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HEALTHCARE COOPERATIVE

PHARMACY POLICY STATEMENT
Common Ground Healthcare Cooperative (CGHC)

DRUG NAME	**Infliximab (Avsola, Inflectra, Remicade, Renflexis, Zymfentra)**
BENEFIT TYPE	Medical: Avsola, Inflectra, Remicade, Renflexis Pharmacy: Zymfentra
STATUS	Prior Authorization Required

Remicade is a tumor necrosis factor (TNF) alpha-inhibitor initially approved by the FDA in 1998 for adults with moderate to severe Crohn's disease. Since that time, infliximab has been approved for five additional indications: rheumatoid arthritis, psoriatic arthritis, plaque psoriasis, ankylosing spondylitis and ulcerative colitis. Multiple biosimilars have been approved for Remicade including Avsola, Inflectra and Renflexis. In 2023, Zymfentra was approved as a "biobetter" of Inflectra designed to be given subcutaneously rather than as an intravenous infusion.

Infliximab (Avsola, Inflectra, Remicade, Renflexis, Zymfentra) will be considered for coverage when the following criteria are met:

Ankylosing Spondylitis (AS)

For **initial** authorization:

1. Member must be 18 years of age or older; AND
2. Medication must be prescribed by or in consultation with a rheumatologist; AND
3. Member has a documented diagnosis of active AS; AND
4. Member shows **ONE** of the following signs or symptoms of inflammation:
   a) Elevated serum C-reactive protein (CRP);
   b) Sacroiliitis on magnetic resonance imaging (MRI); AND
5. Member has had a trial and failure of **TWO** NSAIDs for 14 days each, taken at the maximum recommended dosages; AND
6. Member has tried and failed **TWO** preferred biologic DMARDs for at least 3 months each, one of which must be a TNF inhibitor; AND
7. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
8. Member has had a negative tuberculosis test within the past 12 months.
9. **Dosage allowed/Quantity limit:** 5 mg/kg intravenously at 0, 2 and 6 weeks, then every 6 weeks thereafter.

If all the above requirements are met, the medication will be approved for 12 months.

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For **reauthorization**:
1. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
2. Chart notes have been provided showing improvement of signs and symptoms of disease such as decreased morning stiffness, tenderness or inflammatory back pain, improved quality of life, etc.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Crohn's Disease (CD)

For **initial** authorization:
1. Member is 6 years of age or older with moderately to severely active CD; AND
2. Medication must be prescribed by or in consultation with a gastroenterologist; AND
3. Member has had a documented trial and inadequate response, or intolerance to **ONE** of the following conventional therapies:
   a) A 4-week trial of a corticosteroid;
   b) A 12-week trial of 6-mercaptopurine, azathioprine, or methotrexate; OR
4. Member has severe disease that requires immediate use of a biologic agent, as indicated by **ONE** of the following:
   a) Extensive small bowel disease involving more than 100 cm;
   b) History of bowel or colon resection and is at high risk for CD recurrence (e.g., smoker, <30 years old, 2 or more resections, penetrating/fistulizing disease, etc.);
   c) Fistulizing disease; AND
5. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
6. If the request is for Zymfentra, member must have a trial and failure of **ALL** preferred IV infliximab products; AND
7. Member has had a negative tuberculosis test within the past 12 months.
8. **Dosage allowed/Quantity limit:** 5mg/kg intravenously at 0, 2, and 6 weeks, then every 8 weeks thereafter. Prior to any dosages or dosing frequencies greater than listed, medical necessity documentation must be supplied to justify coverage.
   Zymfentra (Adults only): after 10 weeks of dosing with an intravenous infliximab product, administer 120 mg subcutaneously once every two weeks. Quantity limit: 2 syringes/pens per 28 days.

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
1. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
2. Chart notes have been provided showing improvement in signs and symptoms of CD such as mucosal healing, fewer flare-ups of symptoms, improved quality of life, etc.

If all the above requirements are met, the medication will be approved for an additional 12 months.

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Plaque Psoriasis (PsO)

For **initial** authorization:

1. Member must be 18 years of age or older; AND
2. Medication must be prescribed by or in consultation with a dermatologist; AND
3. Member has clinical documentation of moderate to severe plaque psoriasis characterized by 3% or more of body surface area (BSA) or disease affecting sensitive areas (e.g., hands, feet, face, genitals, etc.); AND
4. Member has tried and failed to respond to treatment with **ONE** of the following:
   a) At least 12 weeks of photochemotherapy (i.e., psoralen plus ultraviolet A therapy);
   b) At least 12 weeks of phototherapy (i.e., UVB light therapy, Excimer laser treatments);
   c) At least a 4-week trial with topical antipsoriatic agents (i.e., anthralin, calcipotriene, coal tar, corticosteroids, tazarotene, tacrolimus, pimecrolimus); AND
5. Member has tried and failed, or unable to tolerate a systemic non-biologic DMARD (i.e., cyclosporine, methotrexate, acitretin) for at least 12 weeks; AND
6. Member has tried and failed at least **TWO** preferred biologic DMARDs for at least 3 months each, one of which must be a TNF inhibitor (same class as Remicade); AND
7. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
8. Member has had a negative tuberculosis test within the past 12 months.
9. **Dosage allowed/Quantity limit:** 5 mg/kg intravenously at 0, 2 and 6 weeks, then every 8 weeks thereafter.

