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Discontinuation of anti-tumour necrosis factor alpha treatment owing to blood test abnormalities, and cost-effectiveness of alternate blood monitoring strategies

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Abstract

Background There is no evidence base to support the use of 6-monthly monitoring blood tests for the early detection of liver, blood and renal toxicity during established anti-tumour necrosis factor alpha (TNFα) treatment.

Objectives To evaluate the incidence and risk factors of anti-TNFα treatment cessation owing to liver, blood and renal side-effects, and to estimate the cost-effectiveness of alternate intervals between monitoring blood tests.

Methods A secondary care-based retrospective cohort study was performed. Data from the British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR) were used. Patients with at least moderate psoriasis prescribed their first anti-TNFα treatment were included. Treatment discontinuation due to a monitoring blood test abnormality was the primary outcome. Patients were followed-up from start of treatment to the outcome of interest, drug discontinuation, death, 31 July 2021 or up to 5 years, whichever came first. The incidence rate (IR) and 95% confidence intervals (CIs) of anti-TNFα discontinuation with monitoring blood test abnormality was calculated. Multivariate Cox regression was used to examine the association between risk factors and outcome. A mathematical model evaluated costs and quality-adjusted life years (QALYs) associated with increasing the length of time between monitoring blood tests during anti-TNFα treatment.

Results The cohort included 8819 participants [3710 (42.1%) female, mean (SD) age 44.76 (13.20) years] that contributed 25 058 person-years (PY) of follow-up and experienced 125 treatment discontinuations owing to a monitoring blood test abnormality at an IR of 5.85 (95% CI 4.91–6.97)/1000 PY. Of these, 64 and 61 discontinuations occurred within the first year and after the first year of treatment start, at IRs of 8.62 (95% CI 6.74–11.01) and 3.44 (95% CI 2.67–4.42)/1000 PY, respectively. Increasing age (in years), diabetes and liver disease were associated with anti-TNFα discontinuation after a monitoring blood test abnormality [adjusted hazard ratios of 1.02 (95% CI 1.01–1.04), 1.68 (95% CI 1.00–2.81) and 2.27 (95% CI 1.26–4.07), respectively]. Assuming a threshold of £20 000 per QALY gained, no monitoring was most cost-effective, but all extended periods were cost-effective vs. 3- or 6-monthly monitoring.

Conclusions Anti-TNFα drugs were uncommonly discontinued owing to abnormal monitoring blood tests after the first year of treatment. Extending the duration between monitoring blood tests was cost-effective. Our results produce evidence for specialist society guidance to reduce patient monitoring burden and healthcare costs.

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What is already known about this topic?

- Hepatic, haematological and renal toxicity due to anti-tumour necrosis factor alpha (TNFα) drugs are uncommon during long-term treatment.
- Despite lack of evidence, all patients established on anti-TNFα treatment in the UK are required to undergo 6-monthly blood tests for the early detection of such toxicity.
- Risk factors for these side-effects are poorly understood and whether it would be cost-effective to reduce the frequency of monitoring blood tests is unknown.

What does this study add?

- It was uncommon for anti-TNFα drugs to be discontinued for hepatic, renal or haematological side-effects; this was even less frequent after 1 year of treatment.
- Age, pre-existing liver disease and diabetes were independent risk factors.
- Assuming a threshold of £20 000/quality-adjusted life years, monitoring 6-monthly, annually and biennially was more cost-effective than monitoring 3-monthly; and monitoring annually and biennially was more cost-effective than monitoring 6-monthly.
- These findings should be used to rationalize monitoring for asymptomatic blood, kidney or liver toxicity during established anti-TNFα treatment.

Anti-tumour necrosis factor alpha (TNFα) drugs are used in the treatment of psoriasis resistant to topical therapies and first-line nonbiologic systemic treatments such as methotrexate.[1] Although effective, they can cause cytopenia and elevated liver enzymes. Concern about these side-effects led the British Association of Dermatology (BAD) to recommend monitoring with full blood count, liver function tests (LFTs), and urea electrolytes and creatinine at least every 6 months during long-term established anti-TNFα treatment.[1] On the contrary, the American Academy of Dermatology does not recommend a fixed monitoring schedule, but leaves the decision on whether to monitor with blood tests – and the frequency of testing – to the patients' dermatologist for all anti-TNFα drugs except for infliximab, for which 6-monthly to annual blood test monitoring is recommended.[2] This is most likely owing to a higher reported risk of thrombocytopenia, neutropenia and hepatotoxicity with infliximab.[3,4]

