Effective Date **7/15/2024**
Coverage Policy Number **IP0229**

Upadacitinib

Table of Contents

Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following upadacitinib products:

- Rinvoq® (upadacitinib extended-release tablets – AbbVie)
- Rinvoq® LQ (upadacitinib oral solution – AbbVie)

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Upadacitinib (Rinvoq, Rinvoq LQ) is considered medically necessary when ONE of the following are met:

1. **Ankylosing Spondylitis [Rinvoq extended-release tablets (not Rinvoq LQ oral solution)].** Individual meets **ALL** of the following:
    A. 18 years of age or older
    B. Documentation of **ONE** of the following:
        i. For Non-axial disease, **ONE** of the following:

a. Failure to **ONE** conventional synthetic disease-modifying anti-rheumatic drug (csDMARD)
b. Contraindication or intolerance to csDMARD therapy

ii. For Axial disease, failure, contraindication or intolerance to **ONE** nonsteroidal anti-inflammatory drug (NSAID)
iii. Already tried a biologic or targeted synthetic DMARD for Ankylosing Spondylitis

C. Documentation of **ONE** of the following:
i. Failure to **ONE** tumor necrosis factor inhibitor (TNFi)
ii. Contraindication or intolerance to TNF inhibitors
D. Medication is being prescribed by, or in consultation with, rheumatologist
E. Preferred Product Step Therapy Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plans]

2. **Atopic Dermatitis, Moderate to Severe [Rinvoq extended-release tablets (not Rinvoq LQ oral solution)].** Individual meets **ALL** of the following criteria:
A. 12 years of age or older
B. Documentation of **ONE** of the following:
i. Failure after at least 3 months to **ONE** conventional systemic therapy
ii. Contraindication or intolerance to **ALL** conventional systemic therapy
iii. Already tried Dupixent (dupilumab) or Adbry (tralokinumab-ldrm)
C. Medication is prescribed by, or in consultation with, an allergist, immunologist or dermatologist

3. **Crohn's Disease [Rinvoq extended-release tablets (not Rinvoq LQ oral solution)].** Individual meets **ALL** of the following criteria:
A. 18 years of age or older
B. Medication is prescribed by, or in consultation, with a gastroenterologist
C. Preferred Product Step Therapy Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plans]

4. **Juvenile Idiopathic Arthritis (JIA) [Rinvoq extended-release tablets or Rinvoq LQ oral solution].** Individual meets **ALL** of the following criteria:
A. **ONE** of the following:
i. Individual has had a 3-month trial of at least one tumor necrosis factor inhibitor
ii. Individual has tried at least one tumor necrosis factor inhibitor but was unable to tolerate a 3-month trial; AND
Note: Refer to Appendix for examples of tumor necrosis factor inhibitors. Conventional synthetic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine do not count.
B. The medication is prescribed by or in consultation with a rheumatologist
C. Preferred Product Step Therapy Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plans]

5. **Non-Radiographic Axial Spondyloarthritis (nr-axSpA) [Rinvoq extended-release tablets (not Rinvoq LQ oral solution)].** Individual meets **ALL** of the following criteria:
A. Has objective signs of inflammation, defined as **ONE** of the following:
i. C-reactive protein (CRP) elevated beyond the upper limit of normal for the reporting laboratory
ii. Sacroiliitis reported on magnetic resonance imaging (MRI)
B. Documentation of **ONE** of the following:
i. Failure after at least 3 months to **ONE** tumor necrosis factor inhibitor (TNFi)
ii. Contraindication or intolerance to TNF inhibitors

