Remicade (infliximab), Inflectra (infliximab-dyyb) Renflexis (infliximab-abda), Ixifi (infliximab-qbtx) Policy Number: C10421-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
11/1/2012	9/25/2019	9/25/2020
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL**
J1745-Injection, infliximab, excludes biosimilar, (Remicade), 10mg Q5103-Injection, infliximab-dyyb, biosimilar, (Inflectra), 10mg Q5104-Injection, infliximab-abda, biosimilar, (Renflexis) 10mg Q5109-Injection, infliximab-qbtx, biosimilar, (Ixifi) 10mg	RxPA	Q2 2019 20191030C10421-A

PRODUCTS AFFECTED:
Remicade (infliximab), Inflectra (infliximab-dyyb), Renflexis (infliximab-abda), Ixifi (infliximab-qbtx)

DRUG CLASS:
Tumor Necrosis Factor Alpha Blockers

ROUTE OF ADMINISTRATION:
Intravenous

PLACE OF SERVICE:
Specialty Pharmacy, Buy and Bill
The recommendation is that medications in this policy will be for medical benefit coverage and the IV infusion products administered in a place of service that is a non-hospital facility based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the therapy/patient meets the Site of Care exceptions. (See appendix for excerpt from Specialty Medication Administration Site of Care Policy)

AVAILABLE DOSAGE FORMS:
Remicade 100MG (infliximab) single vial, Renflexis 100mg (infliximab-abda), Inflectra 100mg (infliximab-dyyb)

FDA-APPROVED USES:
Infliximab (Inflectra, Remicade, and Renflexis) is indicated for the following conditions: in combination with methotrexate (MTX) for reducing signs and symptoms, inhibiting the progression of structural damage and improving physical function in patients with moderately to severely active rheumatoid arthritis, reducing the signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients ≥ 6 years of age with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy, reduction in the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adults with fistulizing

Crohn's disease, reducing signs and symptoms in adults with active ankylosing spondylitis (AS), reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage and improving physical function in adults with psoriatic arthritis, treatment of adults with chronic severe

(i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are less appropriate, reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adults with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to conventional therapy

Remicade (infliximab): has marketing exclusivity and is also indicated for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients ≥ 6 years of age with moderately to severely active UC who have had an inadequate response to conventional

COMPENDIAL APPROVED OFF-LABELED USES:
Graft V Host Disease, Hidradenitis Suppurativa

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
Rheumatoid Arthritis, Psoriatic Arthritis, Psoriasis, Ulcerative Colitis, Plaque Psoriasis, Ankylosing Spondylitis, Crohn's Disease, Behcet Syndrome.

REQUIRED MEDICAL INFORMATION:
FOR ALL INDICATIONS:

1. (a) Negative TB test within the last 12 months for initial and continuation of therapy requests
   OR
   (b) If member tests positive for latent TB, there must be documentation showing member completed a treatment course for TB OR that member has been cleared by an infectious disease specialist to begin treatment with INFLIXIMAB
   OR
   (c) For members who have tested positive for latent TB and have been treated, a negative chest x-ray is required every 12 months
   AND
2. Patient has been evaluated and screened for the presence of hepatitis B virus (HBV) prior to initiating treatment
   AND
3. Patient is not on concurrent treatment or will be used in combination with other TNF-inhibitor, biologic response modifier or other other biologic DMARDs, Janus kinase Inhibitors, or Phosphodiesterase 4 inhibitor (i.e., apremilast, tofacitinib, baricitinib)
   AND
4. Patient does not have an active infection, including clinically important localized infections

A. MODERATE TO SEVERE RHEUMATOID ARTHRITIS:
   1. Documentation of moderate to severe rheumatoid arthritis diagnosis
      AND
   2. Prescriber has assessed baseline disease severity utilizing an objective measure/tool
      AND

3. (a) Patient tried, failed or has a contraindication or intolerance to methotrexate, as determined by the prescribing physician; OR Patient is concurrently receiving MTX AND
   Patient has tried one additional disease-modifying antirheumatic drug (DMARD) (brand or generic; oral or injectable) for at least 3 months, [this includes patients who have tried other biologic DMARDs for at least 3 months]
   (NOTE: An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already has a 3-month trial at least one biologic. These patients who have already tried a biologic for RA are not required to "step back" and try a conventional synthetic DMARD)
   OR
   (b) Patient has early RA (defined as disease duration of < 6 months) with at least one of the following features of poor prognosis: functional limitation (e.g., based on Health Assessment Questionnaire Disability Index [HAQ-DI] score); extra articular disease such as rheumatoid nodules, RA vasculitis, or Felty's syndrome; positive rheumatoid factor or anti-cyclic citrullinated protein (anti-CCP) antibodies; or bony erosions by radiograph; AND

4. Patient tried, failed or has a contraindication or intolerance to methotrexate, as determined by the prescribing physician; or patient is concurrently receiving MTX
   AND
5. IF THIS IS A NON-FORMULARY PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. If yes, please submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s).

