

PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Cosentyx Subcutaneous Prior Authorization Policy

- Cosentyx® (secukinumab subcutaneous injection – Novartis)

REVIEW DATE: 11/01/2023; selected revision 11/15/2023

OVERVIEW

Cosentyx subcutaneous, an interleukin (IL)-17A antagonist, is indicated in the following conditions:¹

- **Enthesitis-related arthritis**, in patients ≥ 4 years of age with active disease.
- **Hidradenitis suppurativa**, in adults with moderate to severe disease.
- **Plaque psoriasis**, in patients ≥ 6 years of age with moderate to severe disease who are candidates for systemic therapy or phototherapy.
- **Psoriatic arthritis**, in patients ≥ 2 years of age with active disease.
- **Ankylosing spondylitis**, in adults with active disease.
- **Non-radiographic axial spondyloarthritis**, in adults with active disease and objective signs of inflammation.

In the pivotal trial for non-radiographic axial spondyloarthritis, patients were required to have objective signs of inflammation, indicated by elevated C-reactive protein and/or sacroiliitis on magnetic resonance imaging.

Guidelines

IL-17 blockers are mentioned in multiple guidelines for treatment of inflammatory conditions.

- **Enthesitis-Related Arthritis:** Guidelines for juvenile idiopathic arthritis from the American College of Rheumatology (ACR) [2018] address treatment of enthesitis-related arthritis.¹⁴ These recommendations were developed prior to approval of Cosentyx. A tumor necrosis factor inhibitor (TNFi) is recommended over use of methotrexate or sulfasalazine in those who have tried a nonsteroidal anti-inflammatory drug (NSAID).
 - **Plaque Psoriasis:** Joint guidelines of care for the management and treatment of psoriasis with biologics were published by the American Academy of Dermatology (AAD) and the National Psoriasis Foundation (2019).³ All of the biologics are generally recommended for treatment of moderate to severe disease. The AAD also recommends methotrexate (unless contraindicated) and other systemic therapies for treatment of moderate to severe psoriasis.⁴ Traditional systemic agents can benefit widespread psoriasis. Studies have assessed response to methotrexate following 6 weeks to 4 months of treatment.
 - **Psoriatic Arthritis:** Guidelines from ACR/National Psoriasis Foundation (2018) generally recommend TNFis as the first-line treatment strategy over other biologics (e.g., IL-17 blockers) with differing mechanisms of action.⁵
 - **Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis:** Guidelines for ankylosing spondylitis and non-radiographic axial spondyloarthritis are published by the ACR/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network (2019).² Following primary nonresponse to a TNFi, either Cosentyx or Taltz® (ixekizumab injection) is recommended; however, if the patient is a secondary nonresponder, a second TNFi is recommended over switching out of the class. In patients with a contraindication to a TNFi, use of an IL-17 blocker is recommended over traditional oral agents such as methotrexate or sulfasalazine.
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POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Cosentyx subcutaneous. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Cosentyx subcutaneous as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Cosentyx subcutaneous to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Cosentyx subcutaneous is recommended in those who meet the following criteria:

FDA-Approved Indications

- 1. Ankylosing Spondylitis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
 - A) Initial Therapy.** Approve for 6 months if prescribed by or in consultation with a rheumatologist.
 - B) Patient is Currently Receiving Cosentyx Subcutaneous or Intravenous.** Approve for 1 year if the patient meets BOTH of the following (i and ii):
 - i.** Patient has been established on Cosentyx subcutaneous or intravenous for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Cosentyx subcutaneous or intravenous is reviewed under criterion A (Initial Therapy).
 - ii.** Patient meets at least ONE of the following (a or b):
 - a)** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Cosentyx subcutaneous or intravenous); OR
Note: Examples of objective measures include Ankylosing Spondylitis Disease Activity Score (ASDAS), Ankylosing Spondylitis Quality of Life Scale (ASQoL), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Global Score (BAS-G), Bath Ankylosing Spondylitis Metrology Index (BASMI), Dougados Functional Index (DFI), Health Assessment Questionnaire for the Spondyloarthropathies (HAQ-S), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).
 - b)** Compared with baseline (prior to initiating Cosentyx subcutaneous or intravenous), patient experienced an improvement in at least one symptom, such as decreased pain or stiffness, or improvement in function or activities of daily living.
- 2. Enthesitis-Related Arthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
 - A) Initial Therapy.** Approve for 6 months if the patient meets both of the following (i and ii):
 - i.** Patient is ≥ 4 years of age; AND
 - ii.** The medication is prescribed by or in consultation with a rheumatologist.
 - B) Patient is Currently Receiving Cosentyx Subcutaneous.** Approve for 1 year if the patient meets BOTH of the following (i and ii):
 - i.** Patient has been established on Cosentyx subcutaneous for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Cosentyx subcutaneous is reviewed under criterion A (Initial Therapy).
 - ii.** Patient meets at least one of the following (a or b):

