HUMIRA® (adalimumab)

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member’s specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.
HUMIRA (adalimumab) (cont.)

**Description:**

HUMIRA is a tumor-necrosis factor (TNF) inhibitor. TNF inhibitors are naturally occurring proteins involved in the body’s normal immune responses. Overproduction of TNF can cause inflammation and tissue damage. TNF inhibition may ease certain inflammatory disease symptoms and prevent disease progression.

**Definitions:**

**Adult:** Age 18 years and older.

**Uveitis:**

Uveitis is characterized by inflammation of the uvea, which is the middle portion of the eye made up of the iris, ciliary body and choroid. The anterior portion of the uvea includes the iris and ciliary body and the posterior portion of the uvea is known as the choroid.

There are several types of uveitis, defined by the part of the eye where it occurs:

- **Iritis** also called anterior uveitis, is the most common type of uveitis
- Intermediate uveitis or pars planitis is inflammation of the uvea in the middle or intermediate region of the eye
- Posterior uveitis affects the back parts of your eye
- Panuveitis occurs when all layers of the uvea are inflamed
HUMIRA (adalimumab) (cont.)

Criteria:

See Resources section for FDA-approved dosage.

- FDA-approved dosage of HUMIRA is considered *medically necessary* with documentation of **ALL** of the following:

  1. **ONE** of the following:

     - Moderate to severely active rheumatoid arthritis in adults
     - Moderate to severely active polyarticular juvenile idiopathic arthritis in individuals 2 years of age and older
     - Psoriatic arthritis in adults
     - Active ankylosing spondylitis in adults
     - Moderate to severely active Crohn’s disease in adults who have had an inadequate response to conventional therapy
     - Moderate to severely active Crohn’s disease in individuals 6 years of age and older who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine (6-MP) or methotrexate
     - Moderate to severely active ulcerative colitis in adults who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP)
     - Moderate to severe chronic plaque psoriasis in adults who are candidates for systemic therapy or phototherapy and when other systemic therapies are less appropriate
     - Moderate to severe hidradenitis suppurativa in adults
     - Non-infectious intermediate uveitis, non-infectious posterior uveitis or non-infectious panuveitis in adults with documentation of **ALL** of the following:

        a. Individual is refractory to a systemic corticosteroid
        b. Use of a systemic immunosuppressant (e.g., methotrexate, cyclosporine, azathioprine, mycophenolate, cyclophosphamide, leflunomide, hydroxychloroquine, sulfasalazine, tacrolimus, sirolimus, or chlorambucil) unless otherwise contraindicated OR intolerant to an immunosuppressant
HUMIRA (adalimumab) (cont.)

Criteria: (cont.)

- FDA-approved dosage of HUMIRA is considered medically necessary with documentation of ALL of the following: (cont.)

  2. No evidence of active serious infections, including clinically important localized infections or sepsis when initiating or continuing therapy
  3. Evidence of testing for latent tuberculosis before HUMIRA use and during therapy and any treatment for latent infection has been initiated prior to HUMIRA therapy
  4. Evidence of ongoing monitoring in individuals who are known hepatitis B carriers for reactivation of this viral infection during HUMIRA therapy
  5. Evidence of close monitoring in individuals who have a history of or develop heart failure while on HUMIRA therapy
  6. No evidence of lupus-like syndrome while on HUMIRA therapy
  7. HUMIRA is not being used concurrently with anakinra (e.g., Kineret®), abatacept (e.g., Oencia®) or live vaccines
  8. Dosage is not greater than the FDA approved dosing for the labeled indication (refer to dosing table)

- HUMIRA is considered medically necessary for individuals 4 through 17 years of age with non-infectious uveitis refractory to a systemic corticosteroid with documentation of ALL of the following:

  1. Use of a systemic immunosuppressant (e.g., methotrexate, cyclosporine, azathioprine, mycophenolate, cyclophosphamide, leflunomide, hydroxychloroquine, sulfasalazine, tacrolimus, sirolimus, or chlorambucil) unless otherwise contraindicated OR intolerant to an immunosuppressant
  2. No evidence of active serious infections, including clinically important localized infections or sepsis when initiating or continuing therapy
  3. Evidence of testing for latent tuberculosis before HUMIRA use and during therapy and any treatment for latent infection has been initiated prior to Humira therapy
  4. Evidence of ongoing monitoring in individuals who are known hepatitis B carriers for reactivation of this viral infection during HUMIRA therapy
  5. Evidence of close monitoring in individuals who have a history of or develop heart failure while on HUMIRA therapy
  6. No evidence of lupus-like syndrome while on HUMIRA therapy
  7. HUMIRA is not being used concurrently with anakinra (e.g., Kineret), abatacept (e.g., Oencia) or live vaccines
HUMIRA (adalimumab) (cont.)

Criteria: (cont.)

Requests for HUMIRA outside of the FDA-approved dosage will be reviewed by the medical director(s) and/or clinical advisor(s).

- HUMIRA outside of the FDA-approved dosage may be considered medically necessary with documentation of ALL of the following:
  1. Loss of response to the FDA-approved dosage
  2. ONE of the following:
     • Alternative drug(s) are not indicated
     • Alternative drug(s) are contraindicated
     • Non-response/loss of response to prior alternative drug(s)

- HUMIRA for all other indications not previously listed or if above criteria not met is considered experimental or investigational based upon:
  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome, and
  3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.

These indications include, but are not limited to:
  • Anterior uveitis (iritis)
  • Infectious uveitis

Measurement of Antibodies to Adalimumab:

- Measurement of antibodies to adalimumab in an individual receiving treatment with adalimumab, either alone or as a combination test, which includes the measurement of serum adalimumab levels, is considered experimental or investigational based upon:
  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome.

