Rheumatology, 2024, **63**, e37–e38
https://doi.org/10.1093/rheumatology/kead384
Advance access publication 31 July 2023
Letter to the Editor

British Society for Rheumatology RHEUMATOLOGY OXFORD

Letter to the Editor (Other)

British Society of Rheumatology guideline working group response to European Medicines Agency safety update on Hydroxychloroquine

Mark D. Russell [1], Mrinalini Dey [2], Julia Flint[3], Philippa Davie[1], Alexander Allen[4], Amy Crossley[5], Margreta Frishman[6], Mary Gayed[7], Kenneth Hodson[8], Munther Khamashta[9], Louise Moore[10], Sonia Panchal[11], Madeleine Piper[12], Clare Reid[5], Katherine Saxby[13], Karen Schreiber [14,15,16], Naz Senvar[17], Sofia Tosounidou[18], Maud van de Venne[19], Louise Warburton[20], David Williams[21], Chee-Seng Yee [22], Caroline Gordon [23] Ian Giles[24,*], on behalf of the BSR and BHPR Standards, Guidelines and Audit Working Group

[1]Centre for Rheumatic Diseases, King's College London, London, UK
[2]Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, UK
[3]Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust, Shropshire, UK
[4]British Society for Rheumatology, Clinical Affairs, London, UK
[5]Patient Representative, London, UK
[6]Queen's Hospital, Maternity Services, Barking Havering & Redbridge University NHS Trust, UK
[7]Rheumatology, Sandwell and West Birmingham Hospital, UK
[8]UK Tetralogy Information Service, London, UK
[9]Department of Women & Children's Health, King's College London, London, UK
[10]Rheumatic and Musculoskeletal Disease Unit, Our Lady's Hospice and Care Service, Dublin, Ireland
[11]Rheumatology, University Hospitals of Leicester, Leicester, UK
[12]Royal National Hospital for Rheumatic Diseases, Royal United Hospital, Bath, UK
[13]University College London Hospitals NHS Foundation Trust, Pharmacy, London, UK
[14]Thrombosis and Haemostasis, Guy's and St Thomas' NHS Foundation Trust, London, UK
[15]Danish Hospital for Rheumatic Diseases, Sonderborg, Denmark
[16]Department of Regional Health Research (IRS), University of Southern Denmark, Odense, Denmark
[17]Obstetrics and Gynaecology, St George's University Hospitals NHS Foundation Trust, London, UK
[18]Lupus UK Centre of Excellence, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK
[19]Obstetrics & Gynaecology, Frimley Park Hospital, Surrey, UK
[20]Primary Care and Health Sciences, Keele University, Keele, UK
[21]Womens Health, University College London Hospitals NHS Foundation Trust, London, UK
[22]Department of Rheumatology, Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust, Doncaster, UK
[23]Rheumatology Research Group, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK
[24]Centre for Rheumatology, Division of Medicine, University College London, London, UK

*Correspondence to: Ian Giles, Room 411, Rayne Institute, 5 University Street, London, UK. Email: i.giles@ucl.ac.uk

Rheumatology key message

- Reassurance that evidence underlying the EMA safety alert on HCQ in pregnancy does not alter the BSR 2022 pregnancy recommendations.

Dear Editor, We are concerned by the European Medicines Agency (EMA) recommendation to update the patient information leaflet for the use of HCQ in pregnancy [1]. HCQ is the antimalarial drug most used to treat rheumatic diseases. It has been extensively studied in pregnancy, and the British Society of Rheumatology guidelines on prescribing antirheumatic drugs in pregnancy recommend its use in pregnancy if required to treat disease at doses up to 400 mg/day [2].

The EMA recommendations from pharmacovigilance monitoring were influenced by a population-based cohort study comparing HCQ-exposed ($n = 2045$) and HCQ-unexposed ($n = 21\,679$) rheumatic disease pregnancies [3]. It found a small increase in risk of congenital malformations from 35.3/1000 in women not taking HCQ to 44.1/1000 in those taking HCQ in the first trimester. Moreover, a statistically significant increase in risk was found only with daily doses $\geq$400 mg of HCQ and no comparison was made between HCQ exposure at typical rheumatology dosing of up to and including 400 mg/day compared with atypical dosing of >400 mg/day.

The patient information leaflet will be revised to describe findings solely from this study and remove mention of other studies with reassuring findings. The revised wording will be:

Accepted: 13 July 2023

'[Hydroxychloroquine] may be associated with a small increased risk of major malformations and should not be used during pregnancy unless your doctor considers the benefits outweigh the risks.' The summary of product characteristics recommendation is unchanged from: 'Hydroxychloroquine should be avoided in pregnancy except when, in the judgement of the physician, the individual potential benefits outweigh the potential hazards. If treatment with hydroxychloroquine is necessary during pregnancy, the lowest effective dose should be used.'