There is no evidence base to support the use of monitoring blood tests for the early detection of toxicity after the first few months of anti-TNFα treatment and the cost-effectiveness of different monitoring strategies has never been evaluated. Previous studies have reported low rates of hepatotoxicity and cytopenia with anti-TNFα drugs in psoriasis, and that the risk of hepatotoxicity was increased in those concomitantly treated with methotrexate.[5,6] To support evidence-based practice and better use of healthcare resources, we conducted a retrospective cohort study to evaluate the incidence of anti-TNFα discontinuation owing to cytopenia, transaminitis or acute kidney injury; to ascertain the risk factors for this outcome; and to perform a health economic evaluation of alternate intervals between monitoring blood tests.

Materials and methods

Data source

Data from the BAD Biologic and Immunomodulators Register (BADBIR) were used in this study.[7] The BAD established an online pharmacovigilance register (BADBIR) to assess the long-term safety of biologics prescribed for patients with moderate-to-severe psoriasis. Following baseline data acquisition, hospital clinicians recorded changes in therapy, disease activity, changes in treatment (including reasons for stopping treatment) and adverse events. Data on death and malignancy were obtained from linkages with the National Health Service Information Centre system.

Study design

This study protocol was approved by the BADBIR steering committee. It was a retrospective cohort study encompassing the period 1 October 2007 to 31 July 2021.

Study population

Adults (aged $\geq$ 18 years) with psoriasis with or without arthritis prescribed their first anti-TNFα drugs were eligible. There were no exclusion criteria in terms of comorbidities or concurrent drug prescriptions. In the UK and Republic of Ireland (ROI), anti-TNFα drugs are prescribed from hospital outpatient clinics. The hospital team also organizes monitoring blood tests and acts on any abnormalities.

Follow-up

Patients were followed-up from their first anti-TNFα prescription until the outcome of interest, death, treatment discontinuation, 31 July 2021 or up to 5 years – whichever came first.

Outcome

Anti-TNFα discontinuation owing to a monitoring blood test abnormality was the outcome of interest and was ascertained using the information about reason(s) for stopping treatment specified in BADBIR. Where the reason for stopping treatment was recorded only as an 'adverse event', 'adverse event and inefficacy', 'other' or 'death',

the descriptions of the adverse event in the free text and MedDRA coding were manually reviewed to ascertain outcomes related to side-effects of interest.

Blood test data from the 6-month period before stopping anti-TNFα treatment were used to ascertain whether the treatment was stopped for leukopenia, thrombocytopenia or elevated liver enzymes. The estimated glomerular filtration rate (eGFR) was calculated using the 2021 CKD Epidemiology Collaboration (CKD-EPI) equation, which does not consider race.[8]

Risk factors

Age at registration (years), sex, body mass index (BMI), alcohol intake [not currently drinking alcohol, and self-reporting low (1–14 units weekly), medium (15–21 units weekly) and high alcohol intake ($\geq$ 21 units weekly)], diabetes, high cholesterol and a recorded clinical diagnosis of liver disease before the date of the first anti-TNFα prescription were the risk factors (Table 1). The recorded height and weight at registration were used to calculate BMI. Age, sex, BMI, alcohol intake and diabetes were included as they are associated with drug-induced liver injury.[3]

Statistical analysis

Mean [standard deviation (SD)] and numbers with percentages were used for descriptive statistics. The incidence rate (IR) and 95% confidence interval (CI) of outcome per 1000 person-years (PY) was calculated for the entire follow-up period, for the first 6 months, for the first 12 months and for the follow-up period after the first 12 months. Multivariable Cox regression was used to examine the association between covariates at baseline and outcome of interest. Missing data for BMI and alcohol were handled by multiple imputation using chained equations. Ten imputations were carried out, and the imputation model included all covariates and the outcome variable. Results from the imputed datasets were combined using Rubin's rule. Data management and analysis were performed in STATA v. 16 (StataCorp, College Station, TX, USA). A P-value < 0.05 was considered to be statistically significant.

