

Pharmacy Management Drug Policy

SUBJECT: Inflectra® (infliximab-dyyb), Infliximab (Remicade® (infliximab)), Renflexis® (infliximab-abda)

POLICY NUMBER: PHARMACY-44

EFFECTIVE DATE: 8/2003

LAST REVIEW DATE: 1/6/2020

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

DESCRIPTION:

Remicade® is a chimeric (murine-human) IgG1k monoclonal antibody produced by recombinant DNA technology by continuous perfusion and is purified by a series of steps that includes measures to inactivate and remove viruses. Remicade neutralizes the biological activity of tumor necrosis alpha (TNF α) by high-affinity binding and inhibits binding of TNF α with its receptors. Inhibiting the binding of TNF α to its receptors prevents the release of the pro-inflammatory cytokines that are involved in the body's immune and inflammatory responses.

Inflectra® (infliximab-dyyb) is the first biosimilar monoclonal antibody (mAb) approved by the FDA. Analytical data demonstrates that it is highly similar in structure and function to Remicade. The FDA's decision follows the February 9, 2016 FDA Arthritis Advisory Committee's recommendation to approve proposed biosimilar infliximab across all eligible indications, by a vote of 21-3. Infliximab-dyyb products neutralize the biological activity of TNF α by binding with high affinity to the soluble and transmembrane forms of TNF α and inhibit binding of TNF α with its receptors. Inhibiting the binding of TNF α to its receptors prevents the release of the pro-inflammatory cytokines are involved in the body's immune and inflammatory responses.

Renflexis® (infliximab-abda) is the second biosimilar monoclonal antibody (mAb) approved by the FDA. Analytical data demonstrates that it is highly similar in structure and function to Remicade. Renflexis was approved by the FDA on April 21, 2017 for all eligible indications. Infliximab-abda products neutralize the biological activity of TN TNF α by binding with high affinity to the soluble and transmembrane forms of TNF α and inhibit binding of TNF α with its receptors. Inhibiting the binding of TNF α to its receptors prevents the release of the pro-inflammatory cytokines are involved in the body's immune and inflammatory responses.

For a biological product to be labeled as a biosimilar, it must be shown that it is highly similar and has no differences from an existing FDA approved reference product (i.e. Remicade) by extensively analyzing the structure, purity, chemical identity, and bioactivity. It has been concluded that there are no clinically meaningful differences demonstrated through human pharmacokinetic/exposure and pharmacodynamic/responses, and assessment of immunogenicity. Biosimilars may be approved for all or a subset of the same indications as the reference product, depending on patent exclusivity. Biosimilars differ from generics in complexity, manufacturing processes, and in the data needed to demonstrate similarity for approval.

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FDA approved indications:

	Remicade	Inflectra	Renflexis
AS	✓	✓	✓
CD	✓	✓	✓
Pediatric CD (6 years and older)	✓	✓	✓
PS	✓	✓	✓
PsA	✓	✓	✓
RA	✓	✓	✓
UC	✓	✓	✓
Pediatric UC (6 years and older)	✓	✓	✓

AS – Ankylosing Spondylitis; CD – Crohn’s Disease; PS – Psoriasis; PsA – Psoriatic Arthritis; RA – Rheumatoid Arthritis; UC – Ulcerative Colitis

Inflectra is the preferred infliximab product and will be covered under the medical benefit without prior authorization. Approval for Remicade and Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra. An adequate trial of Inflectra is defined as:

- For infliximab naïve (new start) patients – Standard induction dosing and two dosing intervals (every 8 weeks, etc.)
- For patients who have previously received infliximab – Two dosing intervals (every 8 weeks, etc.)

PLEASE NOTE: the below criteria applies to –

- Requests for Remicade and Renflexis for all lines of business
- Requests for Inflectra for Managed Medicaid (MMC)/Child Health Plus (CHP)*
 - Inflectra does not require prior authorization for lines of business other than MMC/CHP

REMICADE (infliximab), RENFLEXIS (infliximab-abda), INFLECTRA (infliximab-dybb)* POLICY:

Based upon our assessment and review of the peer-reviewed literature infliximab has been medically proven to be effective and therefore, medically necessary for any of the following indications if all of the following criteria are met:

