MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY:	Psoriatic Arthritis (PsA)	**P&T DATE**	5/11/21
CLASS:	Rheumatology/Anti-Inflammatory Disorders	**REVIEW HISTORY**	5/20, 5/19, 2/18, 2/17, 2/16, 5/15, 10/14, 2/13, 2/12, 11/12, 5/10, 2/08, 6/08, 2/07
LOB:	MCL		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

OVERVIEW

Psoriatic arthritis (PsA) is an inflammatory condition that usually involves small joints and skin. Individuals with PsA exhibit both arthritis and psoriasis (PsO) symptoms (i.e. joint pain/stiffness, joint swelling, psoriatic plaque development, and/or nail disfiguration). This review will examine the treatment guidelines of PsA, the currently available PsA drug products, and their coverage criteria.

Severe Psoriatic Arthritis*	Severe Psoriasis*
Erosive disease	Psoriasis area & Severity Index (PASI) ≥12
Elevated markers of inflammation (ESR, CRP)	Body surface area (BSA) ≥ 10
Long-term damage that interferes with function and causing major impairment in quality of life	Significant involvement in specific areas (e.g, face, hands or feet, nails intertriginous areas, scalp)
Many affected sites including dactylitis, enthesitis	Burden of the disease causing significant disability
Function-limiting PsA at a few sites, rapidly progressive disease	Impairment of physical or mental function and the designation of moderate-to-severe disease despite lower BSA

*The definition of severe PsA and psoriasis as the presence of 1 or more of the items listed. This is not a formal definition. Table adapted from the 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis.

Available Psoriatic Arthritis Agents *(Current as of 02/2021)*

Systemic Agents					
Therapeutic Class	**Generic Name (Brand Name)**	**Available Strengths**	**Fml Limits**	**Cost/ Month***	**Notes**
Oral DMARDs	Azathioprine (Imuran)	50mg, 75mg, 100mg	-	$24.20	
	Cyclosporine, micronized	25mg, 100mg Capsule	-	$152.81	Regular cyclosporine is non-formulary.
	Leflunomide (Arava)	10mg Tablet	-	$37.62	
	Methotrexate Tablet, Vial	2.5mg; 25mg/2ml	-	$15.27	
	Sulfasalazine Tablet, DR Tablet	500mg	-	$23.65	
PDE-4 Inhibitor	Apremilast (Otezla)	30mg	PA; PL; SP	$3,660.05	Reserved for treatment failure to one or more oral DMARD but unable to use biologics.
Biologics	Adalimumab (Humira, Humira CF)	20mg/0.4ml, 40mg/0.8ml 40mg/0.4ml	PA; PL; SP	$5,464.64	Reserved for treatment failure to adequate trial of DMARD therapy.
	Etanercept (Enbrel)	25mg/ml, 50mg/ml	PA; PL; SP	$5,713.68	Reserved for treatment failure to adequate trial of DMARD therapy.
	Infliximab-dyyb (Inflectra) Infliximab-abda (Renflexis)	100mg IV vial	PA; PL; SP	--	Reserved for treatment failure to one oral DMARD for 3 months.
	Infliximab (Remicade)	100mg IV vial	NF	$8,858.05	Non-Formulary

	Abatacept (Orencia)	125mg/ml; 250mg IV vial	PA; PL; SP	$4,624.90	Reserved for treatment failure to either Adalimumab, Etanercept, or Infliximab.
	Certolizumab (Cimzia)	200mg	PA; PL; SP	$4,583.16	Reserved for treatment failure to Adalimumab, Etanercept, OR Infliximab.
	Golimumab (Simponi)	50mg/0.5ml, 100mg/ml	PA; PL; SP	$4,749.38	Reserved for treatment failure to Adalimumab, Etanercept, OR Infliximab.
	Secukinumab (Cosentyx)	150mg/ml	PA; PL; SP	$6,068.65	Reserved for treatment failure to Adalimumab, Etanercept, OR Infliximab.
	Guselkumab (Tremfya)	100mg/mL	PA; PL; SP	$5,537.00	Reserved for treatment failure to Adalimumab, Etanercept, OR Infliximab.
	Ixekizumab (Taltz)	80mg/ml	PA; PL; SP	$57,963.91	Reserved for treatment failure to two 1st line agents OR one 1st line agent and one 2nd line agent.
	Ustekinumab (Stelara)	45mg/0.5ml, 90mg/ml	PA; PL; SP	$10,958.30 $22,048.62	Reserved for treatment failure to two 1st line agents OR one 1st line agent and one 2nd line agent.
JAK-Inhibitor	Tofacitinib (Xeljanz, Xeljanz XR)	IR: 5mg, XR: 10mg	PA; PL;QL	$4,688.19	Reserved for treatment failure to two 1st line agents OR one 1st line agent and one 2nd line agent.