Health economic methods

Patients were monitored according to each strategy for a period of 5 years. An additional monitoring appointment after the cessation of treatment as a result of an abnormal blood test was assumed. The probability that an abnormal blood test would result in an illness because of the extended monitoring period was estimated by the clinical team members, based on their experience. This involved a remote videoconference followed by asynchronous email discussion. The rates are provided in Table S1 (see Supporting Information). The clinicians erred toward overestimating the risks rather than underestimating them. The costs and quality-adjusted life year (QALY) losses associated with each condition were estimated following targeted literature reviews (Table S2; see Supporting Information). A monitoring appointment with blood tests was estimated to cost £24.09; details on this estimation are provided in Appendix S1 (see Supporting Information). No disutility was assumed for attending a monitoring appointment. To account for uncertainty in outcome incidence, health economic analyses considered the midpoint and upper and lower 95% CI of the IR from start of treatment, from 1 year after the start of treatment and within the first year of treatment. It was assumed that these risks were distributed exponentially.

For each strategy the costs associated with both monitoring and illness were estimated, as was the loss in QALYs. All values were discounted at a value of 3.5% per annum, as recommended by the National Institute for Health and Care Excellence.[9] The results were presented in terms of incremental net monetary benefit (iNMB), assuming a cost per QALY threshold of £20 000, compared with monitoring every 3 months. The strategy with the greatest iNMB value was estimated to be the most cost-effective treatment. Sensitivity analysis considered threefold higher risks of illnesses than estimated by the clinicians.

Results

Data for 8819 participants with psoriasis (42.1% female) prescribed their first anti-TNFα agent that contributed 25 058 PY of follow-up were included in this study. Mean (SD) age and BMI were 44.76 (13.20) years and 31.15 (9.44) kg m^{-2}, respectively. Of the included participants 6744 (76.5%), 1718 (19.5%), 281 (3.2%) and 76 (0.9%) were prescribed adalimumab, etanercept, infliximab and certolizumab or their biosimilars, respectively. Diabetes, high cholesterol, liver disease and renal disease were present in 738 (8.4%), 742 (8.4%), 419 (4.8%) and 131 (1.5%) participants, respectively.

There were 125 anti-TNFα treatment discontinuations for abnormal monitoring blood test results at an IR of 5.85 (95% CI 4.91–6.97)/1000 PY. The IRs of discontinuation of etanercept, infliximab, certolizumab and adalimumab or their biosimilars for abnormal monitoring blood test results were 8.04 (95% CI 5.55–11.65), 18.55 (95% CI 10.53–32.66), 9.79 (95% CI 1.38–69.53) and 4.90 (95% CI 3.96–6.07)/1000 PY, respectively.

Forty-one, 64 and 61 discontinuations owing to abnormal blood test results occurred in the first 6 months, in the first year and after the first year of first prescription during 4111, 7428 and 17 751 PY of follow-up at IRs of 9.97 (95% CI 7.34–13.54), 8.62 (95% CI 6.74–11.01) and 3.44 (95% CI 2.67–4.42)/1000 PY, respectively. The IRs for the discontinuation of etanercept, infliximab, certolizumab and adalimumab or their biosimilars owing to abnormal blood test results after the first year of treatment were 4.63 (95% CI 2.63–8.16), 12.30 (95% CI 5.87–25.81), 23.60 (95% CI 3.32–167.55) and 2.82 (95% CI 2.07–3.83) per 1000 PY.

Blood test results from within the 6 months prior to the stop date were available for 75 patients who stopped treatment. Among them, 51 had an alanine transaminase (ALT) level of > 40 IU L^{-1} (of these, 29 had an ALT level > 80 IU L^{-1} and 7 had an ALT level > 200 IU L^{-1}); 5 had a total white blood cell (WBC) count $< 4.0 \times 10^3$ cells mL^{-1} and none had a WBC count $< 3.0 \times 10^3$ cells mL^{-1}; 8 had a platelet count $< 150 \times 10^3$ cells mL^{-1} (of these, 4 had a platelet count $< 100 \times 10^3$ cells mL^{-1} and none had a platelet count $< 50 \times 10^3$ cells mL^{-1}); 2 had an eGFR < 60 mL min^{-1}, with none having an eGFR < 30 mL min^{-1}.

Increasing age, diabetes and liver disease associated with anti-TNFα discontinuation with abnormal blood tests

in the model adjusted for age, sex, BMI, alcohol intake, pre-existing liver disease, diabetes and hypercholesterolaemia [adjusted hazard ratios (HRs) 1.02 (95% CI 1.01–1.04), 1.68 (95% CI 1.00–2.81) and 2.27 (95% CI 1.26–4.07) respectively]. Infliximab was statistically significantly associated with a higher likelihood of stopping treatment owing to abnormal monitoring blood test results than etanercept [unadjusted HR 2.38 (95% CI 1.21–4.67); adjusted HR 2.21 (95% CI 1.12–4.34)]. Patients on adalimumab had a significantly lower risk of stopping treatment owing to abnormal monitoring blood test results compared with etanercept on univariate analysis (unadjusted HR 0.63, 95% CI 0.41– 0.97); the data became nonsignificant after adjustment for covariates (adjusted HR 0.66, 95% CI 0.43–1.03).