- a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Cosentyx subcutaneous); OR
Note: Examples of objective measures include the Juvenile Arthritis Disease Activity Score (JADAS); Physician Global Assessment (MD global), Parent/Patient Global Assessment of Overall Well-Being (PGA), Parent/Patient Global Assessment of Disease Activity (PDA), Juvenile Arthritis Disease Activity Score (JDAS), Clinical Juvenile Arthritis Disease Activity Score (cJDAS), Juvenile Spondyloarthritis Disease Activity Index (JSpADA), serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), and/or reduced dosage of corticosteroids.
 - b) Compared with baseline (prior to initiating Cosentyx subcutaneous), patient experienced an improvement in at least one symptom, such as improvement in limitation of motion, less joint pain or tenderness, decreased duration of morning stiffness or fatigue, improved function or activities of daily living.

 3. **Hidradenitis Suppurativa.** Approve for the duration noted if the patient meets ONE of the following criteria (A or B):
 - A) Initial Therapy. Approve for 3 months if the patient meets BOTH of the following (i, ii, and iii):
 - i. Patient is \geq 18 years of age; AND
 - ii. Patient has tried at least one other therapy; AND
Note: Examples include intralesional or oral corticosteroids (e.g., triamcinolone, prednisone), systemic antibiotics (e.g., clindamycin, dicloxacillin, erythromycin), and isotretinoin.
 - iii. The medication is prescribed by or in consultation with a dermatologist.
 - B) Patient is Currently Receiving Cosentyx Subcutaneous. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
 - i. Patient has been established on therapy for at least 90 days; AND
Note: A patient who has received < 90 days of therapy or who is restarting therapy with Cosentyx subcutaneous is reviewed under criterion A (Initial Therapy).
 - ii. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Cosentyx subcutaneous); AND
Note: Examples of objective measures include Hurley staging, Sartorius score, Physician Global Assessment, and Hidradenitis Suppurativa Severity Index.
 - iii. Compared with baseline (prior to initiating Cosentyx subcutaneous), patient experienced an improvement in at least one symptom, such as decreased pain or drainage of lesions, nodules, or cysts.

 4. **Non-Radiographic Axial Spondyloarthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
 - A) Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):
 - i. Patient has objective signs of inflammation, defined as at least ONE of the following (a or b):
 - a) C-reactive protein elevated beyond the upper limit of normal for the reporting laboratory; OR
 - b) Sacroiliitis reported on magnetic resonance imaging; AND
 - ii. The medication is prescribed by or in consultation with a rheumatologist.
 - B) Patient is Currently Receiving Cosentyx Subcutaneous or Intravenous. Approve for 1 year if the patient meets BOTH of the following (i and ii):
 - i. Patient has been established on Cosentyx subcutaneous or intravenous for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Cosentyx subcutaneous or intravenous is reviewed under criterion A (Initial Therapy).
 - ii. Patient meets at least ONE of the following (a or b):
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- a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Cosentyx subcutaneous or intravenous); OR
Note: Examples of objective measures include Ankylosing Spondylitis Disease Activity Score (ASDAS), Ankylosing Spondylitis Quality of Life Scale (ASQoL), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Global Score (BAS-G), Bath Ankylosing Spondylitis Metrology Index (BASMI), Dougados Functional Index (DFI), Health Assessment Questionnaire for the Spondyloarthropathies (HAQ-S), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).
 - b) Compared with baseline (prior to initiating Cosentyx subcutaneous or intravenous), patient experienced an improvement in at least one symptom, such as decreased pain or stiffness, or improvement in function or activities of daily living.
- 5. Plaque Psoriasis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
- A) Initial Therapy. Approve for 3 months if the patient meets ALL of the following criteria (i, ii, and iii):
 - i. Patient is ≥ 6 years of age; AND
 - ii. Patient meets ONE of the following conditions (a or b):
 - a) Patient has tried at least at least one traditional systemic agent for psoriasis for at least 3 months, unless intolerant; OR
Note: Examples include methotrexate, cyclosporine, acitretin, or psoralen plus ultraviolet A light (PUVA). An exception to the requirement for a trial of one traditional systemic agent for psoriasis can be made if the patient has already had a 3-month trial or previous intolerance to at least one biologic other than Cosentyx. A biosimilar of Cosentyx does not count. Refer to [Appendix](#) for examples of biologics used for psoriasis. A patient who has already tried a biologic for psoriasis is not required to “step back” and try a traditional systemic agent for psoriasis.
 - b) Patient has a contraindication to methotrexate, as determined by the prescriber; AND
 - iii. The medication is prescribed by or in consultation with a dermatologist.
 - B) Patient is Currently Receiving Cosentyx Subcutaneous. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
 - i. Patient has been established on Cosentyx subcutaneous for at least 90 days; AND
Note: A patient who has received < 90 days of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).
 - ii. Patient experienced a beneficial clinical response, defined as improvement from baseline (prior to initiating Cosentyx subcutaneous) in at least one of the following: estimated body surface area, erythema, induration/thickness, and/or scale of areas affected by psoriasis; AND
 - iii. Compared with baseline (prior to initiating Cosentyx subcutaneous), patient experienced an improvement in at least one symptom, such as decreased pain, itching, and/or burning.
- 6. Psoriatic Arthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
- A) Initial Therapy. Approve for 6 months if the patient meets both of the following (i and ii):
 - i. Patient is ≥ 2 years of age; AND
 - ii. The medication is prescribed by or in consultation with a rheumatologist or a dermatologist.
 - B) Patient is Currently Receiving Cosentyx Subcutaneous or Intravenous. Approve for 1 year if the patient meets BOTH of the following (i and ii):
 - i. Patient has been established on Cosentyx subcutaneous or intravenous for at least 6 months; AND
Note: A patient who has received < 6 months of therapy with Cosentyx subcutaneous or intravenous or who is restarting therapy is reviewed under criterion A (Initial Therapy).
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- ii. Patient meets at least ONE of the following (a or b):
 - a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Cosentyx subcutaneous or intravenous); OR
Note: Examples of standardized measures of disease activity include Disease Activity Index for Psoriatic Arthritis (DAPSA), Composite Psoriatic Disease Activity Index (CPDAI), Psoriatic Arthritis Disease Activity Score (PsA DAS), Grace Index, Leeds Enthesitis Score (LEI), Spondyloarthritis Consortium of Canada (SPARCC) enthesitis score, Leeds Dactylitis Instrument Score, Minimal Disease Activity (MDA), Psoriatic Arthritis Impact of Disease (PsAID-12), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).
 - b) Compared with baseline (prior to initiating Cosentyx subcutaneous or intravenous), patient experienced an improvement in at least one symptom, such as less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Cosentyx subcutaneous is not recommended in the following situations:

1. **Concurrent Use with other Biologics or Targeted Synthetic Disease-Modifying Antirheumatic Drugs (DMARDs).** Cosentyx should not be administered in combination with another biologic or targeted synthetic DMARD used for an inflammatory condition (See [Appendix](#) for examples). Combination therapy is generally not recommended due to the potential for a higher rate of adverse effects with combination therapies and lack of evidence for additive efficacy.
Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Cosentyx.
 2. **Crohn's Disease.** Exacerbations of Crohn's disease, in some cases serious, occurred in clinical trials in patients treated with Cosentyx.¹ In a Phase II published study in patients with Crohn's disease (n = 59), an intravenous formulation of Cosentyx did not reduce the Crohn's disease activity index by ≥ 50 points compared with placebo and the study was terminated prematurely.⁶
 3. **Rheumatoid Arthritis.** In a published, double-dummy Phase III study, Cosentyx was less effective than current treatments in patients with rheumatoid arthritis who were previously treated with a tumor necrosis factor inhibitor (TNFi).⁷ Patients were randomized to one of four treatment groups: 1) induction with an intravenous formulation of Cosentyx (10 mg/kg) followed by Cosentyx 150 mg subcutaneously given once every 4 weeks (Q4W) [n = 137]; 2) secukinumab intravenous induction (10 mg/kg) followed by Cosentyx 75 mg subcutaneously Q4W (n = 138). At Week 24, ACR 20 response was significantly better with Cosentyx 150 mg subcutaneous (31%) and Orencia (abatacept intravenous [IV] injection) [43%] vs. placebo (18%). ACR 20 response with Cosentyx 75 mg was 28%, which was not significantly better than the placebo group. ACR 50/70 responses were 17%/10%, respectively, with Cosentyx 150 mg and 12%/5%, respectively, with Cosentyx 75 mg which were not significantly different from that of placebo (9%/5%, respectively). The group treated with Orencia intravenous had significantly improved ACR 50/70 responses at Week 24 (28%/12%). Using as observed data, ACR 20/50/70 responses at Week 52 were 63%/46%/19%, respectively, with Cosentyx 150 mg, 57%/26%/7%, respectively, with Cosentyx 75 mg, and 75%/52%/23%, respectively, with Orencia intravenous. There is a published Phase II dose-ranging study (n = 237) evaluating Cosentyx in rheumatoid arthritis.⁸⁻¹⁰ The ACR 20 response at Week 16 (using last observation carried forward analysis) was 34%, 46.9%, 46.5%, 53.7% for the 25, 75, 150, and 300 mg doses, respectively, vs. 36% for placebo; however, this did not achieve statistical significance. After Week 16, patients who
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responded to Cosentyx had sustained response through Week 52, with patients on the 150 mg dose having the greatest improvement over time (55% and 40% of patients with ACR 50 and ACR 70 responses, respectively, at Week 52). In another Phase II study, Cosentyx did not achieve higher ACR 20 response rates at Week 12 vs. placebo.¹¹ There was an open-label treatment period where ACR responses were generally maintained through Week 52. Some patients were treated with an intravenous formulation of secukinumab and generally responded similarly to those treated with Cosentyx. In another Phase II study, an intravenous formulation of secukinumab demonstrated limited efficacy in biologic-naïve patients with rheumatoid arthritis associated with the HLA-DRB1 allele.¹²