These measurements include, but are not limited to:
  • Anser™ ADA
HUMIRA (adalimumab) (cont.)

Resources:

Literature reviewed 12/13/16. We do not include marketing materials, poster boards and non-published literature in our review.

The BCBS Association Medical Policy Reference Manual (MPRM) policy is included in our guideline review. References cited in the MPRM policy are not duplicated on this guideline.


HUMIRA (adalimumab) (cont.)

Resources: (cont.)


- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult moderately to severely active rheumatoid arthritis</td>
<td>HUMIRA is administered by subcutaneous injection. 40 mg every other week. In rheumatoid arthritis, some patients not taking concomitant methotrexate may derive additional benefit from increasing the dosing frequency of HUMIRA to 40 mg every week.</td>
</tr>
<tr>
<td>Adult moderately to severely active ankylosing spondylitis</td>
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<tr>
<td>Adult moderately to severely active psoriatic arthritis</td>
<td></td>
</tr>
<tr>
<td>Pediatric moderately to severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age and older</td>
<td>HUMIRA is administered by subcutaneous injection. 10 kg (22 lbs) to &lt; 15 kg (33 lbs): 10 mg every other week. 15 kg (33 lbs.) to &lt;30 kg (66 lbs.): 20 mg every other week. ≥30 kg (66 lbs.): 40 mg every other week.</td>
</tr>
</tbody>
</table>
HUMIRA (adalimumab) (cont.)

Resources: (cont.)

- FDA-approved indication and dosage: (cont.)

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Adult Crohn’s Disease</td>
<td>HUMIRA is administered by subcutaneous injection. Initial dose (Day 1): 160 mg Second dose two weeks later (Day 15): 80 mg. Two weeks later (Day 29): Begin a maintenance dose of 40 mg every other week.</td>
</tr>
<tr>
<td>Pediatric moderately to severely active Crohn’s Disease in patients 6 years of age and older</td>
<td>HUMIRA is administered by subcutaneous injection. 17kg (37 lbs) to &lt; 40 kg (88 lbs): Initial dose (Day 1): 80 mg Second dose two weeks later (Day 15): 40mg Two weeks later (Day 29): Begin a maintenance dose of 20 mg every other week. ≥ 40 kg (88 lbs): Initial dose (Day 1): 160 mg (given in one day or split over two consecutive days) Second dose two weeks later (Day 15): 80mg Two weeks later (Day 29): Begin a maintenance dose of 40 mg every other week.</td>
</tr>
<tr>
<td>Adult moderately to severely active ulcerative colitis (UC)</td>
<td>HUMIRA is administered by subcutaneous injection. Initial dose (Day 1): 160 mg Second dose two weeks later (Day 15): 80 mg. Two weeks later (Day 29): Begin a maintenance dose of 40 mg every other week. Only continue HUMIRA in patients who have shown evidence of clinical remission by eight weeks (Day 57) of therapy.</td>
</tr>
<tr>
<td>Adult moderately to severely chronic plaque psoriasis</td>
<td>HUMIRA is administered by subcutaneous injection. Initial dose of 80 mg, followed by 40 mg given every other week starting one week after the initial dose.</td>
</tr>
</tbody>
</table>
HUMIRA (adalimumab) (cont.)

Resources: (cont.)

- FDA-approved indication and dosage: (cont.)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult moderate to severe hidradenitis suppurativa</td>
<td>HUMIRA is administered by subcutaneous injection.</td>
</tr>
<tr>
<td></td>
<td>Initial dose (Day 1): 160 mg</td>
</tr>
<tr>
<td></td>
<td>Second dose two weeks later (Day 15): 80 mg</td>
</tr>
<tr>
<td></td>
<td>Third (Day 29) and subsequent does: 40 mg every week.</td>
</tr>
<tr>
<td>Adult non-infectious intermediate, posterior and panuveitis</td>
<td>HUMIRA is administered by subcutaneous injection.</td>
</tr>
<tr>
<td></td>
<td>Initial dose of 80 mg, followed by 40 mg given every other week starting one week after the initial dose</td>
</tr>
</tbody>
</table>
HUMIRA (adalimumab) (cont.)

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ’s Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ’s Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díi kwe’é atah níiníigíí Blue Cross Blue Shield of Arizona haada yit’éego bina’íidilíkgo ei dodoog Háida bijá ańilyeedíegií t’aadoo le’é yina’ídilíkgo beehaz’áanii hóló díí t’aá hazaad’ek’ehjí háká a’doowolgo be haz’á doo baq’á ilílnígó. A tá’hain’éegi kojí bích’į’ hodiilíih 877-475-4799.

Chinese: 如果您，或您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thợ ngôn viên, xin gọi 877-475-4799.

Arabic: إن كان لديك أو لدى شخص تساعده أسئلة بخصوص Blue Cross Blue Shield of Arizona غير مضمونة، قد يطلب من دو للكفالة، للتحدث مع مترجم يصل إلى 877-475-4799.
HUMIRA (adalimumab) (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutulungan, ay maa ma mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuhang tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관련해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 이용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 통해서와 얘기하기 위해서는 877-475-4799로 전화하십시오.

French: Si vous, ou quelqu'un que vous êtes en train d'aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d'obtenir de l'aide et l'information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizonaについてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi:
آگر شما، یا کسی که شما به آن کمک می‌کنید، سوال در مورد اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799.
[بی‌پاسخ مداخله نمایید.]

Assyrian:

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiciem, nazovite 877-475-4799.

Thai: หากคุณ หรือคนที่คุณช่วยเหลือเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณมีสิทธิ์ได้รับความช่วยเหลือและข้อมูลภาษาของเครือไดโอมิคไปจาก พลังงานของ โทร 877-475-4799