ST = Step Therapy; QL = Quantity Limit; PL = Prescriber Limit (Must be prescribed by Rheumatologist/Dermatologist);
PA = Prior Authorization Required; NF = Non-Formulary; SP = Specialty; DMARDs = Disease Modifying Anti-Rheumatic Drugs;
PDE-4 = Phosphodiesterase-4 Inhibitor

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

Oral DMARDs

Azathioprine, Cyclosporine (Modified), Leflunomide, Methotrexate 25mg/ml Vial, Methotrexate Tablets, Sulfasalazine IR/DR Tablets

- ❒ **Coverage Criteria:** None.
- ❒ **Limits:** None.
- ❒ **Required Information for Approval:** None.
- ❒ **Non-Formulary*:*** Otrexup, Cyclosporine (Regular)

Phosphodiesterase-4 Inhibitor (PDE-4 Inhibitor)

Apremilast (Otezla)

- ❒ **Coverage Criteria:** Apremilast is reserved for patients with PsA who have tried an adequate trial of oral DMARD but cannot use biologics (e.g. history of severe infection, etc). Must be prescribed by a rheumatologist or dermatologist.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Clinic notes or prescription history indicating patient has tried at least 12 weeks of dose-optimized oral DMARD (Methotrexate, Cyclosporine, Leflunomide, etc). If patient is unable to tolerate one oral DMARD, a second oral DMARD must be tried.
- ❒ **Other Notes:** Medication is to be dispensed by HPSJ's designated specialty pharmacy.

Biologics

1st line—Adalimumab (Humira), Etanercept (Enbrel), Infliximab-dyyb (Inflectra), Infliximab-abda (Renflexis)

- ❒ **Coverage Criteria:** Reserved for treatment failure to 12 weeks of dose-optimized, oral DMARD therapy (Methotrexate 15-25mg/week, Cyclosporine, Acitretin, and Leflunomide). If patient is unable to tolerate one oral DMARD, a second oral DMARD must be tried. Must be prescribed by a rheumatologist or dermatologist.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Clinic notes or prescription history indicating patient has tried at least 12 weeks of dose-optimized oral DMARD (Methotrexate, Cyclosporine, Leflunomide, etc).
- ❒ **Other Notes:**
  - Medication is to be dispensed by HPSJ's designated specialty pharmacy.
  - Biologics exceeding labeled standard maintenance doses may be approved 1 month at a time. Subsequent fills of the increased maintenance dose will require documentation of symptom improvement.
  - Remicade is non-formulary.

2nd line—Cimzia (Certolizumab), Simponi (Golimumab), Abatacept (Orencia), Secukinumab (Cosentyx), Gulselkumab (Tremfya)

- ❒ **Coverage Criteria:** Reserved for treatment failure/documented intolerance to Adalimumab, Etanercept, or Infliximab. Must be prescribed by a rheumatologist or dermatologist.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Prescription history of Adalimumab, Etanercept, or Infliximab.
- ❒ **Other Notes:** Medication is to be dispensed by HPSJ's designated specialty pharmacy. Biologics exceeding labeled standard maintenance doses may be approved 1 month at a time. Subsequent fills of the increased maintenance dose will require documentation of symptom improvement.