I. Ankylosing Spondylitis

- a. Member must be followed by and the drug prescribed a rheumatologist or a recognized expert with treatment in inflammatory back pain **AND**
- b. There must be presence of refractory disease defined by failure or at least two NSAIDs at maximum strength for at least 1 month each **AND**
- c. Member must have documentation of serious side effects or drug failure after an adequate trial of Inflectra
- d. Infliximab dosing will be authorized for ankylosing spondylitis (AS) as 5mg/kg at weeks 0, 2, and 6, and every 6 weeks thereafter
- e. Dosing for arthritis associated with gastrointestinal disease may be dosed similar to Rheumatoid Arthritis regimens.
- f. Recertification for Remicade or Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra

II. Crohn’s Disease

- a. Member must be actively followed by and the drug prescribed by a gastroenterologist **AND**

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- b. Member must have a diagnosis of moderate to severe disease defined as Crohn's Disease Activity Index (CDAI) score of 220-450. Typically described as having more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting or significant anemia **AND**
- c. Member must meet at least **ONE** of the following criteria:
 - i. Patient continues to experience disease flare despite complete and adequate therapy with a corticosteroid (such as prednisone or budesonide) **OR**
 - ii. Treatment with an immunomodulator (such as azathioprine or 6-mercaptopurine) fails to maintain remission in a case of steroid dependent or steroid refractory CD. **OR**
 - iii. Documentation is provided that azathioprine, 6-mercaptopurine, or methotrexate is not effective, contraindicated, or not tolerated **AND**
- d. Member must have documentation of serious side effects or drug failure after an adequate trial of Inflectra
- e. Authorization Period and Limitations for patients with Crohn's Disease:
 - i. **Initial therapy:** A maximum of 4 infusions in a 4 month period may be authorized when criteria are met. The recommended initial dose for adult and pediatric patients age 6 and older is 5mg/kg administered at weeks 0, 2, and 6 and then every 8 weeks thereafter. Patients who do not respond by week 14 are unlikely to respond to continued dosing and consideration should be given to discontinue infliximab in these patients.
 - ii. **Dose Escalation:** For patients who respond and then lose their response, consideration may be given to increase either the dose or the frequency. Requests to increase both the dose and the frequency at the same time will not be authorized. A dosing regimen of greater than 10mg/kg at any frequency interval will not be authorized. A dosing regimen of less than every 4 weeks at any strength will not be authorized.
- f. Recertification for Remicade or Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra

III. Plaque Psoriasis

- a. Member must be actively followed by and the drug prescribed by a dermatologist or rheumatologist **AND**
- b. Member must be at least 18 years of age **AND**
- c. Member must have moderate to severe chronic plaque psoriasis that involves at least 10% of their body surface area. Consideration will be given to those who have severe disease of the hands or feet or other areas causing disruption in normal activities, but have less than 10% body surface area involvement **AND**
- d. Member must be a candidate for systemic therapy (i.e., acitretin, methotrexate, or cyclosporine therapy) **AND** had a trial period of at least a 3 months or had developed severe intolerance or contraindications to the above mentioned agents (if contraindicated, trial of one of the other two criteria listed below must be present)
 - i. If systemic therapy is contraindicated, then one of the following must be attempted for a reasonable period of time (at least 3 months):
 1. UVB in combination with a topical therapy such as coal tar, steroids or tazarotene **OR**
 2. PUVA in combination with topical corticosteroids **OR**

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3. Medium/High potency topical steroids in combination with anthralin, calcipotriene, or tazarotene **AND**
 - e. Member must have documentation of serious side effects or drug failure after an adequate trial of Inflectra
 - f. Infliximab dosing will be authorized for plaque psoriasis as 5 mg/kg at 0, 2, 6 weeks followed by maintenance therapy every 8 weeks.
 - g. Recertification for Remicade or Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra

IV. Psoriatic Arthritis

- a. Member must be actively followed by and the drug prescribed by a dermatologist or rheumatologist **AND**
- b. Member must have some clinical features of psoriatic arthritis such as: involvement of the DIP joints, an asymmetric distribution of joint disease, spondyloarthritis, sausage digits, new bone formation on radiographs, cutaneous findings, and the characteristic nail manifestations of psoriatic arthritis (nail pitting, onycholysis & other lesions, which include leukonychia, red spots in the lunula, and nail plate crumbling) all may be present **AND**
- c. Member must have documentation of serious side effects or drug failure after an adequate trial of Inflectra
- d. Infliximab dosing will be authorized at a dose of 5mg/kg at weeks 0, 2, and 6 weeks and then every 8 weeks thereafter. Infliximab can be used with or without methotrexate.
- e. Recertification for Remicade or Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra

V. Rheumatoid Arthritis

- a. Member must be actively followed by and the drug prescribed by a rheumatologist **AND**
- b. Member must have had failure to methotrexate alone at a minimum dose of 12.5 – 15mg weekly after at least a 12 week period **AND**
- c. Member must have documentation of serious side effects or drug failure after an adequate trial of Inflectra **AND**
- d. Member must be receiving concomitant methotrexate therapy (at least 7.5mg to 10mg per week) and will continue methotrexate therapy (at least 7.5mg to 10mg per week) for the duration of infliximab use
 - i. **Note:** For patients that have a contraindication to or documented side effects to methotrexate the expectation is that infliximab will NOT be used as monotherapy. Alternative DMARDs (leflunomide, hydroxychloroquine, sulfasalazine, etc) can be used in place of methotrexate. Each case will be reviewed individually and the facts and merits of each case will be fully considered.
- e. Authorization Period and Limitations for Patients with Rheumatoid Arthritis
 - i. **Initial therapy:** A maximum of 5 infusions in a 6 month period may be authorized when criteria are met. Note: The recommended initial dose is 3mg/kg administered at weeks 0, 2, and 6 and then every 8 weeks thereafter.
 - ii. **Continued therapy:**

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1. After the initial 6 months of therapy, a maximum of 7 infusions in a 1 year period may be authorized when documentation (including chart notes) indicates that there is disease stability or improvement **OR**
 2. A maximum of 6 infusions in a 6 month period may be considered medically necessary for patients who have had an incomplete response to administration (up to 10 mg/kg) every 8 weeks. NOTE: Available data do NOT support increasing both the dose (to 10 mg/kg) AND dosing frequency (to every 4 weeks) at the same time. A dosing regimen of greater than 10mg/kg at any frequency interval will not be authorized. A dosing regimen of less than every 4 weeks at any strength will not be authorized.
- f. Low disease activity or remission should be considered treatment targets for members receiving infliximab. Members with moderate or high disease activity >3 months due to lack of or loss of benefit should discontinue infliximab and switch to another biologic agent.
 - g. Members with high disease activity who fail infliximab therapy due to a serious adverse effect should switch to a non-TNF biologic. Member with moderate or high disease activity who fails infliximab therapy due to non-serious adverse effects should switch to another TNF-blocker or a non-TNF biologic agent.
 - h. Recertification for Remicade or Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra

VI. Ulcerative Colitis

- a. Member must be actively followed by and the drug prescribed by a gastroenterologist **AND**
- b. Member must have failure or intolerance to at least 2 of the following conventional therapies for at least 3 months:
 - i. Thiopurines: Azathioprine/6-mercaptopurine (6-MP)
 - ii. 5-Aminosalicylates: Sulfasalazine, Mesalamine (asacol, colazol), Olsalazine
 - iii. Cyclosporine
 - iv. IV or oral steroids **AND**
- c. Member must have documentation of serious side effects or drug failure after an adequate trial of Inflectra
- d. A diagnosis of pediatric ulcerative colitis will **NOT** require trial and failure of Inflectra in children younger than 18 years
- e. Infliximab dosing will be authorized for UC as 5 mg/kg at 0, 2, and 6 weeks and every 8 weeks thereafter.
- f. Recertification for Remicade or Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra

The following are **non-FDA approved indications** which **may be considered medically appropriate**:

VII. Behcet's disease

- a. Member must have a confirmed diagnosis of Behchet's disease with ocular involvement (uveitis) **AND**
- b. Member must be actively followed by and the drug prescribed by a rheumatologist **AND**

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- c. Member must be refractory to corticosteroids and at least one immunosuppressive agent **AND**
- d. Member must have documentation of serious side effects or drug failure after an adequate trial of Inflectra
- e. Initial dosing will be authorized at 5mg/kg. The typical schedule of weeks 0, 2, and 6 and then every 8 weeks thereafter is common regimen associated with this disease state.
- f. Recertification for Remicade or Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra

VIII. Hidradenitis Suppurativa

- a. Member must be actively followed by and the drug prescribed by a dermatologist **AND**
- b. Member must have a diagnosis of stage II, stage III, or severe refractory hidradenitis suppurativa with recurrent abscesses **AND**
- c. Member must have had a minimum of a three month trial of systemic antibiotics (such as minocycline, doxycycline, clindamycin, or rifampin) which failed to provide clinical improvement **AND**
- d. Member must have documentation of serious side effects or drug failure after an adequate trial of Inflectra
- e. Initial approval will be for 6 months - 5 infusions of 5mg/kg week 0, week 2 and week 6; then maintenance doses at week 14 and week 22. Recertification will require progress notes showing a therapeutic response to initial dosing, and if approvable, will be authorized for 5 years per MSD guidelines.
- f. Recertification for Remicade or Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra

IX. Noninfectious Uveitis

- a. Member must be actively followed by and the drug prescribed by a rheumatologist or ophthalmologist **AND**
- b. Member must have a previous trial of ALL of the following:
 - i. A topical or injected ophthalmic steroid (unless contraindications are present)
 - ii. An oral systemic steroid
 - iii. An adequate trial of an immunosuppressive agent, such as but not limited to, azathioprine, mycophenolate, or methotrexate **AND**
- c. Member must have documentation of serious side effects or drug failure after an adequate trial of Inflectra
- d. Initial approval will be for 6 months – 5mg/kg IV infusion at weeks 0, 2, 6 – then a maintenance dose of 5 mg/kg IV infusion every 8 weeks thereafter. Recertification will require progress notes showing a therapeutic response to initial dosing, and if approvable, will be authorized for 5 years per MSD guidelines.
- e. Recertification for Remicade or Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra

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APPROVAL TIME PERIODS:

Line of Business	Medical Initial approval (IV)	Medical Recertification (IV)
Medicaid Managed Care (MMC)/Child Health Plus (CHP)	6 months	12 months
Commercial/Exchange	Outpatient hospital: 1 year	Outpatient hospital: 1 year
	Home Care/Office based: 2 years	Home Care/Office based: 2 years
Medicare	Outpatient hospital: 2 years	Outpatient hospital: 2 years
	Home Care/Office based: 2 years	Home Care/Office based: 2 years

POLICY GUIDELINES:

1. Prior-authorization is contract dependent.
 - Requests for Remicade and Renflexis for all lines of business
 - Requests for Inflectra for Managed Medicaid (MMC)/Child Health Plus (CHP)*
 - Inflectra does not require prior authorization for lines of business other than MMC/CHP
2. Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e.; generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.
3. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required.
 - The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
 - The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
 - The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
 - The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
 - The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rationale for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
 - The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.

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4. The patient has no contraindications to the use of infliximab, including:
 - a. Class III or IV CHF, or in subjects with an ejection fraction less than 50%
 - b. Patient must be free of clinically important active infection.
 - c. Infliximab should not be administered to patients with known hypersensitivity to any murine proteins or other components of the product.
5. Infliximab carries a Black Box Warning for risk of infection. Tuberculosis, invasive fungal infections, and other opportunistic infections have been observed in patients receiving infliximab.
6. All patients should be evaluated for latent tuberculosis with a tuberculin skin test. Treatment of latent tuberculosis infection should be initiated prior to therapy with Infliximab. Annual testing is recommended for patients who live, travel, or work in situations where tuberculosis exposure is likely.
7. Caution should be exercised in patients with a clinically important chronic infection or a history of recurrent infection.
8. Rare post-marketing cases of hepatosplenic T-cell lymphoma have been reported in adolescent and young adults with Crohn's disease treated with Infliximab. All of these cases have occurred in patients on concomitant treatment with azathioprine or mercaptopurine.
9. Severe hepatic reactions including acute liver failure, jaundice, hepatitis, and cholestasis have been reported in post marketing data. This has occurred between 2 weeks to more than 1 year after initiation of therapy. Patients with signs or symptoms of liver dysfunction should be evaluated for liver injury if jaundice and/ or marked liver enzyme elevations (≥ 5 x upper limit of normal) develops. Infliximab should be discontinued and a thorough investigation of the abnormality should be undertaken.
10. Infliximab has been associated with the reactivation of chronic hepatitis B in patients who are chronic carriers of the virus. Chronic carriers should be appropriately evaluated and monitored prior to the initiation of therapy. Patients with psoriasis who are candidates for anti-TNF therapy should undergo hepatitis B screening prior to initiating therapy. Patients who are seropositive for hepatitis B surface antigen with inactive disease should undergo a course of antiviral therapy 2 – 4 weeks prior to initiation of anti-TNF therapy.
11. Safety and efficacy of Remicade in juvenile rheumatoid arthritis has not been established. The merits of each case will be evaluated individually.
12. Involvement of the DIP joints, an asymmetric distribution of joint disease, spondyloarthritis, sausage digits, new bone formation on radiographs, cutaneous findings, and the characteristic nail manifestations of psoriatic arthritis all help to distinguish psoriatic arthritis from other inflammatory arthritis, including RA.
13. A diagnosis of Irritable Bowel Disease associated arthritis will be evaluated using criteria for Ankylosing Spondylitis. Recent data suggest following dosing regimens developed for patients with Rheumatoid Arthritis. (Allowing dose increases above 5mg/kg.)
14. Remicade, Inflectra, or Renflexis will not be authorized when used in combination with other biologics such as Enbrel (etanercept), Kineret (anakinra), Orencia (abatacept), Rituxan (rituximab), or Humira (adalimumab).
15. Patients should not receive live attenuated herpes zoster vaccine while receiving anti-TNF therapy.
16. Approval of Remicade and Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra. An adequate trial is defined as:
 - a. For infliximab naïve (new start) patients – Standard induction dosing and two dosing intervals (every 8 weeks, etc.)
 - b. For patients who have previously received infliximab – Two dosing intervals (every 8 weeks, etc.)

