Subject: Arcalyst (rilonacept)	**Original Effective Date:** 6/29/2012
Policy Number: MCP-110	**Revision Date(s):**
Review Date(s): 12/16/2015; 6/15/2016; 3/21/2017; 3/8/2018; Q3 2020	
MCPC Approval Date: 3/8/2018	
P&T Approval Date: Q4 2019, Q3 2020	

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP document and provide the directive for all Medicare members.

Contents

SUMMARY OF EVIDENCE/POSITION

This policy addresses **Arcalyst (rilonacept)** for the treatment of **Cryopyrin-Associated Periodic Syndromes (CAPS)** when appropriate criteria are met.

- There have been no head-to-head trials comparing the efficacy of rilonacept, or canakinumab against each other or any other medication in the management of CAPS. At this time, there is insufficient clinical evidence to establish or conclude the superiority in effectiveness of one agent over another for the management of patients Cryopyrin-Associated Periodic Syndromes (CAPS). **Therefore, when there is no proven or demonstrated difference in clinical safety or efficacy, Molina Healthcare reserves the right to prefer the most cost-effective agent that provides the best value for members.**

- Arcalyst is not indicated for the treatment of neonatal onset multisystem inflammatory disorder (NOMID) or chronic infantile neurological cutaneous and articular syndrome (CINCA). **Molina Healthcare will not authorize either medication for these indications.**

FDA INDICATIONS

Cryopyrin-associated Periodic Syndromes (CAPS) Treatment of CAPS, including Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older.

Available as: Single-use 20-mL, glass vial containing 220 mg of rilonacept as a lyophilized powder for reconstitution for subcutaneous injection

Approved by the FDA: February 27, 2008

COVERAGE CRITERIA FOR INITIAL AUTHORIZATION

Initiation of therapy with may be authorized for members who meet **ALL** of the following criteria **[ALL]**

1. **Prescriber specialty [ONE]**

   - ❒ Prescribed by, or in consultation with a board-certified rheumatologist, immunologist, or genetic specialist. Submit consultation notes if applicable.

2. **Diagnosis/Indication [ALL]**
   Documentation of diagnosis required and may include clinical notes from the member's medical records including any relevant labs and/or tests, supporting the diagnosis **[ALL]**

   - ❑ Confirmed diagnosis of one Cryopyrin-Associated Periodic Syndromes disorder (CAPS): Familial Cold Auto-inflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS)
     - *Arcalyst is not indicated for use in, and have not been studied in, patients with NOMID/CINCA.*

   - ❑ Genetic mutation in the NLRP3 gene (also called CIAS1)
     - *There is currently no reliable evidence that rilonacept or canakinumab are efficacious in patients who do not exhibit the NLRP3 (nucleotide-binding domain, leucine-rich family [NLR], pyrin domain containing 3) gene (formerly the* CIAS1 *[cold-induced autoinflammatory syndrome 1] gene) mutation.*
     - *In addition to clinical symptoms, a diagnosis should be made using a combination of procedures including laboratory assessments, skin biopsy, and genetic testing.*

- ❑ Symptom presentation consistent with a diagnosis of Familial Cold Auto-inflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS) **[ONE]**

  - ❍ FCAS: recurrent intermittent fever and urticarial rash that followed generalized cold exposure
    - *Symptoms are mild and episodes last < 24 hours, are preceded by exposure to cold temperatures or a rapid decrease in temperature, may not be recognized until adulthood, even if having started much earlier*

  - ❍ MWS: recurrent intermittent fever and urticarial rash; hearing loss or amyloidosis may also be present
    - *Symptoms are moderate and occur in 2-3 day flares (usually not related to cold exposure), may also have chronic daily symptoms, are accompanied by conjunctivitis with episcleritis, sensorineural hearing loss, and mild symptoms of bone and joint disease and renal amyloid A (AA) amyloidosis*

NOTE: Arcalyst (rilonacept) is not indicated for use in patients with neonatal-onset multisystem inflammatory disease (NOMID), another syndrome that is included in CAPS.