3rd line—Ustekinumab (Stelara), Ixekizumab (Taltz), Tofacitinib (Xeljanz, Xeljanz XR)

- ❒ **Coverage Criteria:** Ustekinumab, Ixekizumab, Tofacitinib IR/XR) are reserved for treatment failure/documented intolerance to two 1st line agents (adalimumab, etanercept, infliximab) OR one 1st line agent (adalimumab, etanercept, infliximab) and one 2nd line agent (certolizumab, golimumab, secukinumab, abatacept). Must be prescribed by rheumatologist or dermatologist.
- ❒ **Limits:** Xeljanz 5mg- 2 tablets per day
  Xeljanz XR 10mg- 1 tablet per day
- ❒ **Required Information for Approval:** Prescription history, medical authorization history, or clinic notes indicating fills of Adalimumab/Etanercept/Infliximab AND/OR Certolizumab/Golimumab/Secukinumab/Abatacept.
- ❒ **Other Notes:** Medication is to be dispensed by HPSJ's designated specialty pharmacy. Biologics exceeding labeled standard maintenance doses may be approved 1 month at a time. Subsequent fills of the increased maintenance dose will require documentation of symptom improvement.

CLINICAL JUSTIFICATION

Psoriatic Arthritis

2018 The American College of Rheumatology (ACR) and the National Psoriasis Foundation (NPF) Guideline for the Treatment of Psoriatic Arthritis[33]

Highlights

- Most recommendations are conditional and applies to the majority of patients but may not be appropriate for all (shared decision-approach).

- Strong recommendations for patients with active PsA and concomitant active inflammatory bowel disease despite treatment with an oral small molecule (e.g. methotrexate)
    - Switch to a TNFi monoclonal antibody biologic over switching to a TNFi biologic soluble receptor biologic (i.e, etanercept).
    - Switch to a TNFi monoclonal antibody over switching to an interleukin (IL)-17 biologic
    - Switch to an IL-12/IL-23i biologic over switching to an IL-17i biologic.
- Other strong recommendations:
    - In adult patients with active PsA and frequent serious infections who are naïve to oral small molecule (OSM) and biologic drugs may start an oral small molecule over a TNFi biologic.
    - Smoking cessation over no smoking cessation.
- Conditional Recommendations
    - Treat-to-target approach for all patients with active PsA.
    - For treatment naïve, active PsA patients- use TNFi biologics as first-line therapy over OSM/DMARDs.
    - OSM drugs may be used instead of a TNFi biologic in patients without severe PsA and without severe psoriasis or in those who prefer an oral drug instead of parenteral therapy, or those with contraindications to TNFi treatment (congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease).
    - For treatment-naïve patients with active PsA, the use of TNFi biologic or OSM is recommended over an interleukin-17.
    - An IL-17i or IL-12/23i may be used instead of TNFi biologics with severe psoriasis or contraindications to TNF biologics.
    - In patients with active PsA despite OSM therapy, switching to a TNFI, IL-17i, or an IL-12/23i biologic is recommended over switching to a different OSM. A different OSM may be used rather than a TNFi, IL17i, or IL-12/23i in patients who prefer an oral medication or those without evidence of severe PsA or severe psoriasis.
    - In patients with active PsA despite TNFi treatment, switching to a different TNFi biologic monotherapy is recommended over switching to IL-12/23i biologic, IL-17i biologic, abatacept, or tofacitnib monotherapy or adding methotrexate to the current TNFi biologic. An IL-12/23i biologic, IL-17i biologic, abatacept, or tofacitnib may be used instead of a different TNFi biologic monotherapy in the case of a primary TNFi biologic failure or serious adverse event to a TNFi.
    - An IL-17i or Il-12/23i biologic may be used instead of a different TNFi biologic, particularly in the presence of severe psoriasis. Abatacept may be used instead of a TNFi biologic in patients with recurrent or serious infections in the absence of severe psoriaisis.
    - In treatment-naïve PsA patients with predominant enthesitis, a TNFi biologic is recommended over an OSM as a first-line option.

- The recommendation to use biologics as first-line treatment diverges from recommendations by the European League for Rheumatism (EULAR) for PsA where oral small molecules drugs are recommended as first-line agents for treatment-naïve patients. This was in part due to the lower cost of conventional oral small molecules agents. However, because the ACR/NPF guidelines note that this is a conditional recommendation due to low-to very-low quality evidence, HPSJ will continue to use oral small molecule drugs as first-line agents from a cost effective standpoint. HPSJ will take into consideration with the use of TNF-inhibitors as first line treatments in patients with predominant enthesitis or severe PsA.

