KINERET® (anakinra)

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.
KINERET (anakinra) (cont.)

Description:

Kineret blocks the activity of IL-1 by competitively inhibiting IL-1 binding to the interleukin-1 type I receptor (IL 1RI), which is expressed in a wide variety of tissues and organs.

Definitions:

Adult: Age 18 years and older

Preferred Tumor Necrosis (TNF) Medications:

- Enbrel®
- Humira®
- Remicade®

Significant Adverse Drug Event:

A significant adverse drug event is when an individual's outcome is death, life-threatening, hospitalization (initial or prolonged), disability resulting in a significant, persistent, or permanent change, impairment, damage or disruption in the individuals' body function/structure, physical activities or quality of life, or requires intervention to prevent permanent impairment or damage.

Cryopyrin Associated Periodic Syndromes (CAPS):

A spectrum of auto-inflammatory syndromes that includes three conditions:

- Familial cold auto-inflammatory syndrome (FCAS). Also known as familial cold induced urticarial.
- Muckle-Wells syndrome (MWS)
- Neonatal onset multisystem inflammatory disease (NOMID). Also known as chronic infantile neurologic cutaneous and articular syndrome (CINCA) and Prier-Griseli syndrome.
KINERET (anakinra) (cont.)

Criteria:

See Resources section for FDA-approved dosage.

Rheumatoid Arthritis:

- FDA-approved dosage of Kineret is considered medically necessary for adults with moderately to severely active rheumatoid arthritis who have failed 1 or more disease modifying anti-rheumatic drugs (DMARDs) as monotherapy or concomitantly with DMARDs other than tumor necrosis factor (TNF) antagonists with documentation of ALL of the following:

  1. Failed response to TWO of the preferred TNF medications Enbrel, Humira, Remicade (unless otherwise contraindicated or not labeled for the indication being prescribed, (refer to, “Small Molecules and Biologics Chart” Administrative Procedure Guideline) with documentation of ANY of the following:

     - Individual’s condition has not improved or has worsened
     - Individual experienced a significant adverse drug event to the preferred TNF medications
     - Individual is intolerant to the preferred TNF medications
     - Individual is non-adherent to the preferred TNF medications

  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 Kineret use and during therapy and any treatment for latent infection has been initiated prior to Kineret therapy

  4. Evidence that neutrophil counts have been assessed prior to initiating Kineret treatment, and while receiving Kineret, monthly for 3 months, and thereafter quarterly for a period up to 1 year

  5. Kineret is not being used concurrently with live vaccines or TNF antagonists

  6. Absence of hypersensitivity to E coli-derived proteins, Kineret, or to any component of the product

  7. Dosage is not greater that the FDA approved dosing for the labeled indication (refer to dosing table)
KINERET (anakinra) (cont.)

Criteria: (cont.)

See Resources section for FDA-approved dosage.

Cryopyrin-Associated Periodic Syndromes (CAPS):

Neonatal-Onset Multisystem Inflammatory Disease (NOMID):

- FDA-approved dosage of Kineret is considered *medically necessary* for individuals 17 years of age and under with Neonatal-Onset Multisystem Inflammatory Disease (NOMID) with documentation of **ALL** of the following:

  1. No evidence of active serious infections including clinically important localized infections or sepsis when initiating or continuing therapy
  2. Evidence of testing for latent tuberculosis before Kineret use and during therapy and any treatment for latent infection has been initiated prior to Kineret therapy
  3. Evidence that neutrophil counts have been assessed prior to initiating Kineret treatment, and while receiving Kineret, monthly for 3 months, and thereafter quarterly for a period up to 1 year
  4. Kineret is not being used concurrently with live vaccines or TNF antagonists
  5. Absence of hypersensitivity to *E. coli*-derived proteins, Kineret, or to any component of the product
  6. Dosage is not greater that the FDA approved dosing for the labeled indication (refer to dosing table)

- Kineret for all other cryopyrin-associated periodic syndromes (CAPS) 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 CAPS include, *but are not limited to*:

- Familial cold auto-inflammatory syndrome (FCAS). Also known as familial cold induced urticarial.
- Muckle-Wells syndrome (MWS)
KINERET (anakinra) (cont.)

Criteria: (cont.)

- Kineret 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.

1 Not applicable for current members on Kineret prior to 07/09/14 or new members who are actively being treated with Kineret prior to their effective date with BCBSAZ. (Excludes any changes in route of administration, such as changing intravenous delivery to subcutaneous delivery)

Refer To:

- “Small Molecules and Biologics Chart” #AP94, BCBSAZ Administrative Procedure Guideline when preferred TNF medications Enbrel, Humira, Remicade are otherwise contraindicated or not labeled for the indication being prescribed
KINERET (anakinra) (cont.)

Resources:

Literature reviewed 01/03/17. We do not include marketing materials, poster boards and non-published literature in our review.

Kineret Package Insert:

- 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 (RA)</td>
<td>Kineret is administered by subcutaneous injection. 100 mg daily. Physicians should consider a dose of 100 mg of Kineret administered every other day for RA patients who have severe renal insufficiency or end stage renal disease (defined as a creatinine clearance &lt;30ml/min, as estimated from serum creatinine levels).</td>
</tr>
<tr>
<td>Neonatal-Onset Multisystem Inflammatory Disease (NOMID)</td>
<td>Kineret is administered by subcutaneous injection. 1-2 mg/kg daily. The dose can be individually adjusted to a maximum of 8 mg/kg daily to control active inflammation. Adjust doses in 0.5 to 1.0 mg/kg increments. Once daily administration is generally recommended, but the dose may be split into twice daily administrations. Each syringe is intended for a single use. A new syringe must be used for each dose. Any unused portion after each dose should be discarded. Physicians should consider administration of the prescribed Kineret dose every other day for NOMID patients who have severe renal insufficiency or end stage renal disease (defined as creatinine clearance &lt; 30 mL/min, as estimated from serum creatinine levels).</td>
</tr>
</tbody>
</table>
KINERET (anakinra) (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 esta 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 nilínígii Blue Cross Blue Shield of Arizona haada yit’éegó bina’i’dilkgdag éi doodago Háida bi’é aniłyeedííi t’áadoo le’é yina’i’dilkgdoo beehaz’áánii hóó díi t’áá hazaad’ehjí háká a’dowolgo bee haz’á doo báqh ilínígó. Atá’ haine’ííi kojí bích’í hódilíih 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，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. Đế nói chuyện với một thống dịch viên, xin gọi 877-475-4799.

Arabic: إن كان لديك أو لدى شخص تساعد أسلة بخصوص خطرة وقعة السرورية من دون أية تقف، للمتحدث مع مترجم النص ب 877-475-4799.
KINERET (anakinra) (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutulungan, ay may 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 makuasaap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 풍부하시기 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 sans 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:
گر شما، یا کسی که شما به او کمک می‌گردید، سوال‌های مورد اطمینانه به زبان خود را به طور رایگان دریافت نمایید. این خدمات حاضر نمی‌باشد. 877-475-4799.

Assyrian:

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

Thai: หากคุณ หรือคนที่คุณช่วยเหลือถามถึง Blue Cross Blue Shield of Arizona คุณมีสิทธิ์ที่จะได้รับความช่วยเหลือและข้อมูลภาษา ของคุณได้โดยไม่เสียเงิน ติดต่อเราที่ 877-475-4799.