Health economic results

The iNMB for each strategy is shown in Figure 1. All extended monitoring periods were more cost-effective than 3-monthly monitoring. For all deciles, no monitoring was estimated to be most cost-effective, although annual and biennial monitoring were a considerable improvement on 3-monthly monitoring. Disaggregated results for the base case are shown in Table S3 (see Supporting Information), with combined results in Table S4 (see Supporting Information). Sensitivity analyses using three times the risk of adverse events are also shown in Figure 1 and showed similar results to the main health economic analysis.

Discussion

In this study of UK and ROI populations we evaluated the incidence and risk factors of clinically significant blood test abnormalities (i.e. ones that required treatment cessation) due to anti-TNFα drugs. We also evaluated the cost-effectiveness of alternate blood test monitoring strategies. Among a cohort of patients with moderate-to-severe psoriasis starting anti-TNFα drugs for the first time, we found that it was uncommon for treatment to be stopped owing to abnormal blood test results, and that this became even less common after the first year of treatment. This is consistent with reports that the median interval between starting anti-TNFα drugs and drug-induced liver injury and neutropenia ranged between 14 to 18 weeks and 12 to 17 weeks, respectively, although late-onset liver enzyme elevations and neutropenia were also reported in these studies.[10–14] Increasing age and pre-existing liver disease were independent risk factors for stopping anti-TNFα drugs owing to abnormal monitoring blood test results, consistent with previous reports.[3] Also consistent with previous reports of a higher risk of drug-induced liver injury with infliximab, we found