The *2015 EULAR PsA Guidelines*[1] recommends the following:

	Recommendations	Level of evidence	Grade of recommendation	Level of agreement (mean±SD
1.	Treatment should be aimed at reaching the target of remission or, alternatively, minimal/low disease activity, by regular monitoring and appropriate adjustment of therapy	1b	A	9.6±0.9
2.	In patients with PsA, NSAIDs may be used to relieve musculoskeletal signs and symptoms	1b	A	9.6±0.8
3.	In patients with peripheral arthritis, particularly in those with many swollen joints, structural damage in the presence of inflammation, high ESR/CRP and/or clinically relevant extra-articular manifestations[a], csDMARDs should be considered[b] at an early stage[a], with methotrexate preferred in those with relevant skin involvement[b]	[a]: 3 [b]: 1b	B	9.4±0.8
4.	Local injections of glucocorticoids should be considered as adjunctive therapy in PsA[a]; systemic glucocorticoids may be used with caution at the lowest effective dose[b]	[a]: 3b [b]: 4	C	9.1±1.2
5.	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, therapy with a bDMARD, usually a TNF inhibitor, should be commenced	1b	B	9.5±0.7
6.	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, in whom TNF inhibitors are not appropriate, bDMARDs targeting IL12/23 or IL17 pathways may be considered	1b	B	9.1±1.1
7.	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, in whom bDMARDs are not appropriate, a targeted synthetic DMARD such as a PDE4-inhibitor may be considered	1b	B	8.5±1.4
8.	In patients with active enthesitis and/or dactylitis and insufficient response to NSAIDs or local glucocorticoid injections, therapy with a bDMARD should be considered, which according to current practice is a TNF inhibitor	1b	B	9.1±1.2
9.	In patients with predominantly axial disease that is active and has insufficient response to NSAIDs, therapy with a bDMARD should be considered, which according to current practice is a TNF inhibitor	1b	B	9.6±0.6
10.	In patients who fail to respond adequately to a bDMARD, switching to another bDMARD should be considered, including switching between TNF inhibitors	1b	B	9.6±0.7

The level of evidence was determined for different parts of the recommendation (referred to as a and b) where necessary.
The level of agreement was computed as a 0–10 scale.
bDMARD, biological DMARD; CRP, C reactive protein; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs, such as methotrexate, sulfasalazine or leflunomide; ESR, erythrocyte sedimentation rate; EULAR, European League Against Rheumatism; NSAIDs, non-steroidal anti-inflammatory drugs; PDE, phosphodiesterase; PsA, psoriatic arthritis; TNF, tumour necrosis factor.

Highlights

- Similar to the 2015 ACR Guidelines[2], the 2015 EULAR Guidelines recommend a "treat-to-target" approach for PsA.
    - Patients with active disease should be monitored every 3 months and treatment should be adjusted when appropriate. The TICOPA trial demonstrated patients who had treatment escalation from DMARD therapy to biologics had better therapeutic outcomes when they were monitored and the treatment regimen was adjusted more vigorously.[3]
- MTX 15-25 mg/week is the preferred oral DMARD, especially for patients with skin involvement.[4]
- Patients with peripheral arthritis who have tried one or more oral for DMARDs 3-6 months should consider therapy with a biologic (i.e. TNF inhibitor).
    - There were no significant differences in efficacy between TNF inhibitors. However, indirect comparison studies found Enbrel to be less efficacious or have a slower onset as compared to the rest of the TNF inhibitors.
- Patients with peripheral arthritis who have tried one or more oral DMARDs for 3-6 months and cannot use TNF inhibitors, non-TNF biologics (i.e. IL 12/23, IL 17 inhibitors) should be considered.
- Patients with peripheral arthritis who have tried one or more oral DMARDs for 3-6 months and cannot use biologics, PDE-4 inhibitor (i.e. Apremilast) should be considered.
    - Based on Apremilast's relatively low efficacy and high cost (relative to the other oral agents), the lack of studies with direct comparison to MTX and other oral DMARDs or biologics, the Task Force concluded that Apremilast should, in most cases, be limited to patients who have tried an adequate trial of oral DMARD but cannot use biologics (e.g. history of severe infection, contraindications to biologics).
- Patients with predominantly axial disease that is active and has insufficient response to NSAIDs, biologics should be considered (TNF inhibitors should be tried first unless inappropriate or contraindicated, in which non-TNF biologics are considered).
    - Patients who failed one TNF inhibitor should consider switching to another TNF inhibitor.

