Clinical Policy Title: Vitiligo and psoriasis

Clinical Policy Number: 16.02.06

Effective Date: October 1, 2017
Initial Review Date: September 17, 2016
Most Recent Review Date: September 17, 2016
Next Review Date: August 2017

Related policies:

None.

ABOUT THIS POLICY: AmeriHealth Caritas Pennsylvania has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas Pennsylvania when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Pennsylvania’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Pennsylvania’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Pennsylvania will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania’s clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas Pennsylvania considers vitiligo and psoriasis to be remediable medical conditions, and the use of treatments specified in this policy to be clinically proven and, therefore, medically necessary when the following criteria are met:

- Diagnosis is made of vitiligo and/or psoriasis by a primary care or specialty physician knowledgeable in the diagnosis (i.e., clinical evaluation, skin biopsy) and treatment of these conditions.

- Treatment administered is an established method of care for vitiligo:
  - Excimer laser (e.g., XTRAC, PhotoMedex, Radnor, PA; EX-308, Ra Medical Systems, Inc., Carlsbad, CA).
  - Narrow-band ultraviolet B (UVB).
  - Topical and oral psoralen photochemotherapy (PUVA).
  - Topical tacrolimus.
  - Topical pimecrolimus.
- Topical and systemic corticosteroids.
- Treatment administered is an established method of care for psoriasis:
  - Anthralin.
  - Corticosteroids (e.g., betamethasone dipropionate ointment and fluocinonide cream).
  - Keratolytic agents (e.g., lactic acid, salicylic acid, and urea).
  - Retinoids (e.g., tazarotene).
  - Tar preparations.
  - Vitamin D derivatives (e.g., calcipotriene).
  - Topical tacrolimus and pimecrolimus
  - Systemic retinoids
  - Methotrexate
  - Systemic cyclosporine
  - Biologic therapies as outlined by PerformRx in “Specialty Biologic Agents for Psoriasis” (Appendix A).

**Limitations:**

All other treatments for vitiligo and psoriasis are considered to be investigational and, therefore, not medically necessary.

Note: The following CPT/HCPCS codes are not listed in the Pennsylvania Medicaid fee schedule:

96913 - Photochemotherapy (Goeckerman and/or PUVA) for severe photoresponsive dermatoses requiring at least four to eight hours of care under direct supervision of the physician (includes application of medication and dressings)

96999 - Unlisted special dermatological service or procedure [excimer laser]

J7507 - Tacrolimus, immediate release, oral 1 mg

J7508 - Tacrolimus, extended release, oral 0.1 mg

**Alternative covered services**

Primary care and specialty physician (including surgical) evaluation and management.

**Background**

Vitiligo is an acquired depigmentary disorder characterized by white areas on the skin due to loss of functional melanocytes. Psoriasis is a common, chronic, disfiguring inflammatory and proliferative
disorder of the skin.

Topical and oral corticosteroids are among several therapeutic agents that have efficacy in these disorders. Very potent topical steroids are widely used to treat vitiligo and psoriasis but the evidence for their effectiveness is limited. Folliculitis is a common side effect of treatment with potent topical steroids. Long-term daily treatment with oral corticosteroids, in most patients, requires continued treatment to maintain response and benefit is usually insufficient to justify the risks.

Photochemotherapy with psoralen plus ultraviolet A has demonstrated therapeutic responses but the relapse rate following treatment is high, and continued treatment is usually needed to maintain control, which may lead to an unacceptably high cumulative UVA dose. Anthralin (Dithranol®, Drithocreme®) are adjunctive therapies but only a small proportion of patients seem to achieve cosmetically worthwhile results. Dithranol needs to be applied sufficiently frequently and in a high enough concentration to produce a brisk irritant reaction in order to be effective. Staining of hair limits its use in fair-haired individuals. Tacrolimus has shown variable response in the treatment of vitiligo and psoriasis. Impressive therapeutic responses have also been seen in those with psoriasis treated with alefacept. In common with other immune-mediated complex diseases, there is no definitive cure for psoriasis, and available treatment is only to decrease disease activity and improve symptoms.

Excimer laser in which “excimer” is a terminological reference of “excited dimer,” composed of a noble gas and halide (e.g., xenon and chloride) which repel each other, is a promising therapeutic choice though laser therapy in general is often compromised by complete or partial response. The advantages of monochromatic 308 nm excimer laser over other phototherapies include lower UV dose exposure, shorter course of therapy and precise definition of treatment area which helps prevent compromise of the adjacent normal skin.