C. Medication is being prescribed by, or in consultation with, a rheumatologist

6. **Psoriatic Arthritis [Rinvoq extended-release tablets or Rinvoq LQ oral solution].** Individual meets **ALL** of the following criteria:
    A. 2 years of age or older
    B. Documentation of **ONE** of the following:
        i. For Non-axial disease, **ONE** of the following:
            a. Failure to **ONE** disease-modifying anti-rheumatic drug (DMARD)
            b. Contraindication or intolerance to **ALL** disease-modifying anti-rheumatic drug (DMARD) therapy
        ii. For Axial disease, **ONE** of the following:
            a. Failure to **ONE** disease-modifying anti-rheumatic drug (DMARD), OR a nonsteroidal anti-inflammatory drug (NSAID)
            b. Contraindication or intolerance to **ALL** systemic therapy such as disease-modifying anti-rheumatic drug (DMARD) therapy, AND nonsteroidal anti-inflammatory drugs (NSAIDs)
        iii. Already tried a biologic or targeted synthetic DMARD
    C. Documentation of **ONE** of the following:
        i. Failure after at least 3 months to **ONE** tumor necrosis factor inhibitor (TNFi)
        ii. Contraindication or intolerance to TNF inhibitors
    D. Medication is being prescribed by, or in consultation with, a rheumatologist or dermatologist
    E. Preferred Product Step Therapy Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plans]

7. **Rheumatoid Arthritis [Rinvoq extended-release tablets (not Rinvoq LQ oral solution)].** Individual meets **ALL** of the following criteria:
    A. 18 years of age or older
    B. Documentation of **ONE** of the following:
        i. Failure after 3 months to **ONE** conventional synthetic disease-modifying anti-rheumatic drug (csDMARD)
        ii. Contraindication or intolerance to **ALL** conventional synthetic DMARDs
        iii. Already tried a biologic or targeted synthetic DMARD
    C. Documentation of **ONE** of the following:
        i. Failure after at least 3 months to **ONE** tumor necrosis factor inhibitor (TNFi)
        ii. Contraindication or intolerance to TNF inhibitors
    D. Medication is being prescribed by, or in consultation with, a rheumatologist
    E. Preferred Product Step Therapy Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plans]

8. **Ulcerative Colitis [Rinvoq extended-release tablets (not Rinvoq LQ oral solution)].** Individual meets **ALL** of the following criteria:
    A. 18 years of age or older
    B. Medication is being prescribed by, or in consultation with, a gastroenterologist
    C. Preferred Product Step Therapy Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plans]

Coverage varies across plans and requires the use of preferred products. Refer to the customer's benefit plan document for coverage details.

Employer Group Plans	
Condition	**Preferred Product with Step Therapy Criteria**
Ankylosing Spondylitis	For Rinvoq extended-release tablets (not Rinvoq LQ oral solution) Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **adalimumab – adbm/ Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Atopic Dermatitis	**Preferred** [requires prior authorization]
Crohn's Disease	For Rinvoq extended-release tablets (not Rinvoq LQ oral solution) Documentation of failure, contraindication, or intolerance to **ONE** of the following **adalimumab products**: A. **Adalimumab-adaz or Hyrimoz** (by Sandoz/Novartis) [requires prior authorization] B. **Adalimumab - adbm or Cyltezo** [requires prior authorization] C. **Adalimumab-ryvk** or **Simlandi** [requires prior authorization] D. **Humira** (by AbbVie) [requires prior authorization]
Juvenile Idiopathic Arthritis (JIA)	For Rinvoq extended-release tablets or Rinvoq LQ oral solution Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **adalimumab – adbm/ Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Psoriatic Arthritis	For Rinvoq extended-release tablets or Rinvoq LQ oral solution Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **adalimumab – adbm/ Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Rheumatoid Arthritis	For Rinvoq extended-release tablets (not Rinvoq LQ oral solution) Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **adalimumab – adbm/ Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Ulcerative Colitis	For Rinvoq extended-release tablets (not Rinvoq LQ oral solution) Documentation of failure, contraindication, or intolerance to **ONE** of the following adalimumab products: A. **Adalimumab-adaz or Hyrimoz** (by Sandoz/Novartis) [requires prior authorization] B. **Adalimumab - adbm or Cyltezo** [requires prior authorization] C. **Adalimumab-ryvk** or **Simlandi** [requires prior authorization] D. **Humira** (by AbbVie) [requires prior authorization]