Safety alerts on medication use in pregnancy have far-reaching consequences on prescribing of drugs used by rheumatologists. In 2019 the EMA [4] and Medicines and Healthcare products Regulatory Agency (MHRA) [5] issued warnings that ondansetron should not be used to treat nausea of pregnancy in the first trimester due to an increased risk of orofacial malformations, specifically oral clefts. These warnings were based on findings that showed a small but statistically significant increase in risk [6], with the absolute increased risk of oral clefts from ondansetron being 3 extra cases per 10 000 women treated. Consequently, healthcare professionals and patients were deterred from use of this drug in pregnancy. As the substantial suffering from hyperemesis gravidarum not infrequently results in termination of pregnancy, expert opinion remains that ondansetron is an effective low-risk treatment of this condition that should be an option to the informed pregnant woman [7].

The Huybrechts study on HCQ was included in the systematic literature review that informed the 2022 BSR pregnancy guideline based on 43 studies of 4701 pregnancy exposures to HCQ. There were no appreciable adverse effects overall of HCQ on pregnancy duration or birth weight, no increased risk of first trimester miscarriages and no specific patterns of congenital malformations in association with HCQ exposure [2].

We would like to reassure healthcare professionals and patients that the evidence under-pinning the EMA safety alert on use of HCQ in pregnancy was considered and does not alter the BSR 2022 pregnancy recommendations. Other examples of regulatory bodies drawing different conclusions from the same data exist within the BSR guideline. The MHRA and EMA have issued guidance for infants exposed to infliximab (a TNF inhibitor) *in utero* [8]. They recommend that infants exposed to infliximab *in utero* should not receive live vaccinations until 12 months of age and that live vaccinations should be avoided in infants exposed to infliximab through breast milk. The systematic review of the same body of evidence led the multi-disciplinary authors of the updated BSR pregnancy guidelines to recommend avoidance of live vaccine use in infants exposed to all TNF inhibitor and non-TNF inhibitor biologic DMARDs with high rates of placental passage, in third trimester of pregnancy until they are 6 months of age [2]. Other, experts have cautioned against a one size fits all approach and suggest that obstetric teams continue to provide well-considered and evidence-based advice on effects of maternal biologic DMARDs on suitability of childhood vaccinations [9].

Our multidisciplinary working group is concerned that a statement emphasizing a possible small risk of harm over established benefit may encourage healthcare professionals and patients to stop HCQ in pregnancy and risk disease relapse to the detriment of mother and fetus. A more supportive wording would acknowledge the potential for a small increased risk of major congenital malformations at doses higher than those normally used in rheumatological conditions and state 'the benefits and risks of HCQ during pregnancy should be considered with your specialist before conception'. It would therefore encourage consultations with specialists to balance the benefits of HCQ to prevent maternal disease flare and harm to the baby that may occur if this drug is stopped in pregnancy against potential small risks of congenital malformations at high dose.

Data availability

Not applicable for this letter.

Funding

No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

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

References

1. CMDh. Report from the CMDh meeting held on 21-22 February 2023 [press release]. https://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/CMDh_pressreleases/2023/CMDh_press_release_-_February_2023.pdf (April 2023, date last accessed).
2. Russell MD, Dey M, Flint J *et al.* Executive Summary: British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids. Rheumatology (Oxford) 2023;62:1370–87.
3. Huybrechts KF, Bateman BT, Zhu Y *et al.* Hydroxychloroquine early in pregnancy and risk of birth defects. Am J Obstet Gynecol 2021;224:290.e1–22.
4. EMA. Updated Signal assessment report on birth defects following in-utero exposure during the first trimester of pregnancy arising from recent publications with ondansetron. 2019. https://www.ema.europa.eu/en/documents/prac-recommendation/updated-signal-assessment-report-birth-defects-following-utero-exposure-during-first-trimester_en.pdf (April 2023, date last accessed).
5. MHRA. Ondansetron: small increased risk of oral clefts following use in the first 12 weeks of pregnancy. 2020. https://www.gov.uk/drug-safety-update/ondansetron-small-increased-risk-of-oral-clefts-following-use-in-the-first-12-weeks-of-pregnancy#:~:text=Recent%20epidemiological%20studies%20suggest%20exposure,lip%20and%2For%20cleft%20palate (April 2023, date last accessed).
6. Huybrechts KF, Hernandez-Diaz S, Straub L *et al.* Association of maternal first-trimester ondansetron use with cardiac malformations and oral clefts in offspring. JAMA 2018;320:2429–37.
7. Damkier P, Kaplan YC, Shechtman S *et al.* Ondansetron in pregnancy revisited: assessment and pregnancy labelling by the European Medicines Agency (EMA) & Pharmacovigilance Risk Assessment Committee (PRAC). Basic Clin Pharmacol Toxicol 2021;128:579–82.
8. EMA. Infliximab (Remicade, Flixabi, Inflectra, Remsima and Zessly): Use of live vaccines in infants exposed in utero or during breastfeeding. 2022. https://www.ema.europa.eu/en/documents/dhpc/direct-healthcare-professional-communication-dhpc-infliximab-remicade-flixabi-inflectra-remsima_en.pdf (April 2023, date last accessed).
9. Selinger CP, Bel Kok K, Limdi JK *et al.* Live vaccinations for infants exposed to maternal infliximab in utero and via breast milk – the need for nuanced decision making. BMJ Open Gastroenterol 2022;9:e001029.