Medium doses of the 308-nm excimer laser have proven to be effective in the treatment of limited vitiligo; however, the rate and speed of repigmentation is highly associated with the site and duration of disease as the face and neck (UV sensitive areas) are the highly respondent areas along with an earlier resolution of the lesions while the joints and extremities (UV resistant areas) exhibit the slightest response to therapy.

**Searches**

AmeriHealth Caritas Pennsylvania searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on August 2, 2016. Search terms were “vitiligo and psoriasis,” “vitiligo” and
“psoriasis.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.

- **Guidelines based on systematic reviews**.

- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

Mehraban (2014) conducted a systematic review of the 308nm xenon-chloride excimer laser in treatment of dermatologic disorders and reported verified efficacy in treating skin conditions such as vitiligo, psoriasis, atopic dermatitis, alopecia areata, allergic rhinitis, folliculitis, granuloma annulare, lichen planus, mycosis fungoides, palmoplantar pustulosis, pityriasis alba, CD30+ lympho proliferative disorder, leukoderma, prurigo nodularis, and localized scleroderma and genital lichen sclerosus.

Wang (2014) treated 170 patients with the 308 nm excimer laser to assess its efficacy and safety for the treatment of vitiligo. The lesions of vitiligo were treated one to two times per week for 10—30 treatments. Efficacies were evaluated every seven days and three days after the treatments were completed. Patients were followed up for two months. The rates of "remarkably improved" and "cured" were 67.97 percent and 32.03 percent in faces, 54.55 percent and 27.27 percent in necks, 63.26 percent and 26.53 percent in trunks, 38.84 percent and 15.70 percent in limbs, and 0 and 0 in hands and feet. The areas of faces had a better response than those of necks, trunks, or limbs (P < 0.01), and the areas of trunks or limbs had better response than that of hands and feet (P < 0.01). The authors concluded that the 308 nm excimer laser is safe and effective in treating stable vitiligo and the efficacy varies in different lesion sites.

A narrative review (DiMeglio, 2014) identified classic therapies of psoriasis that span from topical treatments (emollients, topical corticosteroids, vitamin D analogs) used in mild-to-moderate psoriasis, to UVA/UVB phototherapy or systemic therapies reserved to moderate-to-severe cases. Among systemic therapies, which include retinoids, methotrexate, and cyclosporine, the folic acid antagonist methotrexate, which has immunosuppressive, cytostatic, and anti-inflammatory activity and is rather inexpensive, is often used as first line of treatment. However, classic therapy has not completely met patients’ needs, especially in the most severe cases. In the past decade, a better understanding of disease immunopathogenesis has been successfully translated into new drugs, known as “biologics,” targeting key inflammatory mediators and currently representing an effective third-line therapy in moderate-to-severe psoriasis patients, unresponsive to nonbiologic systemic agents.
Leonardi (2003) demonstrated that tumor necrosis factor (TNF) blockade, using etanercept, is an effective therapeutic strategy for psoriasis. Etanercept is a human p75 TNF receptor fusion protein, similar in therapeutic concept to infliximab, a humanized chimeric anti-TNF monoclonal antibody, or adalimumab, a fully human monoclonal antibody. Etanercept efficacy has been shown in three phase III trials with about 50 percent of patients achieving good responses at week 12 of therapy. TNF neutralization causes early down-modulation of myeloid cell-related genes, with decrease of Th17 cell products and downstream molecules in just 2 weeks after commencing therapy. Interestingly, only patients who downregulate the expression of Th17 pathway genes successfully respond to etanercept treatment.

The latest biologic to be approved for psoriasis, ustekinumab, is a monoclonal antibody simultaneously blocking the heterodimeric proteins IL-12 and IL-23 via its bidding to the shared subunit p40. Its efficacy is quite high, with 67 percent of patients achieving response at 12 weeks of treatment (Leonardi 2008).

Shen (2007), treated a total of 187 patients with the 308-nm excimer laser for 20 sessions at different frequencies (0.5, 1.0, 2.0, and 3.0 per week) in a study designed to determine the optimal treatment frequency for vitiligo and identify key clinical variable(s) associated with treatment efficacy at the optimal frequency. The repigmentation rate was graded on a six-point scale and was blindly evaluated by independent physicians. The final percentage of repigmentation for group 0.5 was statistically lower than those for group 1.0, 2.0, and 3.0, and percentages of final levels of repigmentation among these three groups were not statistically different. The onset of repigmentation correlated with the area of vitiliginous patches treated, not with the other clinical variables.