B. PSORIATIC ARTHRITIS (PsA):
   1. Documentation of active and progressive PsA, evidenced by one (1) of the following: ≥3 swollen joints and 3 tender joints, Axial involvement that has not responded to NSAIDs, A high Psoriasis Area and Severity Index (PASI) score and a severely affected quality of life, Enthesitis (inflammation of the insertion of tendons or ligaments into bone) and dactylitis (inflammation of the whole digit) that has not responded to NSAIDs and locally injected glucocorticoids, and for which there is no evidence for non-biologic DMARD efficacy
      AND
   2. (a) Treatment failure with or a clinical contraindication to a minimum 3-month trial of two (2) of the following DMARDs (standard target doses must have been taken for ≥2 months): Leflunomide, Methotrexate, Sulfasalazine, Cyclosporine
      OR
      (b) Documentation of predominant axial PsA (see appendix for definitions) and Treatment failure with NSAIDs (does NOT require trial of DMARD therapy)
      OR
      (c) Documentation of peripheral joint arthritis (see appendix for definitions) and documentation of treatment failure with or a clinical contraindication to a minimum 3-month trial of one (1) of the following DMARDs (standard target doses must have been taken for ≥2 months): Leflunomide, Methotrexate, Sulfasalazine, Cyclosporine)
      AND
   3. IF THIS IS A NON-FORMULARY PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. If yes, please submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s)

C. ULCERATIVE COLITIS:
   1. Documentation of moderate to severely active ulcerative colitis

AND

2. (a) Patient has had a 2-month trial of one systemic agent (e.g., 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone, methylprednisolone) or was intolerant to one of these agents for ulcerative colitis or will continue to take concurrently.
   NOTE: A previous trial of a biologic (e.g., an adalimumab product [e.g., Humira], Simponi SC [golimumab SC injection], or Entyvio [vedolizumab IV infusion] also counts as a trial of one systemic agent for UC)
   OR
   b) The patient has pouchitis AND has tried therapy with an antibiotic (e.g., metronidazole, ciprofloxacin), probiotic, corticosteroid enema [for example, Cortenema® {hydrocortisone enema, generics}], or Rowasa® (mesalamine) enema
   AND
3. Will not be used with biologic DMARDs (e.g., Cimzia, Enbrel, Kineret, Remicade) or potent immunosuppressant drugs (such as azathioprine and cyclosporine)
   AND

4. IF THIS IS A NON-FORMULARY PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. If yes, please submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s)

D. CHRONIC PLAQUE PSORIASIS:
1. Documentation of moderate to severe disease activity for ≥6 months, evidenced by one (1) of the following: >10% body surface area with plaque psoriasis, ≤10% body surface area with plaque psoriasis that involves sensitive areas or areas that would significantly impact daily function (e.g., extensive recalcitrant facial involvement, pustular involvement of the hands or feet, or genital involvement), Psoriasis Area and Severity Index (PASI) score ≥12
   AND
2. Documentation of treatment failure with or a clinical contraindication to ≥3 of the following topical therapies for ≥6 months: Corticosteroids, Tazorac, Dovonex, Anthralin, Salicylic acids, Tars, Other topical therapies [DOCUMENTATION REQUIRED]
   AND
3. Documentation of treatment failure with or a clinical contraindication to TWO of the following systemic therapies for ≥3 months: Methotrexate (oral or IM at a minimum dose of 15 mg/week), cyclosporine, acitretin, azathipoprine, hydroxyurea, leflunomide, mycophenolate mofetil, sulfasalazine, or tacrolimus
   AND
4. Documentation of treatment failure with or a clinical contraindication to Phototherapy for ≥3 months with either psoralens with ultraviolet A (PUVA) or ultraviolet B (UVB) radiation (provider to submit documentation of duration of treatment, dates of treatment, and number of sessions; contraindications include type 1 or type 2 skin, history of photosensitivity, treatment of facial lesions, presence of premalignant lesions, history of melanoma or squamous cell carcinoma, or physical inability to stand for the required exposure time)
   AND
5. IF THIS IS A NON-FORMULARY PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. If yes, please submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s)

E. MODERATE TO SEVERE ANKYLOSING SPONDYLITIS:

1. Documentation of a Bath AS Disease Activity Index (BASDAI) score ≥4 on a 10-point scale
   AND
2. Inadequate response to ≥2 NSAIDs (e.g., ibuprofen, naproxen, etodolac, meloxicam, indomethacin) for ≥3 consecutive months at maximal recommended or tolerated anti-inflammatory doses
   AND
3. IF THIS IS A NON-FORMULARY PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. If yes, please submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s)

F. MODERATE TO SEVERE ACTIVE CROHN'S DISEASE:
1. Documentation of a diagnosis of currently ACTIVE moderate to severely active Crohn's Disease (Crohn's disease activity index-CDAI score of 221-450)
   AND
2. Patient has had a trial and inadequate response (or is currently taking) corticosteroids, or corticosteroids are contraindicated in this patient
   AND
3. (a) Documentation patient will be using infliximab in combination with azathioprine or 6-mercaptopurine or has a labeled contraindication to both agents.
   OR
   (b) The patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas
   OR
   (c) The patient has had ileocolonic resection (to reduce the chance of Crohn's disease recurrence

G. BEHCET SYNDROME:
1. Documented diagnosis of Behcet Syndrome with the following present: recurrent oral aphthae (at least three times in one year) plus two of the following clinical features: Recurrent genital aphthae (aphthous ulceration or scarring), Eye lesions (including anterior or posterior uveitis, cells in vitreous on slit lamp examination, or retinal vasculitis observed by an ophthalmologist), Skin lesions (including erythema nodosum, pseudofolliculitis, papulopustular lesions, or acneiform nodules consistent with Behçet syndrome), OR A positive pathergy test.
   AND
2. (a) The patient has tried at least ONE conventional therapy (e.g., systemic corticosteroids [for example, methylprednisolone], immunosuppressants [azathioprine, methotrexate {MTX}, mycophenolate mofetil, cyclosporine, tacrolimus, Leukeran® [chlorambucil], cyclophosphamide], interferon alfa).