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:

1. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
2. Chart notes have been provided showing improvement of signs and symptoms of disease such as documented member's BSA improvement, etc.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Psoriatic Arthritis (PsA)

For **initial** authorization:

1. Member must be 18 years of age or older; AND
2. Medication must be prescribed by or in consultation with a rheumatologist or a dermatologist; AND
3. Member has a documented diagnosis of active PsA; AND
4. Member has met a 4-week trial of an NSAID taken at maximally tolerated doses **AND** a 3-month trial of a non-biologic DMARD agent (e.g., methotrexate, sulfasalazine, cyclosporine, etc.) unless **ONE** of the following situations is met:
   a) Non-biologic DMARD is **NOT** required for:
      i) Concomitant axial disease (i.e., involving sacroiliac joint and spine) or enthesitis; OR
   b) NSAID and non-biologic DMARD are **NOT** required for:
      i) Severe PsA (defined as having at least one of the following: erosive disease, active PsA at many sites including dactylitis or enthesitis, elevated levels of ESR or CRP, joint deformities, or major impairment in quality of life); AND
5. Member has tried and failed **TWO** preferred biologic DMARDs for at least 3 months each, one of which must be a TNF inhibitor; AND

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6. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
7. Member has had a negative tuberculosis test within the past 12 months.
8. **Dosage allowed/Quantity limit:** 5 mg/kg intravenously at 0, 2 and 6 weeks, then every 8 weeks thereafter.

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
1. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
2. Chart notes have been provided showing improvement of signs and symptoms of disease such as decreased joint swelling and pain, improved skin appearance, improved quality of life, etc.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Rheumatoid Arthritis (RA)

For **initial** authorization:
1. Member must be 18 years of age or older; AND
2. Medication must be prescribed by or in consultation with a rheumatologist; AND
3. Member has a documented diagnosis of moderately to severely active RA; AND
4. Member must have a trial and failure of, or intolerance to methotrexate for at least 3 months; *Note*: If methotrexate is contraindicated, one of the following conventional DMARDs must be trialed instead: leflunomide, sulfasalazine, or hydroxychloroquine; AND
5. Medication is being given in combination with methotrexate or with another conventional DMARD if unable to tolerate methotrexate; AND
6. Member has tried and failed **TWO** preferred biologic DMARDs for 3 months each, one of which must be a TNF inhibitor; AND
7. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
8. Member has had a negative tuberculosis test within the past 12 months.
9. **Dosage allowed/Quantity limit:** 3 mg/kg intravenously at 0, 2 and 6 weeks, then every 8 weeks thereafter. Prior to any changes in dose or frequency, documentation of medical necessity for increase is required (including assessment for adherence and description of residual symptoms, etc.). The max that will be considered is up to 10 mg/kg every 8 weeks or treating as often as every 4 weeks.

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
1. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
2. Chart notes demonstrate improvement of RA signs and symptoms such as fewer number of painful and swollen joints, achievement of remission, slowed progression of joint damage, etc.

If all the above requirements are met, the medication will be approved for an additional 12 months.

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Ulcerative Colitis (UC)

For **initial** authorization:

1. Member is 6 years of age or older with moderately to severely active UC; AND
2. Medication must be prescribed by or in consultation with a gastroenterologist; AND
3. Member must have a documented trial and inadequate response with **ONE** of the following:
   a) 3 months of 6-mercaptopurine or azathioprine;
   b) 30 days of corticosteroid (e.g., budesonide, prednisone, methylprednisolone, etc.);
   c) 3 months of 5-aminosalicylate (e.g., Asacol HD, Lialda, Pentasa, Delzicol, mesalamine, etc.); AND
4. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
5. If the request is for Zymfentra, member must have a trial and failure of **ALL** preferred IV infliximab products; AND
6. Member has had a negative tuberculosis test within the past 12 months.
7. **Dosage allowed/Quantity limit:** 5 mg/kg intravenously at 0, 2, and 6 weeks, followed by 5 mg/kg every 8 weeks thereafter. Prior to any dosages or dosing frequencies greater than listed, medical necessity documentation must be supplied to justify coverage.
   Zymfentra (Adults only): after 10 weeks of dosing with an intravenous infliximab product, administer 120 mg subcutaneously once every two weeks. Quantity limit: 2 syringes/pens per 28 days.