Finally, the shorter the course of disease, the more promising the treatment of vitiligo using a 308 nm excimer laser. Zhang (2010) studied 36 patients with 44 vitiligo patches who were treated using a 308 nm excimer laser twice a week. After 30 treatments: 27/44 patches (61.4 percent) achieved more than 75 percent repigmentation, 4/44 lesions (9.1 percent) showed 51—75 percent repigmentation, 10/44 (22.7 percent) showed 26-50 percent repigmentation and 3/44 (6.8 percent) showed 1—25 percent repigmentation. Of the 44 patches of vitiligo, 20/27 (74.1 percent) lesions on the face/neck, 9/9 (100 percent) on the trunk and 2/8 (25.0 percent) on the extremities showed ≥50 percent repigmentation. The repigmentation (≥50 percent) in face/neck and trunk were much higher than that in the extremities (P<0.05). The repigmentation ≥50 percent) in disease duration of ≤2 years and >2 years were 100.0 percent and 46.2 percent (P<0.05). The average cumulative doses in the face/neck, trunk and extremities were 7.92+/-5.26, 9.93+/-7.36 and 22.13+/-8.15 J/cm². The doses in the face/neck and trunk were much lower than those in the extremities. (P<0.05). Side effects were limited mainly to symptomatic erythema.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mehraban (2014)</td>
<td>Key points:</td>
</tr>
</tbody>
</table>
### The 308nm excimer laser in dermatology

- Systematic review on 308-nm excimer laser in dermatological disorders.
- Showed efficacy in treating vitiligo, psoriasis, atopic dermatitis, alopecia areata, allergic rhinitis, folliculitis, granuloma annulare, lichen planus, mycosis fungoides, palmoplantar pustulosis, pityriasis alba, CD30+ lymphoproliferative disorder, leukoderma, prurigo nodularis, localized scleroderma and genital lichen sclerosus.

### Di Meglio (2014)

**Psoriasis**

**Key points:**
- Narrative review of classic therapies of psoriasis identified topical treatments (emollients, topical corticosteroids, vitamin D analogs) used in mild-to-moderate psoriasis, to UVA/UVB phototherapy or systemic therapies reserved to moderate-to-severe cases.
- Among systemic therapies, which include retinoids, methotrexate, and cyclosporine, the folic acid antagonist methotrexate, which has immunosuppressive, cytostatic, and anti-inflammatory activity is often used as first line of treatment.
- Targeting key inflammatory mediators currently represents an effective third-line therapy in moderate-to-severe psoriasis patients, unresponsive to nonbiologic systemic agents.

### Zhang (2010)

**Clinical efficacy of a 308 nm excimer laser in the treatment of vitiligo**

**Key points:**
- RCT of 36 patients with 44 vitiligo patches who were treated using a 308 nm excimer laser twice a week.
- After 30 treatments: 27/44 patches (61.4%) achieved more than 75% repigmentation, 10/44 lesions (22.7%) showed 26-50% repigmentation and 3/44 (6.8%) showed 1-25% repigmentation.
- Of the 44 patches of vitiligo, 20/27 (74.1%) lesions on the face/neck, 9/9 (100% on the trunk and 2/8 (25.0%) on the extremities showed ≥50% repigmentation.
- The repigmentation (≥50%) in face/neck and trunk were much higher than that in the extremities (P<0.05).
- The repigmentation (≥50%) in disease duration of ≤2 years and >2 years were 100.0% and 46.2% (P<0.05). The average cumulative doses in the face/neck, trunk and extremities were 7.92+/−5.26, 9.93+/−7.36 and 22.13+/−8.15 J/cm².
- The doses in the face/neck and trunk were much lower than those in the extremities (P<0.05).
- Side effects were limited mainly to symptomatic erythema.

### Wang (2009)

**Efficacy and safety of 308 nm excimer laser for vitiligo.**

**Key points:**
- Efficacies and safety of 308 nm excimer laser for vitiligo.
- Patients were followed up for two months.
- The rates of "remarkably improved" and "cured" were 67.97% and 32.03% in faces, 54.55% and 27.27% in necks, 63.26% and 26.53% in trunks, 38.84% and 15.70% in limbs, and 0% and 0% in hands and feet.
- The areas of faces had a better response than those of necks, trunks, or limbs (P < 0.01), and the areas of trunks or limbs had better response than that of hands and feet (P < 0.01).
- The authors concluded that the 308 nm excimer laser is safe and effective in treating stable vitiligo and the efficacy varies in different lesion sites.