NOTE: An exception to the requirement for a trial of one conventional therapy can be made if the patient has already had a trial of at least one tumor necrosis factor inhibitor (e.g., an adalimumab product [e.g., Humira], an etanercept product [e.g., Enbrel]). These patients who have already tried a biologic for Behcet's disease are not required to "step back" and try a conventional therapy)

OR

b) The patient has ophthalmic manifestations of Behcet's disease

H. HIDRADENITIS SUPPURATIVA:
1. Documentation of Hurley stage II (moderate recurrent) or stage III (severe diffuse) disease
AND
2. For current smokers: Documentation indicating smoking cessation has been addressed
AND
3. Documentation indicating the member has been counseled on the use of general supportive measures (e.g., education and support, avoidance of skin trauma, hygiene, dressings, smoking cessation, weight management, diet)
AND
4. Documentation of treatment failure with or a clinical contraindication to a 3-month trial of the following three (3) medications: Oral tetracycline (e.g., minocycline, doxycycline) AND Topical antibiotic AND Antiandrogen (e.g., finasteride) OR clindamycin/rifampin OR oral isotretinoin
AND
5. Documentation of treatment failure with or a clinical contraindication to intralesional corticosteroids
AND
6. Documentation of treatment failure with or a clinical contraindication to procedural interventions (e.g., punch debridement)

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy: 12 months

QUANTITY[1,2]:
Dosing in Crohn's Disease or Ulcerative Colitis:
Initial dose is 5 mg per kg IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then every 8 weeks thereafter. If the patient has an inadequate response to the initial dosage, the dose may be adjusted:
i. The dose can be increased up to a maximum of 10 mg/kg.

ii. In patients who lose response before the next dose is scheduled, the interval can be decreased to every 7, 6, 5, or 4 weeks or the dose per infusion can be increased.
iii. The maximum dose is 10 mg/kg and the shortest interval is every 4 weeks

Dosing in Rheumatoid Arthritis:
Initial dose is 3 mg per kg IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then every 8 weeks thereafter. If the patient has an inadequate response after ≥ 2 months of therapy, the dose may be adjusted:
i. The dose can be increased up to a maximum of 10 mg/kg.
ii. In patients who lose response before the next dose is scheduled, the interval can be decreased to every 7, 6, 5, or 4 weeks or the dose per infusion can be increased.
iii. The maximum dose is 10 mg/kg and the shortest interval is every 4 weeks.
It has been shown that increasing the dose or shortening the dosing interval of Infliximab may be beneficial in patients with RA.1, 40 The criteria for an inadequate response after ≥ 2 months of therapy are recommended based on the professional opinion of specialized physicians.

Dosing in AS[1,2]
Initial dose is 5 mg per kg IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then every 6 weeks thereafter. If the patient has an inadequate response after ≥ 2 months of therapy, the dose may be adjusted:
i. The dose can be increased up to a maximum of 10 mg/kg.

ii. In patients who lose response before the next dose is scheduled, the interval can be decreased to every 5 or 4 weeks or the dose per infusion can be increased.
iii. The maximum dose is 10 mg/kg and the shortest interval is every 4 weeks.

In certain cases, changes in infliximab dosage or dosing interval are recommended for patients with AS who initially respond and then lose that response. The criteria for dosing ranges and an inadequate response after ≥ 2 months of therapy are recommended based on the professional opinion of specialized physicians.

Dosing in Plaque or Psoriatic Psoriasis:
Initial dose is 5 mg per kg IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then every 8 weeks thereafter. If the patient has an inadequate response to ≥ 2 months of therapy, the dose may be adjusted:
i. The dose can be increased up to a maximum of 10 mg/kg.
ii. In patients who lose response before the next dose is scheduled, the interval can be decreased to every 7, 6, 5, or 4 weeks or the dose per infusion can be increased.
iii. The maximum dose is 10 mg/kg and the shortest interval is every 4 weeks.

Dosing in Behcet's Disease: [36,37]
Initial dose is 3 to 5 mg per kg IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, then every 6 to 8 weeks thereafter. If the patient has an inadequate response after ≥ 2 months of therapy, the dose may be adjusted (i, ii, or iii):
i. The dose can be increased up to a maximum of 10 mg/kg with the same treatment interval (every 6 to 8 weeks) OR
ii. The dose may remain the same (3 to 5 mg/kg) and the interval can be decreased to every 7, 6, 5, or 4 weeks;
OR
iii. In selected case, patients may be titrated to the maximum dose (10 mg/kg) and the shortest dosing interval (every 4 weeks).

Dosing in Hidradenitis Suppurativa. Dosing must meet the following: The initial dose is 5 mg per kg IV infusion followed by additional similar doses 2 and 6 weeks after the first infusion, and then every 8 weeks thereafter.

PRESCRIBER REQUIREMENTS:
CROHNS DISEASE AND ULCERATIVE COLITIS: Prescribed by or in consultation with a board-certified gastroenterologist, colorectal surgeon or specialist who is consulting with a board certified gastroenterologist or colorectal surgeon (consultation notes to be submitted)

MODERATE TO SEVERE RHEUMATOID ARTHRITIS: Prescribed by or in consultation with a board-certified rheumatologist

PSORIATIC ARTHRITIS (PsA): Prescribed by or in consultation with a board-certified rheumatologist or dermatologist

CHRONIC PLAQUE PSORIASIS: Prescribed by or in consultation with a board-certified dermatologist

MODERATE TO SEVERE ANKYLOSING SPONDYLITIS: Prescribed by or in consultation with a board-certified rheumatologist

BEHCET'S SYNDROME: Prescribed by or in consultation with a rheumatologist, dermatologist, ophthalmologist, gastroenterologist, or neurologist.