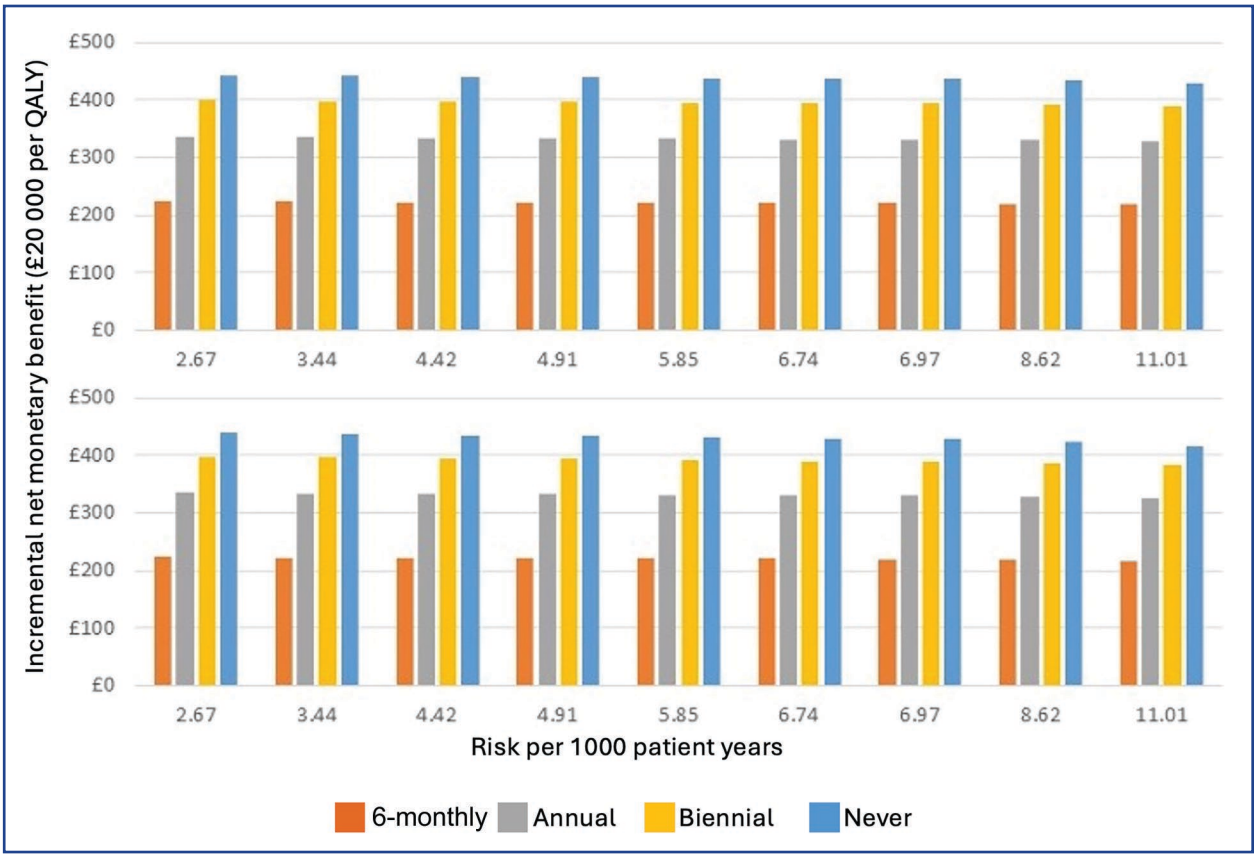

Figure 1 Incremental net monetary benefit associated with extended monitoring periods vs. 3-monthly monitoring across different estimated risks (top panel). Sensitivity analyses assuming a triple rate of adverse events (bottom panel). The values on the horizontal axes are the incidence and upper and lower 95% confidence intervals (CIs) of anti-tumour necrosis factor alpha discontinuations owing to abnormal monitoring blood test results during the 5-year follow-up period [5.85 (95% CI 4.91–6.97)/1000 person-years (PY)], during the first year of treatment [8.62 (95% CI 6.74–11.01)/1000 PY] and after the first year of treatment [3.44 (95% CI 2.67–4.42)/1000 PY)].

Table 1 Risk factors associated with the discontinuation of anti-tumour necrosis factor alpha (TNFα) drugs owing to abnormal blood test results

	HR (95% CI)	aHR (95% CI)
Age, years	1.03 (1.01–1.04)	1.02 (1.01–1.04)
Sex		
Female	1	1
Male	1.25 (0.88–1.78)	1.31 (0.91–1.89)
BMI (kg m^{-2})[a]	1.01 (1.00–1.02)	1.01 (0.99–1.02)
Alcohol (units weekly)[b]	1.01 (1.00–1.02)	1.01 (1.00–1.02)
Nondrinker	1	1
≤ 14	0.98 (0.64–1.51)	1.09 (0.71–1.69)
15–21	1.22 (0.67–2.21)	1.39 (0.76–2.56)
≥ 21	0.89 (0.44–1.76)	1.03 (0.50–2.10)
Diabetes[c]		
No	1	1
Yes	2.16 (1.34–3.49)	1.68 (1.00–2.81)
Liver disease[c]		
No	1	1
Yes	2.66 (1.50–4.72)	2.27 (1.26–4.07)
High cholesterol[c]		
No	1	1
Yes	1.01 (0.54–1.87)	0.69 (0.36–1.31)

aHR, adjusted hazard ratio; BMI, body mass index; CI, confidence interval; HR, hazard ratio. [a]BMI was calculated using height in meters/(weight in kg × weight in kg). Data for BMI were missing for 620 participants. [b]Data for alcohol intake were missing for 848 participants. [c]Comorbidities were defined as present if their year of onset preceded the year of anti-TNFα prescription, else they were defined as absent. No person with kidney disease experienced the outcome of interest.

a significantly higher risk of stopping infliximab treatment associated with abnormal monitoring blood test results.[11,15]

Our cost-effectiveness analysis showed that monitoring with blood tests every year and every 2 years was more cost-effective than monitoring with blood tests every 3–6 months, and monitoring every 6 months was more cost-effective than monitoring every 3 months, although no monitoring was most cost-effective. This is a novel finding and may be used to reduce the frequency of monitoring blood tests in those established on anti-TNFα treatment (e.g. after the first 6 months). However, such changes in clinical practice should only be implemented once the findings of this study have been considered by the relevant specialist societies.