### Leonardi (2008)

**PHOENIX 1 study investigators.**

**Key points:**
- Multicenter study of TNF blockade, using etanercept, a human p75 TNF receptor fusion protein.
- Etanercept achieved response in 50% of patients at week 12.
**Shen (2007)**

Optimal frequency of treatment with the 308-nm excimer laser for vitiligo on the face and neck

**Key points:**
- RCT treated a total of 187 patients with the 308-nm excimer laser for 20 sessions at different frequencies (0.5, 1.0, 2.0, and 3.0 per week).
- Repigmentation rate was graded on a six-point scale and was blindly evaluated by independent physicians.
- The final percentage of repigmentation for group 0.5 was statistically lower than those for group 1.0, 2.0, and 3.0, and percentages of final levels of repigmentation among these three groups were not statistically different.
- The onset of repigmentation correlated with the area of vitiliginous patches treated, not with the other clinical variables.

<table>
<thead>
<tr>
<th>Leonardi (2003)</th>
<th>Key points:</th>
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</table>
| Etanercept as monotherapy in patients with psoriasis | - Clinical trial report suggested TNF blockade is an effective therapeutic strategy for psoriasis.  
- Three phase III trials with about 50% of patients achieved good responses at week 12 of therapy. |

**Glossary**

**Phototherapy** — Uses UVB light, categorized as either wide-band or narrow-band, which refers to the wavelengths included in the UV light source. The Goeckerman regimen combines UVB treatments with coal tar applications.

**Photochemotherapy** — Uses UVA in conjunction with a photosensitizer called psoralen (also known as psoralen with ultraviolet A, or PUVA. The photo-sensitizer is a medication that can be applied directly to the skin or taken orally and makes the skin more sensitive to the ultraviolet light. PUVA is usually a second-line treatment, reserved for patients who have failed to improve with conventional therapy. PUVA may be used to treat psoriasis, atopic dermatitis (eczema) and other conditions. Complications of PUVA may include skin damage, premature skin aging, cataracts and increased risk of melanoma and squamous cell carcinoma.

**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


**Clinical trials:**

Searched clinicaltrials.gov on August 17, 2016 using terms “vitiligo and psoriasis,” | Open Studies. Five studies found, two relevant.


CMS National Coverage Determinations (NCDs):

No NCDs found for treatment of vitiligo and psoriasis.

Local Coverage Determinations (LCDs):

No LCDs found for treatment of vitiligo and psoriasis.

Commonly submitted codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comment</th>
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<tr>
<td>96999</td>
<td>Unlisted special dermatological service or procedure [excimer laser]</td>
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<tr>
<td>96910</td>
<td>Photochemotherapy; tar and ultraviolet B (Goeckerman treatment) or petrolatum and ultraviolet B</td>
<td></td>
</tr>
<tr>
<td>96912</td>
<td>Photochemotherapy; psoralens and ultraviolet A (PUVA)</td>
<td></td>
</tr>
<tr>
<td>96913</td>
<td>Photochemotherapy (Goeckerman and/or PUVA) for severe photoresponsive dermatoses requiring at least four to eight hours of care under direct supervision of the physician (includes application of medication and dressings)</td>
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<tr>
<td>96920</td>
<td>Laser treatment for inflammatory skin disease (psoriasis); total area less than 250 sq cm</td>
<td></td>
</tr>
<tr>
<td>96921</td>
<td>Laser treatment for inflammatory skin disease (psoriasis); 250 sq cm to 500 sq cm</td>
<td></td>
</tr>
<tr>
<td>96922</td>
<td>Laser treatment for inflammatory skin disease (psoriasis); over 500 sq cm</td>
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<table>
<thead>
<tr>
<th>ICD-10 Code</th>
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<tr>
<td>L40.0-L40.9</td>
<td>Psoriasis</td>
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<tr>
<td>L80</td>
<td>Vitiligo</td>
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<td>---------</td>
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</tr>
<tr>
<td>J0135</td>
<td>Injection, adalimumab, 20 mg</td>
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<tr>
<td>J1438</td>
<td>Injection, etanercept, 25 mg</td>
<td>Not covered for Medicare when self-administered</td>
</tr>
<tr>
<td>J1745</td>
<td>Injection, infliximab, 10 mg</td>
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<tr>
<td>J3357</td>
<td>Injection, ustekinumab, 1 mg</td>
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</tr>
<tr>
<td>J3380</td>
<td>Injection, vedolizumab, 1 mg</td>
<td></td>
</tr>
<tr>
<td>J8449</td>
<td>Apremilast 30 mg tablet</td>
<td></td>
</tr>
<tr>
<td>J7507</td>
<td>Tacrolimus, immediate release, oral 1 mg</td>
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<tr>
<td>J7508</td>
<td>Tacrolimus, extended release, oral 0.1 mg</td>
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**Appendix A**

