	
Rheumatology	5 (38)
Dermatology	3 (23)
Gastroenterology	2 (15)
Primary care	3 (23)
Female, n (%)	7 (54)
Years in speciality	
<5 years	1
5-10 years	2
10-20 years	5
>20 years	5

[a] Three participants were taking a DMARD and anti-TNF-alpha (combined therapy).

[b] No risk-score for anti-TNF-alpha monotherapy.

Table 2: Themes, subthemes and supporting quotes.

Theme: Benefits and challenges to current monitoring
Subtheme 1: Reassurance and continuity of care
a. *It's more the peace of mind and just knowing that everything is okay. Patient 5, RA*
b. *I saw it as the medication was what was going to help me, and if one of the requirements was to have regular blood tests then so be it. Patient 17, AS*
c. *It does give me that reassurance that you're still part of that system, that someone's still looking out for you. Patient 12, IBD*
Subtheme 2: Incidental findings leading to the diagnosis of another condition
d. *Incidental findings that the physicians are not aware of and then that allows early interventions… but they might be few and far between. HCP 2, dermatologist*
Subtheme 3: Practical challenges of frequent monitoring
e. *When it's time to get my prescription every third month, there's always a hiccup, it's always late and I always have to chase it. So, I'm at the stage of running out or not having any [medication] to take, because the results aren't filtering through. Patient 13, PsO*
f. *The powers that be just don't consider how many people are involved in the stage of getting the drug to the person and how much time it takes for each person to do that. HCP 12, GP*
Subtheme 4: Remembering to book a test and consequences of non-compliance
g. *In my case, you've got other things wrong with you as well. And depending on how severe they are at the time I can sort of prioritise those, so you then suddenly forget about the need to do your blood test. Patient 15, AS*
h. *Patients will often flare in terms of their disease, so that causes issues that could have been prevented if they continued on their regimen. HCP 10, rheumatology pharmacist*
Subtheme 5: Clinicians' interpretation and actioning of monitoring results
i. *We don't have any consistent guidelines on what to action and what not to action, so then I feel like a lot of the time we're probably doing unnecessary bloods… every consultant will do things differently here. HCP 6, dermatology nurse*

Theme: Questioning the need for the current frequency of monitoring

j. *Because I've been on azathioprine for a few years now, you know, I seem to have settled with it. I think a six-monthly blood test would be better. Patient 8, IBD*

k. *I can't remember the last time I saw an abnormal [result]… we're just taking tonnes of bloods, and nothing happens. HCP 13, GP*

l. *During COVID time… our patients could not go in… so that prompted you to say, "Do we need to have blood monitoring that frequently?" … for the last two years, how many bad side effects or problems you were faced with? That is negligible. HCP 3, rheumatologist*

Theme: Adopting a risk-stratified monitoring plan

Subtheme 1: Views on risk scores and acceptability of proposed frequencies

m. *One out of 100, that doesn't seem like a large amount. That gives me a bit of reassurance. Patient 1, PsO (risk score 1); So, I'm quite low risk then really. Patient 3, IBD (risk score 3)*

n. *I think it's too big a jump and I think if there were any issues, one year since the last test, who knows what could have happened. Whereas if you have the test sooner, things are picked up and can be treated. Patient 3, IBD*

o. *We treat lots of patients with anti-TNF drugs. Although they have lots of other issues, we seldom stop it because of repeat blood test abnormalities. I would be happy with once a year on that basis. HCP 8, gastroenterologist*

p. *You could do it to six months and do that for three years or two years and then move to a year if it seems safe and appropriate. HCP 11, GP*

q. *I suppose if you just questioned the 1 out of 100, then I'd be more inclined to say okay six monthly or once a year is fine, less frequent. But if you gave me the specific context of the medication, then I would change my view. Only because I personally don't think from anecdotal clinical practice that it is 1 out of 100 in this situation, it's probably more. HCP 9, gastroenterologist*

Subtheme 2: Provisos to accepting a reduced monitoring schedule

	r. *I think six months with good feedback is acceptable absolutely, I would be happy with that if I was, as long as I could get the results and I know what was going on, I'd be very happy with six months. Patient 6, RA*
	s. *This needs to be consistent across every indication for this drug, rheumatological, dermatological, hepatological, whatever it is, it needs to be the same. HCP 8, gastroenterologist*
Subtheme 3: Perceived impact of proposed strategy	
	t. *The less that psoriasis can get in the way of my everyday life, the better, and that includes like hospital appointments and blood tests. Patient 4, PsO*
	u. *Where consultants will prescribe, one of the biggest factors will be that they can use that time to actually see more of the patients who are being referred to them. So those patients get treated faster. HCP 7, rheumatology pharmacist*
Theme: Communicating a change in practice	
	v. *There's a lot of difficulty letting go of the old ways… You might need the odd champion to go round and speak to people in person. HCP 4, dermatologist*
	w. *Definitely like a good leaflet or a handout that we could send to the patients would be really good, explaining the reasons why we've decided to change the frequency. HCP 6, dermatology nurse*

Patient participant quotes identified by participant number and inflammatory condition; HCP participant quotes identified by participant number, job role and specialism. RA = rheumatoid arthritis, IBD = inflammatory bowel disease, PsO = skin psoriasis, AS = ankylosing spondylitis.

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

Cosentyx® secukinumab

1,000,000 patients treated globally, and counting*[4]

100+ clinical trials*[5]

8+ years of real-world evidence[1–3]

8 indications[1–3]

Click here to visit our HCP portal and learn more

Real-world evidence shows a consistent safety profile over 6 years[6,7]

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

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

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

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

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

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

Cosentyx® (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.

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. 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.

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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. 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