Individual and Family Plan	
Condition	**Preferred Product with Step Therapy Criteria**
Ankylosing Spondylitis	For Rinvoq extended-release tablets (not Rinvoq LQ oral solution) Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **Adalimumab – adbm/Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Atopic Dermatitis	**Preferred** [requires prior authorization]
Crohn's Disease	For Rinvoq extended-release tablets (not Rinvoq LQ oral solution) Documentation of failure, contraindication, or intolerance to **ONE** of the following **adalimumab products:** A. **Adalimumab-adaz or Hyrimoz** (by Sandoz/Novartis) [requires prior authorization] B. **Adalimumab - adbm or Cyltezo** [requires prior authorization] C. **Adalimumab-ryvk** or **Simlandi** [requires prior authorization] D. **Humira** (by AbbVie) [requires prior authorization]
Juvenile Idiopathic Arthritis (JIA)	For Rinvoq extended-release tablets or Rinvoq LQ oral solution Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **Adalimumab – adbm/Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Psoriatic Arthritis	For Rinvoq extended-release tablets or Rinvoq LQ oral solution Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **Adalimumab – adbm/Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Rheumatoid Arthritis	For Rinvoq extended-release tablets (not Rinvoq LQ oral solution) Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **Adalimumab – adbm/Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Ulcerative Colitis	For Rinvoq extended-release tablets (not Rinvoq LQ oral solution) Documentation of failure, contraindication, or intolerance to **ONE** of the following **adalimumab products:** A. **Adalimumab-adaz or Hyrimoz** (by Sandoz/Novartis) [requires prior authorization] B. **Adalimumab - adbm or Cyltezo** [requires prior authorization] C. **Adalimumab-ryvk** or **Simlandi** [requires prior authorization]

Individual and Family Plan	
Condition	**Preferred Product with Step Therapy Criteria**
	D. **Humira** (by AbbVie) [requires prior authorization]

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of upadacitinib (Rinvoq) is considered medically necessary for **ALL** covered diagnoses when initial criteria are met AND beneficial response is demonstrated.

Authorization Duration

Initial approval duration is up to 12 months.
Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Alopecia.** Insufficient efficacy and safety data to support use in alopecia. Rinvoq is not indicated for this use.[1]

2. **Concurrent Use with a Biologic or with a Targeted Synthetic Disease-Modifying Antirheumatic Drug (tsDMARD).** Rinvoq should not be administered in combination with a biologic used for an inflammatory condition (see Appendix for examples).[1] Combination therapy is generally not recommended due to a potential for a higher rate of adverse effects with combinations and lack of evidence supporting additive efficacy. There are no data evaluating combination of Rinvoq with other targeted synthetic DMARD (e.g., Otezla [apremilast tablets], Xeljanz/XR [tofacitinib tablets/extended-release tablets], Olumiant [baricitinib tablets]); therefore, safety and efficacy of this combination is unknown.

3. **Concurrent use with an Anti-Interleukin Monoclonal Antibody.** Rinvoq is not recommended in combination with biologic immunomodulators such as Dupixent® (dupilumab subcutaneous injection or Adbry® (tralokinumab-ldrm subcutaneous injection).[1]

4. **Concurrent use with Xolair® (omalizumab subcutaneous injection**). Rinvoq is not recommended in combination with biologic immunomodulators such as Xolair.[1]

5. **COVID-19 (Coronavirus Disease 2019).** This includes requests for cytokine release syndrome associated with COVID-19.