This promotional material has been created and funded by Novartis Pharmaceuticals UK Ltd. for UK healthcare professionals only.

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

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

Joint relief in PsA:

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

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

Click here to visit our HCP portal and learn more

Skin clearance in PsO:

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

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

Axial joint relief in PsA:

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

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

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

8 years

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

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

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

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

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

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

NOVARTIS

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

UK | May 2024 | 425034

Cosentyx® (secukinumab) Great Britain Prescribing Information.

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

Indications: Treatment of: moderate to severe plaque psoriasis in adults, children and adolescents from the age of 6 years who are candidates for systemic therapy; active psoriatic arthritis in adults (alone or in combination with methotrexate) who have responded inadequately to disease-modifying anti-rheumatic drug therapy; active ankylosing spondylitis in adults who have responded inadequately to conventional therapy; active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence in adults who have responded inadequately to non-steroidal anti-inflammatory drugs; active enthesitis-related arthritis and juvenile psoriatic arthritis in patients 6 years and older (alone or in combination with methotrexate) whose disease has responded inadequately to, or who cannot tolerate, conventional therapy; active moderate to severe hidradenitis suppurativa (acne inversa) in adults with an inadequate response to conventional systemic HS therapy. **Presentations:** Cosentyx 75 mg solution for injection in pre-filled syringe; Cosentyx 150 mg solution for injection in pre-filled syringe; Cosentyx 150 mg solution for injection in pre-filled pen; Cosentyx 300 mg solution for injection in pre-filled pen. **Dosage & Administration:** Administered by subcutaneous injection at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Consider discontinuation if no response after 16 weeks of treatment. Each 75 mg dose is given as one injection of 75 mg. Each 150 mg dose is given as one injection of 150 mg. Each 300 mg dose is given as two injections of 150 mg or one injection of 300 mg. If possible avoid areas of the skin showing psoriasis. *Plaque Psoriasis:* Adult recommended dose is 300 mg. Based on clinical response, a maintenance dose of 300 mg every 2 weeks may provide additional benefit for patients with a body weight of 90 kg or higher. Adolescents and children from the age of 6 years: if weight ≥ 50 kg, recommended dose is 150 mg (may be increased to 300 mg as some patients may derive additional benefit from the higher dose). If weight < 50 kg, recommended dose is 75 mg. *Psoriatic Arthritis:* For patients with concomitant moderate to severe plaque psoriasis see adult plaque psoriasis recommendation. For patients who are anti-TNFα inadequate responders, the recommended dose is 300 mg, 150 mg in other patients. Can be increased to 300 mg based on clinical response. *Ankylosing Spondylitis:* Recommended dose 150 mg. Can be increased to 300 mg based on clinical response. *nr-axSpA:* Recommended dose 150 mg. *Enthesitis-related arthritis and juvenile psoriatic arthritis:* From the age of 6 years, if weight ≥ 50 kg, recommended dose is 150 mg. If weight < 50 kg, recommended dose is 75 mg. *Hidradenitis suppurativa:* Recommended dose is 300 mg monthly. Based on clinical response, the maintenance dose can be increased to 300 mg every 2 weeks. **Contraindications:** Hypersensitivity to the active substance or excipients. Clinically important, active infection. **Warnings & Precautions:** *Infections:* Potential to increase risk of infections; serious infections have been observed. Caution in patients with chronic infection or history of recurrent infection. Advise patients to seek medical advice if signs/symptoms of infection occur. Monitor patients with serious infection closely and do not administer Cosentyx until the infection resolves. Non-serious mucocutaneous candida infections were more frequently reported for secukinumab in the psoriasis clinical