AGE RESTRICTIONS:
CROHNS DISEASE, ULCERATIVE COLITIS: 6 years of age and older
RHEUMATOID ARTHRITIS, ANKLYOSING SPONDYLISITS, PLAQUE PSORIASIS, PSORIATIC ARTHRITIS, ANKYLOSING SPONDYLITIS: 18 years and older

GENDER:
Male and female

CONTINUATION OF THERAPY:
A. MODERATE TO SEVERE RHEUMATOID ARTHRITIS:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required) AND
2. Documentation of no intolerable adverse effects or drug toxicity
AND
3. Documentation of disease stabilization or improvement in clinical signs and symptoms of RA compared to baseline, evidenced by ANY of the following: Improvement in any objective measurement score (see Appendix A), Reduction in clinical signs and symptoms of RA (e.g., 20% improvement in painful joint count, ESR, CRP, or morning stiffness), Improvement in physical functioning

B. PSORIATIC ARTHRITIS (PsA):
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member's medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required)

AND
2. Documentation of no intolerable adverse effects or drug toxicity
AND
3. Documentation of a positive response to treatment, evidenced by at least one (1) of the following: Demonstrated stabilization or improvement in joint pain and inflammation and reduction in skin lesions, Improvement in the number of tender joints, Improvement in the

C. ULCERATIVE COLITIS:
1. Documentation that member has had a response (e.g., maintained remission, decrease in stool frequency, rectal bleeding, improved endoscopy findings, improvement in physician global assessment, etc.) as determined by the prescriber
AND
2. Adherence to therapy at least 85% of the time as verified by the prescriber or member's medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required)
AND
3. Documentation of no intolerable adverse effects or drug toxicity

D. CHRONIC PLAQUE PSORIASIS:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member's medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required)

AND
2. Documentation of no intolerable adverse effects or drug toxicity
AND
3. Documentation of symptomatic improvement or disease stabilization compared to baseline status, evidenced by one (1) of the following: Body surface area with plaque psoriasis, Dermatology Life Quality Index (DLQI), 75% reduction in PASI score (PASI75), 50% reduction in PASI score (PASI50) and 5-point reduction in DLQI

E. MODERATE TO SEVERE ANKYLOSING SPONDYLITIS:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member's medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required)
AND
2. Documentation of no intolerable adverse effects or drug toxicity
AND
3. Documentation of a positive response to therapy after ≥12 weeks, evidenced by ≥1 of the following: 50% relative improvement, or a decrease of ≥2 points on the BASDAI scale compared with the pre-treatment score, Significant functional improvement measured by outcomes such as HAQ or the ability to return to work, Recommendation from the prescriber to continue therapy due to a documented positive response

F. MODERATE TO SEVERE ACTIVE CROHN'S DISEASE:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member's medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required)
AND
2. Documentation of no intolerable adverse effects or drug toxicity
AND
3. Documentation patient has had an improvement in signs and symptoms since initial authorization as evidence by at least a 5 point decrease in CDAI score

G. BEHCET SYNDROME
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member's medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required)
AND
2. Documentation of no intolerable adverse effects or drug toxicity
AND
3. Documentation patient has had an improvement in signs and symptoms since initial authorization (e.g. reduction in inflammation and/or lesions, dose reduction of oral glucocorticoids and/or immunosuppressive agents, improvement in vitreous haze, improvement in best corrected visual acuity (BCVA), disease stability and/or reduced rate of decline)

H. HIDRADENITIS SUPPURATIVA:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member's medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required)
AND
2. Documentation of no intolerable adverse effects or drug toxicity
AND

3. Documentation of ≥20% improvement in symptoms

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Remicade (infliximab), Inflectra (infliximab-dyyb), Renflexis (infliximab-abda), Ixifi (infliximab-qbtx) that are not an FDA-approved indication or not included in the 'Coverage Criteria' section of this policy are considered not medically necessary. This is subject to change based on research and medical literature, or at the discretion of Molina Healthcare.

BACKGROUND:
Infliximab is a chimeric (murine-human) Immunoglobulin (Ig) G1κ monoclonal antibody produced by recombinant DNA technology that binds specifically with human tumor necrosis factor-alpha (TNF-α). The recommended dose of infliximab is weight-based and varies slightly by indication. Dosing increase, interval shortening, or changing to another therapy is generally recommended for attenuation of response. Inflectra and Renflexis were approved as biosimilar to Remicade, indicating no clinically meaningful differences in safety and effectiveness and the same mechanism of action, route of administration, dosage form, and strength as Remicade.
However, minor differences in clinically inactive components are allowed. At this time, Inflectra and Renflexis have only demonstrated biosimilarity, not interchangeability

Disease Overview
Increased levels of TNF are found in the joints of patients with rheumatoid arthritis (RA) and the stools of patients with Crohn's disease and correlate with elevated disease activity. TNF has an important role in both the pathologic inflammation and the joint destruction that are characteristic of RA. TNF is a naturally occurring cytokine that mediates inflammation and modulates cellular immune responses. Increased levels of TNF have been implicated in the pathology of inflammatory conditions such as psoriasis, psoriatic arthritis, inflammatory bowel disease, and rheumatoid arthritis (RA). Increased levels of TNF are found in the synovial fluid of patients with RA, JIA, AS, and PsA; TNF has an important role in both the pathologic inflammation and the joint destruction that are characteristic of this disease. In psoriasis, increased levels of TNF are found in the blood and skin lesions. Infliximab products binds to TNFα and inhibits binding of TNFα with its receptors.

Risk of tuberculosis during infliximab therapy for inflammatory bowel disease, rheumatoid arthritis, and spondyloarthropathy: A meta-analysis.

In conclusion, the present meta-analysis of 24 RCTs, comprising details from >6,340 patients with RA, SpA and IBD, demonstrated that the OR of tuberculosis infection was markedly increased with

infliximab therapy, as compared with placebo therapy. The overall rates of tuberculosis infection were low (0.51%).