6. **Vitiligo.** Insufficient efficacy and safety data to support use in vitiligo. Rinvoq is not indicated for this use.[1] A small case series of 10 individuals with vitiligo were treated with JAK inhibitors. Five subjects achieved some repigmentation at sites of either sunlight exposure or low dose nbUVB light. The authors stated that JAK monotherapy does not seem to be effective but appears to need concurrent nbUVB phototherapy or sunlight exposure. The authors concluded that prospective clinical trials are necessary to evaluate the use of JAK inhibitors in vitiligo. This study was limited by small sample size, retrospective design and no control group.[11]

Background

OVERVIEW

Rinvoq, a Janus kinase inhibitor (JAKi), is indicated for the following uses:[1]

- **Ankylosing spondylitis**, for treatment of active disease in adults who have had an inadequate response or intolerance to one or more tumor necrosis factor inhibitors (TNFis).
- **Atopic dermatitis**, for treatment of refractory, moderate to severe atopic dermatitis in patients ≥ 12 years of age, whose disease is not adequately controlled with other systemic drug products (including biologics) or when those therapies are not advisable.
- **Crohn's disease**, for treatment of moderately to severely active disease in adults who have had an inadequate response or intolerance to one or more TNFis.
- **Non-radiographic axial spondyloarthritis**, in adults with objective signs of inflammation who have had an inadequate response or intolerance to one or more TNFis.
- **Polyarticular juvenile idiopathic arthritis (JIA)**, in patients ≥ 2 years of age with active disease who have had an inadequate response or intolerance to one or more TNFis.
- **Psoriatic arthritis**, for treatment of active disease in in patients ≥ 2 years of age who have had an inadequate response or intolerance to one or more TNFis.
- **Rheumatoid arthritis**, for treatment of moderately to severely active disease in adults who have had an inadequate response or intolerance to one or more TNFis.
- **Ulcerative colitis**, for treatment of moderately to severely active disease in adults who have had an inadequate response or intolerance to one or more TNFis.

Rinvoq LQ oral solution is only indicated for use in **polyarticular JIA** and **psoriatic arthritis in patients 2 to < 18 years of age**.[1] Rinvoq LQ oral solution is not substitutable with Rinvoq extended-release tablets.

For all indications, Rinvoq/Rinvoq LQ is not recommended for use in combination with other JAKis, biologics, or potent immunosuppressants such as azathioprine or cyclosporine.[1]

Guidelines

Guidelines are available for treatment of inflammatory conditions:

- **Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis:** Current guidelines do not address Rinvoq. Guidelines from the American College of Rheumatology (ACR)/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network (2019) recommend a TNFi as the initial biologic.[2] In those who are secondary non-responders to a TNFi, a second TNFi is recommended over switching out of the class. Both TNFis and interleukin (IL)-17 blockers are recommended over Xeljanz®/Xeljanz® XR (tofacitinib tablets/tofacitinib extended release tablets).
- **Atopic Dermatitis:** Guidelines for the care and management of atopic dermatitis from the American Academy of Dermatology (2023) and the American Academy of Allergy, Asthma and Immunology (2023) have been updated to address Rinvoq.[3,4] Systemic therapies are recommended in patients with moderate to severe or widespread disease, in those with impaired quality of life, and those whose atopic dermatitis is refractory to topical therapies. Biologic agents, such as Dupixent® (dupilumab subcutaneous injection) or Adbry® (tralokinumab-ldrm subcutaneous injection), are recommended as initial systemic treatment due to their favorable efficacy and safety profiles compared to traditional systemic therapies (e.g., azathioprine, cyclosporine, methotrexate, mycophenolate mofetil). Rinvoq may be considered in adults refractory or intolerant to Dupixent or Adbry.
- **Crohn's Disease:** Current guidelines do not address Rinvoq. The American College of Gastroenterology (ACG) has guidelines for Crohn's disease (2018).[5] TNFis are listed as an option for disease that is resistant to corticosteroids, severely active disease, perianal fistulizing disease, and maintenance of remission. In post-operative Crohn's disease, a TNFi should be started within 4 weeks of surgery to prevent recurrence. Guidelines from the American Gastroenterological Association (AGA) [2021] include TNFis among the therapies for moderate to severe Crohn's disease, for induction and maintenance of remission.[6]
- **JIA:** Rinvoq is not addressed in ACR/Arthritis Foundation guidelines for the treatment of JIA (2019) specific to juvenile non-systemic polyarthritis, sacroiliitis, and enthesitis.[11] TNFis are the biologics recommended for polyarthritis, sacroiliitis, and enthesitis. Actemra® (tocilizumab intravenous infusion, tocilizumab