In this study, among those who stopped treatment as a result of abnormal blood test results, most did so due to abnormal LFT results, and of these the vast majority had mildly elevated liver enzymes. Only a few participants stopped their treatment owing to low WBC and low platelet counts. No participant in this study had either leukopenia or thrombocytopenia that was severe enough to increase the risk of infection and bleeding, respectively. Previous studies have reported occasional patients with severe neutropenia and infection,[13] although severe thrombocytopenia increasing the risk of bleeding was not reported previously, to the best of our knowledge. Two patients stopped treatment owing to abnormal renal function. This is not unexpected as anti-TNFα drugs are occasionally associated with granulomatous interstitial nephritis.[16,17]

The strengths of this study included the use of a nationwide cohort of patients with psoriasis from the UK and ROI, increasing the generalizability of the study findings. Furthermore, the reasons for stopping treatment were systematically documented in BADBIR. Free-text reasons for stopping treatment and MedDRA coding were individually reviewed when there was diagnostic uncertainty. This reduced the chances of missing outcome data. Another strength was the large sample size – to the best of our knowledge this is the largest study of its kind to date. Nevertheless, several limitations need to be considered when interpreting the results. Some patients who stopped treatment owing to inefficacy and mildly abnormal monitoring blood test results were considered to have stopped treatment for abnormal blood test results. This may have increased the event rate and biased the health economic gain from less-frequent monitoring toward null. Lack of information on blood test results is another limitation. Information on disease severity and concurrent medications was not included in the data analysis. Few participants were treated with infliximab and certolizumab, which increased the imprecision around estimates of the incidence of side-effects with these drugs.

In conclusion, this study has shown that anti-TNFα drugs are uncommonly stopped owing to abnormal monitoring blood test results and our health economic analysis showed that it is more cost-effective to undertake monitoring blood tests annually and biennially than the current practice of monitoring every 6 months. The results of this study ought to be considered by guideline writing groups so that the frequency of monitoring blood tests may be reduced.

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Conflicts of interest

A.A. reports personal fees from UpToDate (royalty), Springer (royalty), Cadilla Pharmaceuticals (lecture fees), NGM Bio (consulting) and Limbic (consulting) and personal fees from Inflazome (consulting), unrelated to this work. G.P.A. has received consulting fees from Abbott, Albereo, Amryth, AstraZeneca, BenevolentAI, DNDI, GlaxoSmithKline, NuCANA, Pfizer, Roche Diagnostics, Servier Pharmaceuticals and W.L Gore & Associates paid to the University of Nottingham, unrelated to this work. C.P.F. has received consultancy/advisory board fees from AbbVie, GenMab, Incyte, Morphosys, Roche, Takeda, Ono, Kite/Gilead, BMS/Celgene and BTG/Veriton; and departmental research funding from BeiGene unrelated to this work. R.B.W. reports research grants from AbbVie, Almirall, Amgen, Celgene, Janssen, Lilly, LEO, Novartis, Pfizer and UCB, and consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, DiCE, GSK, Janssen, Lilly, LEO, Novartis, Pfizer, Sanofi, Sun Pharma, UCB and UNION. The other authors declare no conflicts of interest.

Data availability

The data included in this study are available from British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR).

Ethics statement

The British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR) received approval from the North West Research Ethics Committee in March 2007. All participants provided written informed consent in accordance with the Declaration of Helsinki.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website.