Guidelines
TNFis feature prominently in guidelines for treatment of inflammatory conditions. Guidelines from the American College of Rheumatology (ACR) [2015] have TNFis (e.g., Cimzia® [certolizumab pegol SC injection], etanercept SC products [e.g., Enbrel®], adalimumab SC products [e.g., Humira®], infliximab IV products [e.g., Remicade®, Renflexis, Inflectra], Simponi® [golimumab SC injection], Simponi Aria® [golimumab IV infusion]) and non-TNF biologics (i.e., Actemra® [tocilizumab IV

infusion, tocilizumab SC injection], Orencia® [abatacept IV infusion, abatacept SC injection], rituximab IV products [e.g., Rituxan®]), administered with or without MTX, equally positioned as a recommended therapy following a trial of a csDMARD (e.g., MTX, leflunomide, hydroxychloroquine, sulfasalazine).18 Other guidelines for inflammatory conditions (e.g., PsA [European Union Against Rheumatism; Group for Research and Assessment of Psoriasis and Psoriatic Arthritis {GRAPPA}] and spondylitis [AS and non-radiographic axial {nr-ax}SpA] {ACR and Spondylitis Association of America/Spondyloarthritis Research and Treatment Network}, inflammatory bowel disease [Crohn's disease, UC] {American Gastroenterological Association} also note the significant place in therapy for TNFis.

Safety

Infliximab has Boxed Warnings concerning risks of serious infection and the risk of malignancy. Prior to initiating therapy with infliximab, patients should be evaluated for active tuberculosis (TB) infection, and periodically during therapy patients should be assessed for latent TB infection. Patients should also be monitored for signs and symptoms of infection during and after treatment with infliximab, and if a serious infection or sepsis develops, infliximab should be discontinued. It is also recommended that patients treated with any TNF antagonist should be monitored for malignancies.

Infliximab is indicated for ankylosing spondylitis.1 Guidelines for axial spondyloarthritis are available from the Assessment of SpondyloArthritis International Society (ASAS)/EULAR (2016).116 The guidelines state that biologics (e.g., TNFis, Cosentyx) should be considered in patients with persistently high disease activity despite traditional conventional treatments (e.g., nonpharmacological management, NSAIDs). For patients with primarily peripheral manifestations of axial spondylitis, local steroid injections and sulfasalazine may be considered as conventional treatment; however, these are not considered for patients who present primarily with axial disease. Furthermore, the guidelines state that patients with purely axial disease should not be treated with conventional synthetic DMARDs. Guidelines from the American College of Rheumatology (ACR) and the Spondyloarthritis Research and Treatment Network (SPARTAN) [2015] make recommendations for treatment of AS.19 TNF inhibitors (e.g., Cimzia, Enbrel, Humira, infliximab, Simponi SC) are recommended for patients who have active disease despite treatment with an NSAID. There is not a preference for TNF inhibitor, except for in the cases of concomitant inflammatory bowel disease or recurrent iritis, when a monoclonal antibody (Humira, infliximab) is recommended over Enbrel. According to Assessments in Ankylosing Spondylitis/European League Against Rheumatism (ASAS/EULAR) 2010 recommendations for ankylosing spondylitis, all patients should have an adequate trial of at least two nonsteroidal antiinflammatory drugs (NSAIDs) for pain and stiffness, unless contraindicated.20-22 Recommendations for other therapies before receiving a TNF blocker vary according to the manifestations of the disease, level of current symptoms, clinical findings, etc. According to these recommendations, patients with pure axial manifestations do not have to try traditional DMARDs before anti-TNF agents such as Infliximab; patients with symptomatic peripheral arthritis should have an insufficient response to at least one local corticosteroid injection, if appropriate; patients with peripheral arthritis should normally have a trial of a DMARD, preferably sulfasalazine; and patients with enthesitis should try appropriate local therapy (e.g., corticosteroid injection in selected cases). In patients with AS, concomitant treatment with a nonbiologic DMARD does not add to the safety or efficacy with an anti-TNF inhibitor.

Infliximab has been shown to reduce the chance of recurrence of symptoms after surgery in patients with Crohn's disease.24-27 In one study, patients treated with infliximab following illeocolonic resection

of Crohn's disease noticed a significant decrease in Crohn's Disease Activity Index (CDAI) score at Month 2 ($P < 0.01$ compared to baseline); this decrease in CDAI was not found in study patients treated post-resection with mesalamine or azathioprine.25 The American College of Gastroenterology (ACG) has guidelines for Crohn's disease (2018).27 Infliximab is listed as an option for severely active disease, fulminant Crohn's disease, enterocutaneous and rectovaginal fistulas, and maintenance of remission. In post-operative Crohn's disease, a TNFi should be started within 4 weeks of surgery to prevent recurrence.

Infliximab is indicated for plaque psoriasis.1 Guidelines for treatment of plaque psoriasis recommend topical therapy for limited disease.28-29 However, for patients with chronic plaque psoriasis that does not respond to topical therapies or patients with more extensive disease, systemic therapy may be used. The traditional systemic agents for plaque psoriasis are MTX, Soriatane, and cyclosporine. A biologic agent such as infliximab is an option for patients who are candidates for phototherapy or systemic therapy, especially those who are intolerant of or unresponsive to traditional systemic agents. The guidelines for the management of psoriasis from the American Academy of Dermatology (2010) note that there is no specific sequence in which the available TNF blockers should be used.29 However, guidelines from the National Psoriasis Foundation for management of plaque psoriasis (2012) note that infliximab is commonly used as a second- or third-line agent whereas Enbrel and Humira are listed as drugs which may be used as first-line systemic agents.In the professional opinion of specialist physicians reviewing the data, we have adopted the criteria requirements for previous therapy.