subcutaneous injection) and Orencia® (abatacept intravenous infusion, abatacept subcutaneous injection) are also among the biologics recommended for polyarthritis. Biologics are recommended following other therapies (e.g., following DMARDs for active polyarthritis or following a nonsteroidal anti-inflammatory drug for active JIA with sacroiliitis or enthesitis). However, there are situations where initial therapy with a biologic may be preferred over other conventional therapies (e.g., if there is involvement of high-risk joints such as the cervical spine, wrist, or hip; high disease activity; and/or those judged to be at high risk of disabling joint damage).

- **Psoriatic Arthritis:** Current guidelines do not address Rinvoq. Guidelines from ACR (2018) recommend TNFis over other biologics and Xeljanz for use in treatment-naïve patients with psoriatic arthritis and in those who were previously treated with an oral therapy.[7]
- **Rheumatoid Arthritis:** Guidelines from ACR (2021) recommend addition of a biologic or a targeted synthetic disease-modifying antirheumatic drug (DMARD) for a patient taking the maximum tolerated dose of methotrexate who is not at target.[8]
- **Ulcerative Colitis:** Rinvoq has not yet been addressed in guidelines. Guidelines from the American College of Gastroenterology for ulcerative colitis (2019) note that the following agents can be used for induction of remission in moderately to severely active disease: budesonide extended-release tablets, oral or intravenous systemic corticosteroids, Entyvio® (vedolizumab intravenous infusion), Xeljanz/Xeljanz XR, or TNFis.[9] Guidelines from the American Gastroenterological Association (2020) recommend Xeljanz only after failure of or intolerance to a TNFi.[10]

References

1. Rinvoq® tablets/Rinvoq LQ oral solution [prescribing information]. North Chicago, IL: AbbVie; April 2024.
2. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*. 2021;73(7):1108-1123.
3. Davis DMR, Drucker AM, Alikhan A, et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *J Am Acad Dermatol*. 2023 Nov 3 [Epub ahead of print].
4. Chu DK, Schneider L, Asiniwasis RN, et al. Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE-and Institute of Medicine-based recommendations. *Ann Allergy Asthma Immunol.* 2023 Dec 18:S1081-1206(23)01455-2.
5. Feuerstein JD, Ho EY, Shmidt E, et al. AGA clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing Crohn's disease. *Gastroenterology*. 2021;160(7):2496-2508
6. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol.* 2018;113(4):481-517.
7. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. *Arthritis Care Res (Hoboken).* 2019;71(1):2-29.
8. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*. 2021;73(7):1108-1123.
9. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.
10. Feuerstein JD, Isaac s KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. *Gastroenterology*. 2020;158:1450-1461.
11. Ward MM, Deodhar A, Gensler LS, et al. 2019 update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol*. 2019;71(10):1599-1613.

APPENDIX

Table 1. Approved TNFis for Targeted Indications.

	Rheumatology					Dermatology	Gastroenterology	
	RA	JIA	AS	nr-axSpA	PsA	PsO	CD	UC
Tumor Necrosis Factor Inhibitors								

Cimzia	√	--	√	√	√	√	√	--
Enbrel	√	√	√	--	√	√	--	--
Adalimumab products (Humira, biosimilars)	√	√	√	--	√	√	√	√
Infliximab Products	√	--	√	--	√	√	√	√
Simponi Subcutaneous	√	--	√	--	√	--	--	√
Simponi Aria	√	√	√	--	√	--	--	--

TNFis – Tumor necrosis factor inhibitors; RA – Rheumatoid arthritis; JIA – Juvenile idiopathic arthritis; AS – Ankylosing spondylitis; nr-axSpA – Non-radiographic spondyloarthritis; PsA – Psoriatic arthritis; PsO – Plaque psoriasis; CD – Crohn's disease; UC – Ulcerative colitis.