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17. Recertification for Remicade or Renflexis will require documentation of serious side effects or drug failure after an adequate trial of Inflectra.
18. All off-label uses of infliximab will be evaluated based on off-label policy criteria. If clinical criteria is met, then Inflectra will be the required product.

CODES

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. Codes may not be covered under all circumstances. Please read the policy and guideline statements carefully. Codes may not all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key: Experimental/Investigational = (E/I). Not medically necessary/appropriate = (NMN).
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<u>HCPCS:</u>	<u>Number</u>	<u>Description</u>
	J1745	Remicade
	Q5103	Inflectra
	Q5104	Renflexis

UPDATES:

Date	Revision
1/20	Revised
7/19	Revised
6/19	Annual Review
2/19	Revised
9/18	Revised
3/18	Revised
1/18	Revised
12/17	Revised
8/17	Revised
5/17	P&T Approval
12/16	Revised
5/16	Revised
10/15	Revised
12/14	Revised
12/13	Revised
10/13	Revised
8/13	Revised
2/13	Reviewed
11/11	Revised
10/10	Revised
6/10	Revised
7/09	Revised
5/09	Revised

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REFERENCES:

1. Remicade [package insert]. Malvern, PA: Centocor Inc; Revised October 2015. Accessed December 2016.
2. Inflectra (infliximab-dyyb) package insert. Republic of Korea: CELLTRION, Inc. Revised April 2016. Accessed December 2016.
3. Renflexis (infliximab-abda) package insert. Republic of Korea: Samsung Bioepis Co. Revised April 2017. Accessed August 2017.
4. U.S. Food and Drug Administration. Biological Product Definitions. <https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM581282.pdf>. Accessed: January 30, 2018.
5. American College of Rheumatology (ACR) Subcommittee on Rheumatoid Arthritis Guidelines. "Guidelines for the management of rheumatoid arthritis. 2002 update" *Arthritis Rheum* 2002 Feb; 46 (2): 328-46.
6. St. Clair. EW, Van der Heijde D, Smolen J, Maini RN, Bathon JM, Emery P, et al. Combination of Infliximab and Methotrexate Therapy for Early Rheumatoid Arthritis. *Arthritis Rheum* 2004 Nov 11; 50 (11):3432-43.
7. Maini RN, Breedveld F, Kalden JR, Smolen JS, Furst D, Weisman MH. Sustained improvement over two years in physical functions, structural damage, and signs and symptoms among patients with rheumatoid arthritis, treated with infliximab and methotrexate. *Arthritis Rheum* 2004 Apr; 50(4):1051-1065.
8. Maini R, St. Clair EW, Breedveld F, Furst D, Kalden J, Weisman E, et al. Infliximab (chimeric anti-tumor necrosis factor α monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomized phase III trial. *Lancet* 1999; 354:1932-9.
9. Lipsky PE, van der Heijde DMFM, St. Clair EW, Furst DE, Breedveld FC, Kalden JR, et al. Infliximab and methotrexate in the treatment of rheumatoid arthritis. *N Engl J Med* 2000; 343:1594-602.
10. Van der Heijde D, Dijkmans B, Geusens P, Sieper J, DeWoody K, Williamson P, et al. Efficacy and safety of infliximab in patients with ankylosing spondylitis. *Arthritis Rheum* 2005 Feb; 52(2): 582-91.
11. Braun, J, Pham T, Sieper J, Davis J, Van der Linden Sj, Dougados M, Van der Heijde D, for the ASAS Working Group. International ASA consensus statement for the use of anti-tumor necrosis factor agents in patients with ankylosing spondylitis. *Ann Rheum Dis* 2003; 62: 817-824.
12. Baraliakos X, Brandt J, Listing M, et al. Clinical response to long-term therapy with infliximab in patients with ankylosing spondylitis-results after 3 years. *Arthritis Rheum*. 2004; 50 (suppl):S217.
13. Hanauer SB, Feagan BG, Lichtenstein GR et al. Maintenance infliximab for Crohn's disease: The ACCENT I randomized trial. *Lancet* 2002; 359; 1541-49.
14. Baert F, Noman M, Vermeire S, et al. Influence of Immunogenicity on the Long-Term Efficacy of Infliximab in Crohn's Disease. *N Engl J Med* 2003; 348:601-8.
15. Rutgeerts P, D'Haens G, Targan S, Vasiliauskas E, Hanauer S, Present DH, et al. Efficacy and safety if retreatment with anti-tumor necrosis factor antibody (Infliximab) to maintain remission in Crohn's disease. *Gastroenterology*. 1999; 117: 761-9.
16. Targan S, Hanauer SB, van Deventer Sander JH, Mayer L, Present DH, Braakman T. A short-term study of chimeric monoclonal antibody CA2 to tumor necrosis factor (alpha) for Crohn's disease. *N Eng J Med*. 1997 Oct; 337(15): 1029-1035.