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:

1. Member has tried and failed **ONE** preferred infliximab product (see appendix); AND
2. Chart notes have been provided showing improvement in signs and symptoms of UC such as clinical remission, decrease in rectal bleeding, decreased corticosteroid use, etc.

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Infliximab (Avsola, Inflectra, Remicade, Renflexis, Zymfentra) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
05/10/2017	New policy for Remicade created. Polices SRx-0041, SRx-0042, and SRx-0043 archived. For diagnosis of AS: trial of Humira and Enbrel requirement was added. For CD: Pediatric Crohn's Disease Activity Index (PCDAI) and Crohn's Disease Activity Index (CDAI) were requirements added; trial of Humira was added. For diagnosis of PP: immunosuppressive drug criterion was separated from phototherapies and topical agents' trials; Psoriasis Area and Severity Index (PASI) score requirement was added; trials of Humira and Enbrel were added. For PsA: trials of Humira and Enbrel were added. For RA: non-biologic DMARDS were listed and criterion was added to use drug in combination with methotrexate, or if intolerant to methotrexate, use another immunosuppressant; trials of Humira and Enbrel were added. For UC: requirement for moderate to severe UC was revised, Pediatric Ulcerative Colitis Activity Index (PUCAI) was added. Trial of Humira required for member ≥ 18 y.o. List of diagnoses considered not medically necessary was added.

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02/26/2019	Humira removed from trial criteria. Actemra, Cimzia, Cosentyx, Enbrel, Kevzara, Olumiant, Otezla, Siliq and Xeljanz added to trial agents list. TB test allowed to be done within 12 months prior to initiation of therapy; chest x-ray option removed. Symptoms of back pain for AS extended till before age of 50. Other drugs options allowed for PsA if there is an intolerance or contraindication to methotrexate.
11/22/2020	Replaced list of excluded diagnoses with the generic statement. Updated references. For all diagnoses: Removed repeat TB in reauth for all diagnoses. AS: Removed list of symptoms of spondyloarthritis because imaging result should be sufficient. Removed peripheral arthritis requirement – not relevant for this diagnosis. Updated maintenance dosing to 6 weeks. CD: Removed PCDAI and CDAI score requirements. Specified length of trials for conventional therapies, previously not specified. Those with severe disease can skip the drug trial. Changed initial approval to 6 months to observe efficacy. PsA: Added requirement of diagnosis of PsA. Changed the trial section to be 4 weeks of an NSAID AND 3 months of a DMARD unless other circumstances apply (e.g., concomitant axial disease, severe PsA, etc.). PsO: Removed rheumatologist from prescriber. Changed BSA to 3% or sensitive area involvement. Removed PASI score requirement. RA: Changed the trials to require methotrexate as one of the non-biologic DMARD trials; only one trial is needed if member has poor prognostic factors. UC: Removed PUCAI and Mayo score requirements. Specified the length of trials for conventional therapies (previously not specified).
01/19/2022	Transferred to new template. RA: Added new reference. Edited the terminology “non-biologic” DMARD to “conventional” DMARD. Changed from requiring 2 csDMARD to just 1. Changed from specific drug names to say 2 preferred biologics one of which is a TNF inhibitor. Modified statement about dose changes and included max dose. AS, PsO, PsA: Clarified DMARD trial wording and reauthorization criteria. Simplified wording for TB test requirement.
01/31/2024	Changed policy name from Remicade (infliximab) to Infliximab (Avsola, Inflectra, Remicade, Renflexis, Zymfentra); combined Remicade, Inflectra and Renflexis policies into one; added Zymfentra to the policy including dosing and quantity limit; updated and added references; added Avsola to policy; removed quantity limit from Inflectra, Renflexis and Remicade; removed pharmacy benefit from Remicade
03/26/2024	Added a trial of preferred IV infliximab products to Zymfentra; added trial of preferred infliximab products; added appendix with preferred and nonpreferred products; added trial of infliximab product into reauthorization criteria.
08/20/2024	AS: changed trial of each NSAID from 4 weeks to 2 weeks for a total of 4 weeks of treatment per EULAR 22 guidelines; removed criteria requiring back pain for 3 or more months before the age of 50 and inflammation of one or both of the sacroiliac joints and added that member must have elevated CRP or sacroiliitis on MRI per EULAR 22 guidelines

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4. Renflexis [prescribing information]. Republic of Korea; Samsung Bioepis Co., Ltd.: 2023.
5. Zymfentra [prescribing information]. Republic of Korea; Celltrion, Inc.: 2023
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Appendix I: Preferred Infliximab Products

Preferred	Non-Preferred
• Inflectra • Avsola	• Remicade • Renflexis • Zymfentra

Effective date: 01/01/2025
Revised date: 08/20/2024