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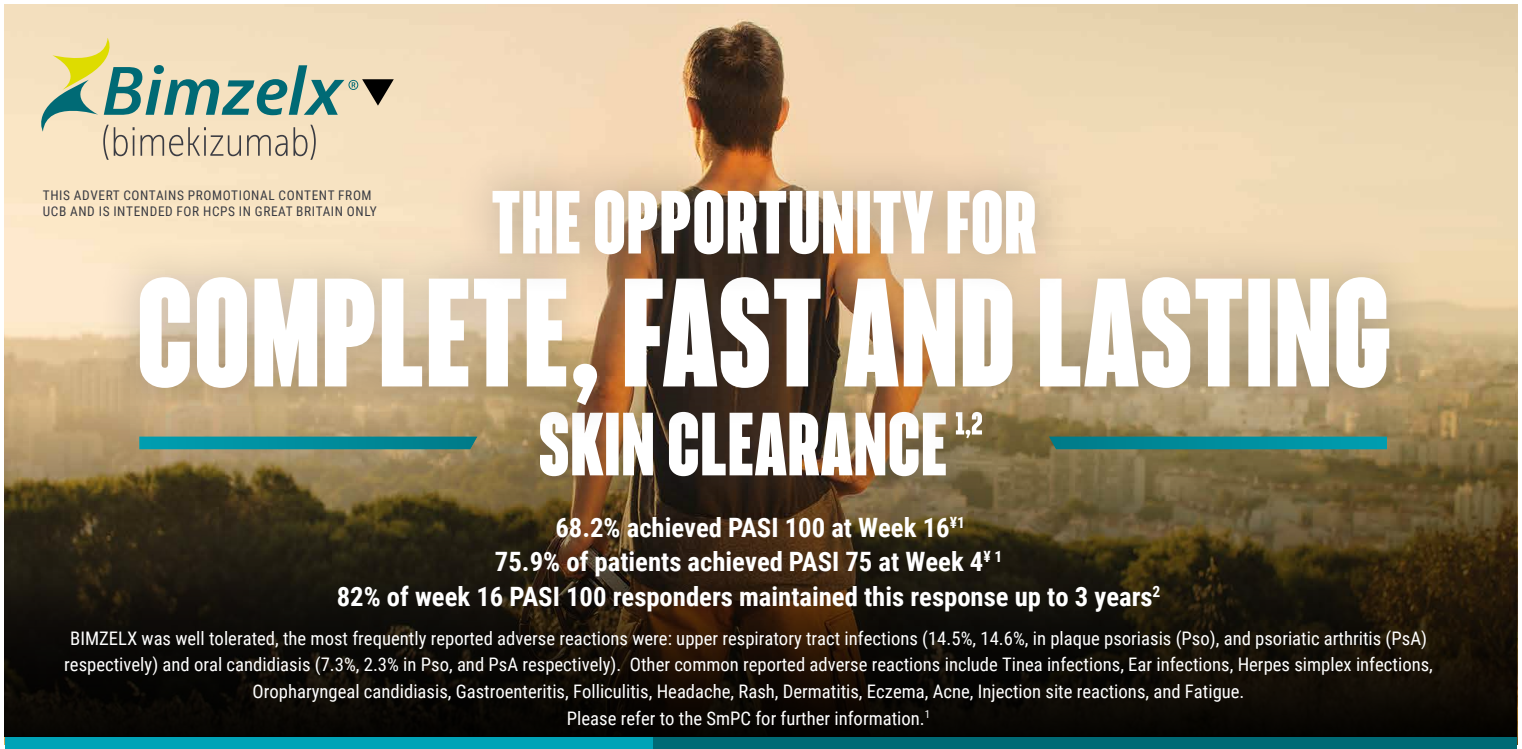

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BIMZELX® ▼ (Bimekizumab) is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy; and for active psoriasis arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs), alone or in combination with methotrexate.[1] (Please consult the Summary of Product Characteristics (SmPC) before prescribing).