Infliximab is indicated for PsA.1 In clinical trials, infliximab was effective in patients with active PsA despite therapy with a DMARD or NSAID. There are few well-controlled, prospective studies with adequate duration that have evaluated the efficacy of the oral DMARDs. Recommendations for the management of PsA have been developed by European League Against Rheumatism (EULAR) [2015] and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) [2015].30-31 According to EULAR, treatment is recommended based on clinical presentation.31 In peripheral arthritis, a biologic (usually a TNF blocker) should be started if there is an inadequate response to at least one conventional synthetic DMARD. This recommendation is supported by the long-term experience and established safety/efficacy balance of TNF blockers vs. other biologics. In patients with enthesitis, dactylitis, or axial disease, the initial DMARD recommended are biologics; according to current practice a TNF blocker would be used. The guidelines note that comparison across trials is difficult because different outcomes were used. For enthesitis/dactylitis, the longest clinical experience is with TNF blockers. For axial disease, limited data exist for IL blockers. In patients who fail to respond to a biologic, switching to another biologic should be considered, including switching between TNF blockers. GRAPPA recommends TNF blockers for patients presenting with various manifestations of PsA (i.e., peripheral arthritis, axial disease, enthesitis, dactylitis, skin, and nail disease)

Infliximab is indicated for adults with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy. Remicade is also approved in pediatric patients ≥ 6 years of age with ulcerative colitis; although Inflectra and Renflexis do not share this indication, the prescribing information notes that pediatric assessment demonstrated safety and efficacy in this indication.117 Infliximab has been effective in cases of refractory pouchitis.34 Clinical guidelines for the management of pouchitis, published in 2009, and ulcerative colitis practice guidelines from the ACG (2010) indicate that first-line therapy for pouchitis is antibiotic therapy (e.g. metronidazole, ciprofloxacin).35-36 Other treatment options include maintenance probiotics, oral or topical budesonide, antiinflammatory drugs (e.g., mesalamine), or immunosuppressive drugs (e.g., infliximab).

Numerous case series have reported that infliximab is effective in producing short-term remission of Behcet's disease, especially uveitis, in patients who were refractory to corticosteroids and conventional immunosuppressive therapy.37-38 EULAR recommendations for the management of Behcet's disease (2018) include infliximab for initial or recurrent episodes of acute sight-threatening uveitis. For patients refractory to first-line treatments (e.g., corticosteroids), infliximab is among the treatment options for mucocutaneous manifestations, venous thrombosis, severe or refractory gastrointestinal disease, and recurrent/chronic joint involvement. .39 Recommendations for the use of TNF blockers in ocular inflammatory disorders from the American Academy of Ophthalmology (AAO) [2014] notes that infliximab may be used first-line in patients with ophthalmic manifestations of Behcet's disease and for acute exacerbations of preexisting Behcet's disease

Psoriatic Arthritis

An estimated 1% of the U.S. adult population harbors cutaneous evidence of psoriasis, characterized by well demarcated erythematous scaly plaques, some of whom develop a related arthritis. In fact, there are several distinct subsets of psoriatic arthritis, including (a) an asymmetric oligoarthritis affecting lower extremity joints; (b) a symmetric polyarthritis affecting upper and lower extremity joints; (c) monoarticular involvement of a distal interphalangeal joint alone; (d) a destructive finger joint arthritis that produces "telescoping," a shortening of the digit as a consequence of aggressive bone destruction and resorption (arthritis mutilans); and (e) axial skeleton involvement (spondylitis, sacroiliitis).

HIDRADENITIS SUPPURATIVA: In a Phase II double-blind, placebo-controlled crossover trial, adult patients with moderate to severe hidradenitis suppurativa were randomized to placebo (n = 23) or infliximab 5 mg/kg (n = 15) at Weeks 0, 2, and 6.47 After Week 8, patients were unblinded, and placebo patients were offered induction with placebo. Maintenance was continued through 22 weeks of treatment. Following Week 8, more patients in the infliximab-treatment group experienced a 50% or greater decrease in the Hidradenitis Suppurativa Severity Index (HSSI) score (approximately 26% and 5% of patients receiving infliximab and placebo, respectively [data presented graphically]; P = 0.092). In post-hoc analysis, significantly more patients treated with infliximab responded with a 25% to < 50% response (60% and 5.6% for infliximab and placebo, respectively; P < 0.001).

Improvement was noted through Week 30. In case series, infliximab has been effective in treating hidradenitis suppurativa that was refractory to other therapies.

APPENDIX:

RAAssessment of Disease Activity

Disease activity indexes have been developed for use in clinical trials and the office setting to standardize definitions and guide treatment. The development of standardized measures of disease activity (which define remission, LDA, and high disease activity [HDA]) allows for a "treat-to-target" strategy using pharmacologic therapy. These targets allow physicians and patients to set goals for treatment. All of these indices are slightly different in the number and type of data points collected. A detailed review of the indices/scales is beyond the scope of this document; however a few of the commonly used measures will be briefly highlighted.

- Disease Activity Score (DAS) 28
  - A scoring of 28 tender or swollen joints, a patient global assessment, and a physician global assessment, along with ESR (DAS28-ESR) or CRP (DAS28-CRP).[24]
- Simplified disease activity index (SDAI)

- The SDAI is the numerical sum of five outcome parameters: tender and swollen joint count (based on a 28-joint assessment), patient and physician global assessment of disease activity [visual analogue scale (VAS) 0–10 cm] and level of C-reactive protein (mg/dl, normal <1 mg/dl).