studies. Should not be given to patients with active tuberculosis (TB). Consider anti-tuberculosis therapy before starting Cosentyx in patients with latent TB. *Inflammatory bowel disease (including Crohn's disease and ulcerative colitis):* New cases or exacerbations of inflammatory bowel disease have been reported with secukinumab. Secukinumab, is not recommended in patients with inflammatory bowel disease. If a patient develops signs and symptoms of inflammatory bowel disease or experiences an exacerbation of pre-existing inflammatory bowel disease, secukinumab should be discontinued and appropriate medical management should be initiated. *Hypersensitivity reactions:* Rare cases of anaphylactic reactions have been observed. If an anaphylactic or serious allergic reactions occur, discontinue immediately and initiate appropriate therapy. *Vaccinations:* Do not give live vaccines concurrently with Cosentyx; inactivated or non-live vaccinations may be given. Paediatric patients should receive all age appropriate immunisations before treatment with Cosentyx. *Latex-Sensitive Individuals:* The removable needle cap of the 75mg and 150 mg pre-filled syringe and 150mg pre-filled pen contains a derivative of natural rubber latex. *Concomitant immunosuppressive therapy:* Combination with immunosuppressants, including biologics, or phototherapy has not been evaluated in psoriasis studies. Cosentyx was given concomitantly with methotrexate, sulfasalazine and/or corticosteroids in arthritis studies. Caution when considering concomitant use of other immunosuppressants. **Interactions:** Live vaccines should not be given concurrently with secukinumab. No interaction between Cosentyx and midazolam (CYP3A4 substrate) seen in adult psoriasis study. No interaction between Cosentyx and methotrexate and/or corticosteroids seen in arthritis studies. **Fertility, pregnancy and lactation:** *Women of childbearing potential:* Use an effective method of contraception during and for at least 20 weeks after treatment. *Pregnancy:* Preferably avoid use of Cosentyx in pregnancy. *Breast feeding:* It is not known if secukinumab is excreted in human breast milk. A clinical decision should be made on continuation of breast feeding during Cosentyx treatment (and up to 20 weeks after discontinuation) based on benefit of breast feeding to the child and benefit of Cosentyx therapy to the woman. *Fertility:* Effect on human fertility not evaluated. **Adverse Reactions**: *Very Common (≥1/10):* Upper respiratory tract infection. *Common (≥1/100 to <1/10):* Oral herpes, headache, rhinorrhoea, diarrhoea, nausea, fatigue. *Uncommon (≥1/1,000 to <1/100):* Oral candidiasis, lower respiratory tract infections, neutropenia, inflammatory bowel disease. *Rare (≥1/10,000 to <1/1,000)*: anaphylactic reactions, exfoliative dermatitis (psoriasis patients), hypersensitivity vasculitis. *Not known:* Mucosal and cutaneous candidiasis (including oesophageal candidiasis). *Infections:* Most infections were non-serious and mild to moderate upper respiratory tract infections, e.g. nasopharyngitis, and did not necessitate treatment discontinuation. There was an increase in mucosal and cutaneous (including oesophageal) candidiasis, but cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in a small proportion of patients (0.015 serious infections reported per patient year of follow up). *Neutropenia:* Neutropenia was more frequent with secukinumab than placebo, but most cases were mild, transient and reversible. Rare cases of neutropenia CTCAE Grade 4 were reported. *Hypersensitivity reactions:* Urticaria and rare cases of anaphylactic reactions were seen. *Immunogenicity:* Less than 1% of patients treated with Cosentyx developed antibodies to secukinumab up to 52 weeks of treatment. *Other Adverse Effects:* The list of adverse events is not exhaustive, please consult the SmPC for a detailed listing of all adverse events before prescribing. **Legal Category:** POM. **MA Number & List Price:** PLGB 00101/1205 – 75 mg pre-filled syringe x 1 - £304.70; PLGB 00101/1029 - 150 mg pre-filled pen x2 £1,218.78; PLGB 00101/1030 - 150 mg pre-filled syringe x2 £1,218.78; PLGB 00101/1198 – 300 mg pre-filled pen x 1 £1218.78. **PI Last Revised:** June 2023. Full prescribing information, (SmPC) is available from: Novartis Pharmaceuticals UK Limited, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, W12 7FQ. Telephone: (01276) 692255.

UK | 290802 | June 2023

Adverse Event Reporting:

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

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

Cosentyx® (secukinumab) Northern Ireland Prescribing Information.

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

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