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17. Chaudhari U, Romanano P, Mulcahy LD et al. Efficacy and safety of Infliximab monotherapy for plaque-type psoriasis. A randomized trial. *Lancet* 2001; 357:1842-47.
18. Shen EH, Das KM. Current therapeutic recommendations: infliximab for ulcerative colitis. *J Clin Gastroenterol.* 2004;38:741-745.
19. Chey WY, Hussein A, Ryan C, et al. Infliximab for refractory ulcerative colitis. *Am J Gastroenterol.* 2001;96:2373-2381
20. Rutgeerts P, Sandborn WJ, Feagan BG, Reinisch W, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. *N Eng J Med.* 2005 Dec 8; 353(23): 2462-76.
21. Jarnerot G, Hertervig E, Friis-Liby I, Blomquist L, Karlen P, et al. Infliximab as rescue therapy in severe to moderately severe ulcerative colitis: a randomized, placebo-controlled study.[see comment]. *Gastroenterology.* 2005 Jun; 128(7): 1805-11,
22. Antoni CE, Kavanaugh A, Kirkham B, et al. Sustained benefits of infliximab therapy for dermatologic and articular manifestations of psoriatic arthritis. Results from the infliximab multinational psoriatic arthritis controlled trial (IMPACT). *Arthritis Rheum.* 2005; 52(4): 1227-36.
23. Gottlieb AB, et al. Infliximab induction therapy for patients with severe plaque-type psoriasis: a randomized, double-blind, placebo-controlled trial. *J Am Acad Dermatol* 2004; 51:534-42.
24. Gottlieb AB, et al. Infliximab monotherapy provides rapid and sustained benefit for plaque-type psoriasis. *J Am Acad Dermatol* 2003, 48: 829-35.
25. Carter MJ, Lobo AJ, Travis SP, on behalf of the IBD section of the British Society of Gastroenterology. Guidelines for the management of inflammatory bowel disease in adults. *Gut.* 2004;53(Suppl V): v1-v16.
26. Bebb JR, Scott BB. How effective are the usual treatments for ulcerative colitis? *Aliment Pharmacol Therap* July 2004; 20(2): 143-149.
27. Baumgart DC, Sandborn WJ. Inflammatory bowel disease: clinical aspects and established and evolving therapies. *Lancet* 2007; 369: 1641-57.
28. Lichtenstein GR, Hanauer SB, Sandborn WJ and the Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's Disease in Adults. ACG Practice Guidelines 2009. *Amer J of Gastroenterology* Accessed March 2009
29. Swaminath A and Kornbluth A. Optimizing Drug Therapy in Inflammatory Bowel Disease. *Current Gastroenterology Reports.* 2007;9:513-520
30. Velayos FS, Sandborn WJ. Positioning Biologic Therapy for Crohn's Disease and Ulcerative Colitis. *Current Gastroenterology Reports.* 2007;9:521-527
31. J L Nam, K L Winthrop, R F van Vollenhoven, et al. Current evidence for the management of rheumatoid arthritis with biologic disease-modifying antirheumatic drugs: a systemic literature review informing the EULAR recommendations for the management of RA. *Ann Rheum Dis* May 2010.