Treatment for PsA is similar to that of PsO. Skin lesion manifestations will be addressed with psoriatic therapies while joint disease is managed like rheumatoid arthritis. Please see the Psoriasis Medication Coverage Policy for PsO treatment with topical agents when a patient with active PsA has major skin involvement. Most cases of mild PsA (no evidence of bone or joint deformity and dysfunction) should not be automatically treated with biologics. In such cases, NSAIDs and intra-articular corticosteroid injections may be used for symptomatic relief for mild PsA or when only a few joints are involved. Sulfasalazine and leflunomide have shown modest benefit with conflicting data for methotrexate. The 2008 American Academy of Dermatology (AAD) and the 2012 British Society for Rheumatology (BSR)/British Health Professionals in Rheumatology (BHPR) PsA treatment guidelines agree that a 12-week trial of dose-optimized oral DMARDs (methotrexate, leflunomide, sulfasalazine, cyclosporine) should be tried prior to use of a biologic agent.[5-6] The exception to this rule is when the patient has extensive joint involvement (at least 3 or more affected joints)—in which case, biologics may be used alone or in combination with an oral DMARD. Otherwise, patients that demonstrated treatment failure to dose-optimized oral DMARDs for 12 weeks should be given a trial of TNF-inhibitor. Partial responders to biologic therapy should be given a 12-week extension and the therapy continued if there continues to be a response measured during the extension period. The efficacy between biologics do not differ significantly but the cost may vary due to differences in administration frequency (twice monthly vs. weekly vs. monthly, and so forth). Therefore, HPSJ's order of preference of the biologic therapies are based on the cost-benefit ratio where the first-line biologics are agents associated with the lowest cost-benefit ratio.

Role of oral agents (DMARDs and immunosuppressants)

Oral DMARDs are commonly used as first-line therapies in many mild-moderate inflammatory disorders with a few exceptions (e.g. Ankylosing Spondylitis). For most patients, treatment with oral agents may be sufficient for their condition. Generally, 12 weeks of continuous DMARD therapy is considered to be an adequate trial—assuming the drug is adequately dosed. In patients with liver and/or renal impairment, DMARDs are not necessarily excluded right away. In most cases, DMARDs can be safely used as long as there is regular monitoring of labs and side effects and the dosing is adjusted accordingly.

Table 1: Commonly used oral agents in chronic inflammatory diseases

Oral Agent	Joint	Skin	GI	liver damage	kidney damage	Pregnancy	Breastfeeding
Azathioprine	X	X*	X	monitor	monitor & dose adjust	Avoid use	Not recommended
Cyclosporine	X*	X	X*	monitor	monitor & dose adjust	Avoid use	Not recommended
Leflunomide	X	X	X*	avoid use	avoid use	Contraindicated	Unknown
Mercaptopurine	X*	X*	X	monitor	monitor & dose adjust	Avoid use	Unknown
Methotrexate	X	X	X	avoid use	monitor & dose adjust	Contraindicated	Contraindicated
Sulfasalazine	X	X*	X	monitor	monitor	Generally safe	Generally safe
**limited evidence*							

Special Populations

Pregnancy

Guidelines for pregnancy, as stated by the Canadian guidelines and the American National Psoriasis Foundation, indicate that 1st line therapy includes low- to moderate potency corticosteroids, 2nd line therapy includes narrow ban UVB, and 3rd line therapy, only to be used if benefits outweigh risks, includes cyclosporine or TNF inhibitors.[20-21] Other DMARDS deemed safe include sulfasalazine and azathioprine, and possibly leflunomide.[22] Azathioprine has a risk for premature births and, although limited animal data contraindicates its use, leflunomide has an apparently low human teratogenicity risk. Cyclosporine and sulfasalazine seem to be the safest or most preferred DMARD agents.[22]

Elevated LFTs

Specific guidelines for patients who have elevated LFTs are not available, but the American Academy of Dermatology guidelines do have suggestions for LFT monitoring and some recommendations on protocol if LFTs are elevated to a certain level. For methotrexate, if elevation exceeds 2x normal levels, LFT monitoring

must be checked more frequently; if elevation exceeds 3x normal levels, consider dose reduction (administer 75% of dose); if elevation exceeds 5x normal, discontinuation of the medication is recommended. No other drugs have specific guidelines for LFT levels.[23] The 2008 ACR guidelines state that leflunomide, methotrexate, and sulfasalazine should not be started nor resumed if liver transaminases were >2x the upper normal limit. Despite this, there are no recommendations on discontinuation.[24] A paper regarding expert opinion on the treatment of psoriasis in special circumstances speaks to the use of biologics in the setting of fatty liver disease. The panel considered etanercept and ustekizumab to be the best options for use in a patient with fatty liver disease.[25]