**PERFORMRx PRIOR AUTHORIZATION CRITERIA for Specialty Biological Agents for Psoriasis**

**PREFERRED STATUS:** Preferred Biological Agents - Require Prior Authorization

- ENBREL® (etanercept): 25 mg vial, 50 mg/mL single-use prefilled syringe
- HUMIRA® (adalimumab): 40 mg/0.8 mL kit, available as pen or syringe, 20 mg prefilled syringe
- PREFERRED STATUS: Non-PREFERRED Biological Agents - Require Prior Authorization (Second Line)
- REMICADE® (Infliximab): 100 mg/20mL vial
- ENTYVIO® (Vedolizumab): 300mg/20ml Vial
- OTEZLA® (Apremilast): 30mg tablet
- COSENTYX® (Secukinumab): 45mg/0.5mL vial
- STELARA® (Ustekinumab): 150mg/ml prefilled syringe

**PA CRITERIA FOR APPROVAL FOR PSORIASIS:**

- The member is an adult (≥18 y/o) and has a documented clinical diagnosis of moderate to severe plaque psoriasis.
- Documentation that the patient has had (consistent with pharmacy claims data, OR for new members to the health plan consistent with medical chart history) adequate trials (including dates and dose/s) of at least 3 of the treatment bullet points listed below:
  - The use of topical steroids or has a documented medical reason for not using this therapy to manage their medical condition.
  - The use of a topical medication [i.e. Dovonex® (calcipotriene), Tazorac® (tazorotene), anthralin or a coal tar preparation] that is indicated for the treatment of psoriasis or has a documented medical reason for not using any of these therapies to manage their medical condition.
  - The use of methotrexate or has a documented medical reason (e.g. history of liver or kidney disease, pregnancy, severe cytopenia, alcoholism) for not using this therapy to manage their medical condition.
  - The use of cyclosporine or has a documented medical reason for not using this therapy to manage their medical condition.
  - The use of Soriatane® (acitretin) or has a documented medical reason for not using this therapy to manage their medical condition.
  - The use of UVB phototherapy or PUVA (psoralen – oral or topical methoxsalen plus UVA therapy) or has a documented medical reason (e.g. pregnancy, skin cancer, hypersensitivity due to preexisting disease state - e.g. systemic lupus erythematus, cataracts) for not undergoing UVB phototherapy or PUVA to manage their medical condition.
condition.
• Documentation was submitted indicating that the member was evaluated for active or latent TB infection (i.e. tuberculin skin test).
• The medication requested has an FDA approved indication for use in patients with moderate to severe plaque psoriasis and is being recommended or prescribed by a dermatologist at an FDA-approved dosage.
• If the request is for a non-preferred agent, documented (consistent with pharmacy claims data, OR for new members to the health plan consistent with medical chart history) If the request is for a non-preferred agent, documented (consistent with pharmacy claims data, OR for new members to the health plan consistent with medical chart history) adequate trial of the preferred biological agents.

If all of the above conditions are met, the request will be approved for up to a 6 month duration. If all of the above criteria are not met, the request is referred to a Medical Director/clinical reviewer for medical necessity review.

PA CRITERIA FOR RE-AUTHORIZATION FOR PSORIASIS:
• The medication is being recommended and prescribed by a dermatologist at an FDA-approved dosage.
• The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy.
• Documentation submitted indicates that the member has obtained clinical benefit from the medication.
If all of the above conditions are met, the request will be approved for a 6-month duration for Remicade requests and for a 12 month duration for requests for all other medications. If all of the above criteria are not met, the request is referred to a Medical director/clinical reviewer for medical necessity review.

NOTE: Medical Director/clinical reviewer must override criteria when, in his/her professional judgment, the requested item is medically necessary.

Revision/Review Date: 9/2015