4. **Uveitis.** Efficacy is not established for this condition. There was not a statistically significant difference between Cosentyx subcutaneous and placebo in three Phase III studies that included patients with Behcet’s uveitis (n = 118); active, noninfectious, non-Behcet’s uveitis (n = 31); and quiescent, noninfectious, non-Behcet’s uveitis (n = 125) [SHEILD, INSURE, and ENDURE studies, respectively].¹³
5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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3. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol.* 2019;80(4):1029-1072.
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12. Burmester GR, Durez P, Shestakova G, et al. Association of HLA-DRB1 alleles with clinical responses to the anti-interleukin-17A monoclonal antibody secukinumab in active rheumatoid arthritis. *Rheumatology (Oxford).* 2016;55(1):49-55.
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14. Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for non-systemic polyarthritis, sacroiliitis, and enthesitis. *Arthritis Rheumatol.* 2019;71(6):846-863.

HISTORY

Type of Revision	Summary of Changes	Review Date
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Inflammatory Conditions – Cosentyx Subcutaneous PA Policy

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Early Annual Revision	Enthesitis-Related Arthritis: Criteria were added for this newly approved condition. Psoriatic Arthritis: A criterion was added to align with the approved age indication for a patient who is ≥ 2 years of age. Previously age was not specifically addressed.	01/26/2022
Annual Revision	No criteria changes.	02/15/2023
Early Annual Revision	Policy name was updated to specify this is for the subcutaneous formulation of Cosentyx. Enthesitis-Related Arthritis: For a patient currently receiving Cosentyx, it was clarified this applies to the subcutaneous formulation. Plaque Psoriasis: For a patient currently receiving Cosentyx, it was clarified this applies to the subcutaneous formulation. Psoriatic Arthritis: For a patient currently receiving Cosentyx, it was clarified this applies to the subcutaneous or intravenous formulation. Ankylosing Spondylitis: For a patient currently receiving Cosentyx, it was clarified this applies to the subcutaneous or intravenous formulation. Non-Radiographic Axial Spondyloarthritis: For a patient currently receiving Cosentyx, it was clarified this applies to the subcutaneous or intravenous formulation.	11/01/2023
Selected Revision	Hidradenitis Suppurativa: This condition and criteria for approval was added to the policy.	11/15/2023

APPENDIX

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		
Adalimumab SC Products (Humira [®] , biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia[®] (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel [®] , biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA
Zymfentra[®] (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC
Infliximab IV Products (Remicade [®] , biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Simponi[®], Simponi[®] Aria[™] (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC IV formulation: AS, PJIA, PsA, RA
Actemra[®] (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA IV formulation: PJIA, RA, SJIA
Kezara[®] (sarilumab SC injection)	Inhibition of IL-6	RA, PMR
Orencia[®] (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan [®] , biosimilars)	CD20-directed cytolytic antibody	RA
Kineret[®] (anakinra SC injection)	Inhibition of IL-1	JIA [^] , RA
Stelara[®] (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC IV formulation: CD, UC
Siliq[™] (brodalumab SC injection)	Inhibition of IL-17RA	PsO
Bimzelx[®] (bimekizumab-bkzx SC injection)	Inhibition of IL-17A and IL-17F	PsO
Cosentyx[®] (secukinumab SC injection, secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA IV formulation: AS, nr-axSpA, PsA
Taltz[®] (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya[™] (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi[®] (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO IV formulation: CD
Tremfya[™] (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio[™] (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	SC formulation: UC IV formulation: CD, UC
Oral Therapies/Targeted Synthetic DMARDs		
Otezla[®] (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo[™] (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant[®] (baricitinib tablets)	Inhibition of JAK pathways	RA
Rinvoq[®] (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, UC
Sotyktu[™] (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz[®] (tofacitinib tablets)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz[®] XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indications (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn’s disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; PMR – Polymyalgia rheumatic; [^] Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; TYK2 – Tyrosine kinase 2.