Table 2. Approved IL-17, IL-23, and IL-12/23 Blockers for Targeted Indications.

	Rheumatology				Dermatology		Gastroenterology	
	Ankylosing Spondylitis	**ERA**	**nr-axSpA**	**PsA**	**AD**	**Plaque Psoriasis**	**Crohn's Disease**	**Ulcerative Colitis**
Interleukin-13 Blocker								
Adbry	--	--	--	--	√	--	--	--
Interleukin-17 Blockers								
Cosentyx	√	√	√	√	--	√	--	--
Siliq	--	--		--	--	√	--	--
Taltz	√	--	√	√	--	√	--	--
Interleukin-23 Blockers								
Ilumya	--	-- --	--	--	--	√	--	--
Skyrizi	--	--	--	√	--	√	√	--
Tremfya	--	--	--	√	--	√	--	--
Interleukin-12/23 Blockers								
Stelara Subcutaneous	--	--	--	√	--	√	√^	√^
Stelara Intravenous	--	--	--	--	--	--	√#	√#

AD - Atopic Dermatitis, ERA - Enthesitis-Related Arthritis, IL – Interleukin; nr-axSpA – Non-radiographic spondyloarthritis; ^ Maintenance dosing only; # Induction dosing only.

Table 3. Approved tsDMARDs for Targeted Indications.

	Rheumatology					Dermatology	Gastro-enterology
	Rheumatoid Arthritis	**Juvenile Idiopathic Arthritis**	**Ankylosing Spondylitis**	**nr-axSpA**	**Psoriatic Arthritis**	**Plaque Psoriasis**	**Ulcerative Colitis**
Janus Kinases Inhibitors							
Olumiant	√	--	--	--	--	--	--
Opzulera	--	--	--	--	--	--	--
Rinvoq	√	--	√	√	√	--	√
Xeljanz tablets	√	√#	√	--	√	--	√
Xeljanz oral solution	--	√#	--	--	--	--	--
Xeljanz XR	√	--	√	--	√	--	√
Phosphodiesterase Type 4 Inhibitor							
Otezla	--	--	--	--	√	√	--
Sphingosine 1-Phosphate Receptor Modulator							
Zeposia	--	--	--	--	--	--	√
Tyrosine Kinase 2 Inhibitor							

	Rheumatology					Dermatology	Gastro-enterology
	Rheumatoid Arthritis	**Juvenile Idiopathic Arthritis**	**Ankylosing Spondylitis**	**nr-axSpA**	**Psoriatic Arthritis**	**Plaque Psoriasis**	**Ulcerative Colitis**
Sotyktu	--	--	--	--	--	√	--

tsDMARDs – Targeted synthetic disease-modifying antirheumatic drugs; # Indicated in polyarticular JIA.

Table 4. Other Approved Biologics for Targeted Indications.

	Rheumatology		
	Rheumatoid Arthritis	**Juvenile Idiopathic Arthritis**	**Psoriatic Arthritis**
Interleukin-6 Blockers			
Actemra Intravenous	√	√^	--
Actemra Subcutaneous	√	√^	--
Kevzara	√	--	--
Interleukin-1 Blocker			
Kineret	√	--	--
T-Cell Costimulation Modulator			
Orencia Intravenous	√	√#	√
Orencia Subcutaneous	√	√#	√
CD20-Directed Cytolytic Antibody			
Rituximab Intravenous Products	√	--	--

^ Indicated in polyarticular and systemic JIA; # Indicated in polyarticular JIA.