32. De Stefano R, Frati E, Nargi F, Baldi C, Menza L, Hammoud M, Galeazzi M. Comparison of combination therapies in the treatment of rheumatoid arthritis: leflunomide-anti-TNF-alpha versus methotrexate-anti-TNF-alpha. *Clin Rheumatol.* 2010 May;29(5):517-24.
33. Wechsler B, Sablé-Fourtassou R, Bodaghi B, Huong DL, Cassoux N, Badelon I, Fain O, LeHoang P, Piette JC. Infliximab in refractory uveitis due to Behçet's disease. *Clin Exp Rheumatol.* 2004;22(4 Suppl 34):S14.
34. Sfikakis PP, Theodossiadis PG, Katsiari CG, Kaklamanis P, Markomichelakis NN. Effect of infliximab on sight-threatening panuveitis in Behçet's disease. *Lancet.* 2001;358(9278):295.
35. Benitez-del-Castillo JM, Martinez-de-la-Casa JM, Pato-Cour E, Méndez-Fernández R, López-Abad C, Matilla M, Garcia-Sanchez J. Long-term treatment of refractory posterior uveitis with anti-TNFalpha (infliximab). *Eye (Lond).* 2005;19(8):841.

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Inflectra® (infliximab-dyyb), Infliximab (Remicade® (infliximab)), Renflexis® (infliximab-abda)

36. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis care & research*. May 2012;64(5):625-639.
37. Hsu S, Papp KA, Lebwohl MG, et al. Consensus guidelines for the management of plaque psoriasis. *Archives of dermatology*. Jan 2012;148(1):95-102.
38. 2010 Rheumatoid Arthritis Classification Criteria. An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative. *Arthritis & Rheumatism*. Vol. 62, No. 9, September 2010, pp 2569–2581.
39. Mekkes JR, Bos JD. Long-term efficacy of a single course of infliximab in hidradenitis suppurativa. *Br J Dermatol* 2008 Feb;158(2):370-4
40. Adams DR, Gordon KB, Devenyi AG, et al: Severe hidradenitis suppurativa treated with infliximab infusion. *Arch Dermatol* 2003; 139(12):1540-1542.
41. Sullivan T.P., Welsh E., Kerdel F.A., et al: Infliximab for hidradenitis suppurativa. *Br J Dermatol* 2003; 149(5):1046-1049.
42. Rosi Y.L., Lowe L., & Kang S.: Treatment of hidradenitis suppurativa with infliximab in a patient with Crohn's disease. *J Dermatolog Treat* 2005; 16(1):58-61.
43. Grant A, Gonzalez T, Montgomery MO, Cardenas V, Kerdel FA. Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: a randomized, double-blind, placebo-controlled crossover trial. *J Am Acad Dermatol*. 2010;62(2):205.
44. Lamprecht P., Voswinkel J., Lilienthal T., et al: Effectiveness of TNF-alpha blockade with infliximab in refractory Wegener's granulomatosis. *Rheumatology (Oxford)* 2002; 41(11):1303-1307.
45. Bartolucci P, Ramanoelina J, Cohen P, et al: Efficacy of the anti-TNF-alpha antibody infliximab against refractory systemic vasculitides: an open pilot study on 10 patients. *Rheumatology* 2002; 41:1126-1132.