- Clinical disease activity index (CDAI)
  - CDAI is based on the simple summation of the count of swollen/tender joint count of 28 joints along with patient and physician global assessment on VAS (0–10 cm) Scale for estimating disease activity.

- RAPID3
  - RAPID3 (routine assessment of patient index data 3) is a pooled index of the 3 patient-reported American College of Rheumatology rheumatoid arthritis (RA) Core Data Set measures: function, pain, and patient global estimate of status. Each of the 3 individual measures is scored 0 to 10, for a total of 30. Disease severity may be classified on the basis of RAPID3 scores: >12 = high; 6.1–12 = moderate; 3.1–6 = low; ≤3 = remission.
- ACR criteria for percent improvement in involved joint count (e.g., ACR20, ACR50, and ACR70)

It should be noted that ACR criteria and CDAI are generally used in randomized clinical trials, whereas RAPID3 is used mostly by US rheumatologists in clinical practice.

Standardized Response Measure in RA

American College of Rheumatology (ACR) 20%, 50%, and 70% response criteria (ACR20/50/70), as well as the European League Against Rheumatism (EULAR) criteria and Disease Activity Score 28-joint count (DAS28), have standardized the evaluation and reporting of response in clinical trials of rheumatoid arthritis (RA).[1,2]

ACR 20/50/70 scores have provided a standardized response measure in RA clinical trials for more than 10 years, allowing for important comparisons of efficacy to be made between treatments and consistency in reporting of clinical trial results, and facilitating approval of 7 disease modifying antirheumatic drugs since 1998.[1]

1. *Felson DT, Anderson JJ, Boers M, Bombardier C, Furst D, Goldsmith C, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum 1995;38:727–35.*
2. *Van Gestel AM, Prevoo ML, van't Hof MA, van Rijswijk MH, van de Putte LB, van Riel PL. Development and validation of the European League Against Rheumatism response criteria for rheumatoid arthritis: comparison with the preliminary American College of Rheumatology and the World Health Organization/International League Against Rheumatism criteria. Arthritis Rheum 1996;39:34–40.*

Molina Healthcare, Inc. covers injectable/infused treatment in a hospital outpatient setting or at a hospital-affiliated infusion suite* when the level of care is determined to be medically necessary.

Considerations used to determine if an alternative level of care is not suitable may include the following findings:

1. The patient is clinically unstable based on documented medical history and susceptible to complication with drug administration (e.g., cardiopulmonary or renal dysfunction, risk for fluid overload)
2. The requested medication is administered as part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer or with dialysis
3. The patient exhibits physical or cognitive impairment and a capable caregiver is not available to assist with safe administration of prescribed medication in the home
4. It is the patient's first dose of the medication or it is being re-initiated after at least 12 months*
5. The patient has experienced adverse events with past administration of the drug and cannot be managed by premedication or resources available at an non-hospital facility based location (NHFBL)
6. Documented history of difficulty establishing and maintaining patent vascular access, or is not a candidate for a mode of long term vascular access during the duration of prescribed treatment

Note: a hospital outpatient setting or a hospital-affiliated infusion suite is expected to have immediate access to specific services of a medical center/hospital setting, including having emergency resuscitation equipment and personnel (ACLS protocol), emergency services, and inpatient admission or intensive care, if necessary

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

REFERENCES:

1. Remicade® injection [prescribing information]. Horsham, PA: Janssen Biotech; June 2018.
2. de Vries HS, van Oijen MG, Driessen RJ, et al. Appropriate infliximab infusion dosage and monitoring: results of a panel meeting of rheumatologists, dermatologists and gastroenterologists.
3. Br J Clin Pharmacol. 2011;71(1):7-19. 3. Lipsky PE, van der Heijde DM, St Clair EW, et al; for the Anti-Tumor Necrosis Factor Trial in Rheumatoid Arthritis with Concomitant Therapy Study Group. Infliximab and methotrexate in the treatment of rheumatoid arthritis. N Engl J Med. 2000;343:1594-1602.
4. Maini R, St Clair EW, Breedveld F, et al. Infliximab (chimeric anti-tumour necrosis factor alpha monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomised phase III trial. ATTRACT Study Group. Lancet.
1999;354:1932- 1939.
5. Maini RN, Breedveld FC, Kalden JR, et al. Sustained improvement over two years in physical function, structural damage, and signs and symptoms among patients with rheumatoid arthritis treated with infliximab and methotrexate. Arthritis Rheum. 2004;50:1051-1065.

6. St Clair EW, van der Heijde DM, Smolen JS, et al. Combination of infliximab and methotrexate therapy for early rheumatoid arthritis: a randomized, controlled trial. Arthritis Rheum. 2004;50:3432-3443.

7. Targan SR, Hanauer SB, van Deventer SJ, et al. A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease. Crohn's Disease cA2 Study Group. N Engl J Med. 1997;337:1029-1035.

8. Hanauer SB, Feagan BG, Lichtenstein GR, et al. Maintenance infliximab for Crohn's disease: the Accent I randomized trial. Lancet. 2002;359:1541-1549.

9. Hyams J, Crandall W, Kugathasan S, et al; REACH Study Group. Induction and maintenance infliximab therapy for the treatment of moderateto-severe Crohn's disease in children. Gastroenterology. 2007;132:863-873.

10. Present DH, Rutgeerts P, Targan S, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med. 1999;340:1398- 1405.

11. Sands BE, Anderson FH, Bernstein CN, et al. Infliximab maintenance therapy for fistulizing Crohn's disease. N Engl J Med. 2004;350:876-885.