Active Ingredient: Bimekizumab – solution for injection in pre-filled syringe or pre-filled pen: *160 mg of bimekizumab in 1 mL of solution (160mg/mL).* **Indications:** Moderate to severe plaque psoriasis in adults who are candidates for systemic therapy. Alone or in combination with methotrexate, for active psoriatic arthritis in adults who have had an inadequate response or intolerant to one or more disease-modifying antirheumatic drugs (DMARDs). Adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) who have responded inadequately or are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs). Adults with active ankylosing spondylitis who have responded inadequately or are intolerant to conventional therapy. **Dosage and Administration:** Should be initiated and supervised by a physician experienced in the diagnosis and treatment of conditions for which Bimzelx is indicated. **Recommended dose:** Plaque Psoriasis: 320 mg (given as two subcutaneous injections of 160 mg each) at week 0, 4, 8, 12, 16 and every 8 weeks thereafter. Psoriatic arthritis: 160 mg (given as 1 subcutaneous injection of 160 mg) every 4 weeks. For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, the recommended dose is the same as for plaque psoriasis. After 16 weeks, regular assessment of efficacy is recommended and if a sufficient clinical response in joints cannot be maintained, a switch to 160 mg every 4 weeks can be considered. Axial spondyloarthritis (nr-axSpA and AS): 160 mg (given as 1 subcutaneous injection) every 4 weeks. For patients with plaque psoriasis (including psoriatic arthritis with coexistent moderate to severe psoriasis) and a body weight ≥ 120 kg who did not achieve complete skin clearance at week 16, 320 mg every 4 weeks after week 16 may further improve treatment response. Consider discontinuing if no improvement by 16 weeks of treatment. Renal or hepatic impairment: No dose adjustment needed. Elderly: No dose adjustment needed. Administer by subcutaneous injection to thigh, abdomen or upper arm. Rotate injection sites and do not inject into psoriatic plaques or skin that is tender, bruised, erythematous or indurated. Do not shake pre-filled syringe or pre-filled pen. Patients may be trained to self-inject. **Contraindications:** Hypersensitivity to bimekizumab or any excipient; Clinically important active infections (e.g. active tuberculosis). **Warnings and Precautions:** Record name and batch number of administered product. *Infection:* Bimekizumab may increase the risk of infections e.g. upper respiratory tract infections, oral candidiasis. Caution when considering use in patients with a chronic infection or a history of recurrent infection. Must not be initiated if any clinically important active infection until infection resolves or is adequately treated. Advise patients to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops an infection, the patient should be carefully monitored. If the infection becomes serious or is not responding to standard therapy do not administer bimekizumab until infection resolves. *TB:* Evaluate for TB infection prior to initiating bimekizumab – do not give if active TB. While on bimekizumab, monitor for signs and symptoms of active TB. Consider anti-TB therapy prior to bimekizumab initiation if past history of latent or active TB in whom adequate treatment course cannot be confirmed. *Inflammatory bowel disease:* Bimekizumab is not recommended in patients with inflammatory bowel disease. Cases of new or exacerbations of inflammatory bowel disease have been reported. If inflammatory bowel disease signs/symptoms develop or patient experiences exacerbation of pre-existing inflammatory bowel disease, discontinue bimekizumab and initiate medical management. *Hypersensitivity:* Serious hypersensitivity reactions including anaphylactic reactions have been observed with IL-17 inhibitors. If a serious hypersensitivity reaction occurs, discontinue immediately and treat. *Vaccinations:* Complete all age appropriate immunisations prior to bimekizumab initiation. Do not give live vaccines to bimekizumab patients. Patients may receive inactivated or non-live vaccinations. **Interactions:** A clinically relevant effect on CYP450 substrates with a narrow therapeutic index in which the dose is individually adjusted e.g. warfarin, cannot be excluded. Therapeutic monitoring should be considered. **Fertility, pregnancy and lactation:** Women of child-bearing potential should use an effective method of contraception during treatment and for at least 17 weeks after treatment. Avoid use of bimekizumab during pregnancy. It is unknown whether bimekizumab is excreted in human milk, hence a risk to the newborn/infant cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Bimzelx therapy. No data available on human fertility. **Driving and use of machines:** No or negligible influence on ability to drive and use machines. **Adverse Effects:** Refer to SmPC for full information. Very Common *(≥ 1/10):* upper respiratory tract infection; Common *(≥ 1/100 to < 1/10):* oral candidiasis, tinea infections, ear infections, herpes simplex infections, oropharyngeal candidiasis, gastroenteritis, folliculitis; headache, rash, dermatitis and eczema, acne, injection site reactions, fatigue; Uncommon *(≥ 1/1,000 to < 1/100):* mucosal and cutaneous candidiasis (including oesophageal candidiasis), conjunctivitis, neutropenia, inflammatory bowel disease. Storage precautions: Store in a refrigerator (2°C – 8°C), do not freeze. Keep in outer carton to protect from light. Bimzelx can be kept at up to 25°C for a single period of maximum 25 days with protection from light. Product should be discarded after this period or by the expiry date, whichever occurs first.

Legal Category: POM

Marketing Authorisation Numbers: PLGB 00039/0802 (Pre-filled Syringe), PLGB 00039/0803 (Pre-filled Pen).

UK NHS Costs: £2,443 per pack of 2 pre-filled syringes or pens of 160 mg each.

Marketing Authorisation Holder: UCB Pharma Ltd, 208 Bath Road, Slough, Berkshire, SL1 3WE, United Kingdom.

Further information is available from: UCB Pharma Ltd, 208 Bath Road, Slough, Berkshire, SL1 3WE. Tel: 0800 2793177 Email: ucbcares.uk@ucb.com

Date of Revision: August 2023 (GB-P-BK-AS-2300047)

Bimzelx is a registered trademark.

Adverse events should be reported. Reporting forms and information can be found at http://www.mhra.gov.uk/yellowcard. Adverse events should also be reported to UCB Pharma Ltd at ucbcares.uk@ucb.com or 0800 2793177.

References: 1. BIMZELX (bimekizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/12834/smpc. Accessed September 2023 **2.** Strober et al. [BE BRIGHT open label extension] Br J Dermatol. 2023. 188(6): 749-759.

GB-BK-2300081 Date of preparation: September 2023.

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