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REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Psoriasis - biologicals 2-20-07.doc	2/2007	Allen Shek, PharmD
Updated Policy	Biological Response Modifiers Review 2-19-08.doc	2/2008	Allen Shek, PharmD
Updated Policy	HPA Suppression among Medium Potency Topical Corticosteroids.doc	6/2008	Allen Shek, PharmD
Updated Policy	Biologic Response Modifiers 2010 final.docx	5/2010	Allen Shek, PharmD
Updated Policy	TNF MUE summary 2-21-2012.docx	2/2012	Allen Shek, PharmD
Updated Policy	Calcipotriene.docx	11/2012	Allen Shek, PharmD
Updated Policy	Biologic Response Modifiers for Psoriasis 2013-2-19.docx	2/2013	Allen Shek, PharmD
Updated Policy	Psoriatic Arthritis & Ankylosing Spondylitis.docx	10/2014	Jonathan Szkotak, PharmD
Updated Policy	Class Review of Topical & Systemic Agents Used for Skin Inflammation Disorders with an Emphasis on Psoriasis.docx	5/2015	Jonathan Szkotak, PharmD
Updated Policy	HPSJ Coverage Policy – Rheum & immuno – Psoriatic Arthritis 2015-05.docx	9/2015	Jonathan Szkotak, PharmD
Updated Policy	Class Review- Biologics, Apremilast, and Tofacitinib in Inflammatory Joint, Skin, and Bowel Diseases.docx	2/2016	Johnathan Yeh, PharmD
Updated Policy	HPSJ Coverage Policy - Rheum & Immuno - Psoriatic Arthritis 2017-02.docx	2/2017	Johnathan Yeh, PharmD
Updated Policy	HPSJ Coverage Policy - Rheum & Immuno - Psoriatic Arthritis 2018-02.docx	02/2018	Johnathan Yeh, PharmD
Updated Policy	HPSJ Coverage Policy - Rheum & Immuno - Psoriatic Arthritis 2019-05.docx	05/2019	Matthew Garrett, Pharm D
Updated Policy	Psoriatic Arthritis 2020-05.docx	05/2020	Matthew Garrett, Pharm D
Updated Policy	Psoriatic Arthritis.docx	05/2021	Matthew Garrett, Pharm D

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy

Appendix:

Switch Studies with Biosimilars launched in the US

Study	Study design	Dosage regimen	Key efficacy outcomes	Immunogenicity	Key safety outcomes	Study conclusions
Yoo et al. PLANETRA study switching extension to week 102	Phase III, open-label, extension study RA patients CT-P13 (n = 302) INX (n = 304) for 54 weeks then CT-P13 maintenance (n = 158) or switch to CT-P13 (n = 144) for up to 102 weeks	3 mg/kg IV CT-P13 or INX, weeks 0, 2, 6 then q8wks + MTX 12.5-25 mg/wk + folic acid 55 mg/wk to week 54 then CT-P13/ MTX/folic acid as above (weeks 64-102)	**ACR20 response rate** CT-P13 maintenance: 71.7% CT-P13 switch: 71.8% (95% CI: -10, 10) **ACR50 response rate** CT-P13 maintenance: 48.0% CT-P13 switch: 51.4% **ACR70 response rate** CT-P13 maintenance: 24.3% CT-P13 switch: 26.1% **Mean improvement in DAS28/CRP** CT-P13 maintenance: -2.40 CT-P13 switch: -2.48 **Good EULAR response (CRP)** CT-P13 maintenance: 40.1% CT-P13 switch: 44.4%	**ADAs at week 78** CT-P13 maintenance: 44.7% CT-P13 switch: 46.2% **ADAs at week 102** CT-P13 maintenance: 40.3% CT-P13 switch: 44.8%	**Overall TEAEs** CT-P13 maintenance: 53.5% CT-P13 switch: 53.8% **TEAEs related to treatment** CT-P13 maintenance: 22.0% CT-P13 switch: 18.9% **Most frequently reported TEAEs related to treatment** **CT-P13 maintenance**: infusion related reaction, latent TB, URTI, LRTI, UTI, bursitis **CT-P13 switch**: infusion-related reaction, latent TB, LRTI, abnormal LFT test, URTI, UTI, urticaria **Serious TEAEs** CT-P13 maintenance: 7.5% CT-P13 switch: 9.1% **Serious TEAEs related to treatment** CT-P13 maintenance: 1.3% CT-P13 switch: 2.8% No deaths	Comparable efficacy and tolerability were observed in patients who switched from INX to CT-P13 for an additional year and in those who had long-term treatment with CT-P13 for 2 years
Tanaka et al. Japanese switching extension study to week 134	Phase I/II open-label, singlearm, multicenter, extension study RA patients CT-P13 (n = 50) INX (n = 51) 54 weeks then CT-P13 maintenance (n = 38) or switch to CT-P13 (n = 33) up to week 134	3 mg/kg IV CT-P13 or INX, weeks 0, 2, 6 then q8wks + MTX 6-16 mg/wk + folic acid 55 mg/wk to week 54 then CT-13/MTX/folic acid as above (weeks 64-104); CT-P13 dose increase allowed to 10 mg/wk	**ACR20 response rate** CT-P13 maintenance: 78.4% CT-P13 switch: 62.5% **ACR50 response rate** CT-P13 maintenance: 70.3% CT-P13 switch: 53.1% **ACR70 response rate** CT-P13 maintenance: 54.1% CT-P13 switch: 40.1% **Mean improvement in DAS28/ESR** CT-P13 maintenance: 3.17	**ADAs at week 110** CT-P13 maintenance: 11.8% CT-P13 switch: 21.7% **ADAs at week 134** CT-P13 maintenance: 15.6% CT-P13 switch: 17.4%	**Overall TEAEs** CT-P13 maintenance: 89.5% CT-P13 switch: 87.9% **Most frequently reported TEAEs related to treatment** **CT-P13 maintenance**: nasopharyngitis, URTI inflammation, herpes zoster, rash	CT-P13 was well tolerated with persistent efficacy in Japanese patients with RA who maintained treatment after 54 weeks and in patients who switched to CT-P13 after 54 weeks of INX treatment

			CT-P13 switch: 3.96		**CT-P13 switch**: nasopharyngitis, infusion-related reaction and Osteoporosis **Serious TEAEs** CT-P13 maintenance: 5.3% CT-P13 switch: 12.1%	
Jorgensen et al. NOR-SWITCH	Phase IV randomized, non-inferiority, double blind study RA, AS, PA, Psoriasis patients stable on INX for 24 weeks, then INX maintenance (n=202) or switch to CT-P13(n=206) for 24 weeks	Dose stayed the same as prior to randomization.	Disease worsening occurred in 53 (26%) patients in the infliximab originator group and in 61 (30%) patients in the CT-P13 group.	INX: 7.1% CT-P13" 7.9%	**Overall AE** INX: 70% CT-P13: 68% **Serious adverse events** INX: 10% CT-P13: 9% AE leading to discontinuation: INX: 4% CT-P13: 3%	CT-P13 was shown to be non-inferior to continued treatment with infliximab according to prespecified non-inferiority margin of 15%.
AS						
Park et al. PLANETAS	Phase I double blind, multicenter, parallel group study CT-P13 (N=125) INX (N = 125)	5 mg/kg IV CT-P13 or INX, weeks 0, 2, 6 then q8wks + continued stable use of glucocorticoids/ NSAIDs allowed	ASAS20 response rate CT-P13: 67.0% INX: 69.4% (95% CI: 0.50, 1.59) ASAS40 response rate CT-P13: 54.7% INX: 49.1% (95% CI: 0.73, 2.15) ASAS partial remission CT-P13: 19.8% INX: 17.6%	ADAs at week 30 CT-P13: 19.5% INX: 23.0%	Overall TEAEs CT-P13: 74.2% INX: 67.2% TEAEs related to treatment CT-P13: 50.0% INX: 51.6%	CT-P13 and INX have highly comparable efficacy, safety and immunogenicity and PK profiles up to week 54