12. van der Heijde D, Dijkmans B, Geusens P, et al; Ankylosing Spondylitis Study for the Evaluation of Recombinant Infliximab Therapy Study Group. Efficacy and safety of infliximab in patients with ankylosing spondylitis: results of a randomized, placebo-controlled trial (ASSERT). Arthritis Rheum. 2005;52:582-591.

13. Antoni C, Krueger GG, de Vlam K, et al; IMPACT 2 Trial Investigators. Infliximab improves signs and symptoms of psoriatic arthritis: results of the IMPACT 2 trial. Ann Rheum Dis. 2005;64:1150-1157.

14. Reich K, Nestle FO, Papp K, et al; EXPRESS study investigators. Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: a phase III, multicentre, double-blind trial. Lancet. 2005;366:1367-1374.

15. Reich K, Nestle FO, Papp K, et al. Improvement in quality of life with infliximab induction and maintenance therapy in patients with moderateto-severe psoriasis: a randomized controlled trial. Br J Dermatol. 2006;154:1161-1168.

16. Menter A, Feldman SR, Weinstein GD, et al. A randomized comparison of continuous vs. intermittent infliximab maintenance regimens over 1 year in the treatment of moderate-to- severe plaque psoriasis. J Am Acad Dermatol. 2007;56:31.e1-15.

17. Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005;353:2462-2476.

18. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol. 2016;68(1):1-26.

19. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 Recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. Arthritis Rheumatol. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis. 2011;70(6):896-904.

20. van den Berg R, Baraliakos X, Braun J, van der Heijde D. First update of the current evidence for the management of ankylosing spondylitis with non-pharmacological treatment and non-biologic drugs: a systematic literature review for the ASAS/EULAR management recommendations in ankylosing spondylitis. Rheumatology (Oxford). 2012;51(8):1388-1396.

21. van der Heijde D, Sieper J, Maksymowych WP, et al. 2010 Update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. Ann Rheum Dis. 2011;70(6):905-908.

22. Baraliakos X, van den Berg R, Braun J, van der Heijde D. Update of the literature review on treatment with biologics as a basis for the first update of the ASAS/EULAR management recommendations of ankylosing spondylitis. Rheumatology (Oxford). 2012;51(8):1378-1387.
23. Regueiro M, Schraut W, Baidoo L, et al. Infliximab prevents Crohn's disease recurrence after ileal resection. Gastroenterology. 2009;136(2):441- 450.
24. Yamamoto T, Umegae S, Matsumoto K. Impact of infliximab therapy after early endoscopic recurrence following ileocolonic resection of Crohn's disease: a prospective pilot study. Inflamm Bowel Dis. 2009;15(10):1460-1466.
25. Sakuraba A, Sato T, Matsukawa H, et al. The use of infliximab in the prevention of postsurgical recurrence in polysurgery Crohn's disease patients: a pilot open-labeled prospective study. Int J Colorectal Dis. 2012;27(7):947-952
26. Sorrentino D, Terrosu G, Paviotti A, et al. Early diagnosis and treatment of postoperative endoscopic recurrence of Crohn's disease: partial benefit by infliximab--a pilot study. Dig Dis Sci. 2012;57(5):1341-1348.
27. 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..
28. Hsu S, Papp KA, Lebwohl MG, et al. Consensus guidelines for the management of plaque psoriasis. Arch Dermatol. 2012;148(1):95-102.
29. American Academy of Dermatology Work Group, Menter A, Korman NJ, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence- based conclusions. J Am Acad Dermatol. 2011;65(1):137-174.
30. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 015 update. Ann Rheum Dis. 2016;75(3):499-510.
31. Coates LC, Kavanaugh A, Mease PJ, et al. Group for research and assessment of psoriasis and psoriatic arthritis: treatment recommendations for psoriatic arthritis 2015. Arthritis Rheumatol. 2016;68(5):1060-1071.
32. Nattiv R, Wojcicki JM, Garnett EA, et al. High-dose infliximab for treatment of pediatric ulcerative colitis: a survey of clinical practice. World J Gastroenterol. 2012;18(11):1229-1234.
33. Ferrante M, D'Haens G, Dewit O, et al. Efficacy of infliximab in refractory pouchitis and Crohn's disease-related complications of the pouch: a Belgian case series. Inflamm Bowel Dis. 2010;16(2):243-249.
34. Pardi DS, D'Haens G, Shen B, et al. Clinical guidelines for the management of pouchitis. Inflamm Bowel Dis. 2009;15(9):1424-1431.
35. Kornbluth A, Sachar DB; Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults: American College of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol. 2010;105(3):501-523.
36. Sfikakis PP, Markomichelakis N, Alpsoy E, et al. Anti-TNF therapy in the management of Behcet's disease--review and basis for recommendations. Rheumatology (Oxford). 2007;46:736-741. 2016;68(2):282-298.
37. Calvo-Río V, Blanco R, Beltrán E, et al. Anti-TNF-α therapy in patients with refractory uveitis due to Behçet's disease: a 1-year follow-up study of 124 patients. Rheumatology (Oxford). 2014;53(12):2223-2231.
38. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis. 2018;77(6):808-818.

39. Levy-Clarke G, Jabs DA, Read RW, et al. Expert panel recommendations for the use of anti- tumor necrosis factor biologic agents in patients with ocular inflammatory disorders. Ophthalmology. 2014;121(3):785-796.

40. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2010. Ann Rheum Dis. 2011;70 Suppl 1:i2-36.

41. Wang, Q., Wen, Z., & Cao, Q. (2016). Risk of tuberculosis during infliximab therapy for inflammatory bowel disease, rheumatoid arthritis, and spondyloarthropathy: A meta-analysis. Experimental And Therapeutic Medicine, 12(3), 1693-1704. doi: 10.3892/etm.2016.3548