Informational Note

- *There is currently no reliable evidence that rilonacept or canakinumab are efficacious in patients who do not exhibit the NLRP3 (nucleotide-binding domain, leucine-rich family [NLR], pyrin domain containing 3) gene (formerly the* CIAS1 *[cold-induced autoinflammatory syndrome 1] gene) mutation.*
- *Arcalyst (rilonacept) is an interleukin-1 (IL-1) blockers indicated for the treatment of CAPS, including FCAS and MWS in adults and children. CAPS refer to rare genetic syndromes generally caused by mutations in the NLRP-3 [nucleotide-binding domain, leucine rich family (NLR), pyrin domain containing 3] gene (also known as Cold-Induced Auto-inflammatory Syndrome-1 [CIAS1]). The NLRP-3 gene encodes the protein cryopyrin, an important component of the inflammasome. Cryopyrin regulates the protease caspase-1 and controls the activation of interleukin-1 beta (IL-1β). Mutations in NLRP-3 result in an overactive inflammasome resulting in excessive release of activated IL-1β that drives inflammation.*

- ❑ Significant functional impairment resulting in limitations of activities of daily living (ADLs)
  - *Arcalyst's approval for the CAPs indication was based on a phase III clinical trial in which effectiveness end points included numbers of multi-symptom and single-symptom disease flare days, single-symptom scores, physician's and patient's global assessments of disease activity, limitations in daily activities, as well as hsCRP and SAA levels.*

3. Age/Gender/Other restrictions [ONE]

- ❑ 12 years of age or older
  - *Safety and effectiveness in children younger than 12 years of age have not been established.*

4. Step/Conservative Therapy/Other condition Requirements [ALL]

❒ No concurrent use of any other biologic DMARD [eg. IL-1 inhibitor Kineret (anakinra); or a TNF-α blocking agent [Enbrel (etanercept), Remicade (infliximab), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]

- *The effectiveness of concurrent use of Arcalyst (rilonacept) with other biologic DMARDs has not been established.*

NOTE: If the member has been previously treated with another IL-1 inhibitor (Kineret [anakinra]) or a TNF-α blocking agent [Enbrel (etanercept), Remicade (infliximab), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] the agent will be discontinued before initiating Arcalyst or Ilaris

- *Concomitant administration of rilonacept with TNF inhibitors is not recommended due to an increased risk of serious infections, neutropenia and toxicity.*
- *The concomitant administration with other Interleukin-1 blockers has not been studied.*

❑ No active or chronic infections [including hepatitis B, hepatitis C, human immunodeficiency virus, or tuberculosis]

NOTE: Member with active or chronic infections including tuberculosis, human immunodeficiency virus, hepatitis B, or hepatitis C will not be authorized for rilonacept therapy since rilonacept (an interleukin-1 blocker) has the potential to increase the risk of infection and reactivate latent, chronic infections.

❒ No evidence of latent tuberculosis infection as evidence by a tuberculin skin test results or chest x-ray within the previous six months.
NOTE: If there is evidence of latent tuberculosis infection, treatment should not be initiated.

- *Current CDC guidelines should be followed to evaluate and to treat possible latent tuberculosis infections prior to initiation of therapy with rilonacept.*
- *Due to the increased risk of infection while on rilonacept, patients should receive all recommended immunizations, as appropriate including pneumococcal vaccine and inactivated influenza vaccine.*

5. Contraindications/Exclusions to therapy [ANY]

There are no contraindications listed in the manufacturer's labeling.

Authorization will **not** be granted if **ANY** of the following conditions apply **[ANY]**

- ❑ Non-FDA approved indications
- ❑ Known hypersensitivity to Arcalyst (rilonacept) or any ingredient in the formulation
- ❒ Active or chronic infections
  - *Patients who develop a new infection while undergoing treatment should be monitored closely. If a patient develops a serious infection, therapy should be discontinued. Therapy should not be initiated in patients with active or chronic infections. May increase risk of reactivation of latent tuberculosis; follow current guidelines for evaluation and treatment of latent tuberculosis prior to initiating rilonacept therapy*
- ❒ Combination therapy with TNF-antagonists
  - *There is an increased risk of serious infection*
- ❒ Concurrent administration of live vaccines
  - *There are no data concerning secondary transmission of live vaccines in patients receiving therapy. Administration of inactivated (killed) vaccines while on therapy may not be effective.*

6. Labs/Reports/Documentation required [ALL]

All documentation for determination of medical necessity must be submitted for review. Prescriber to submit documentation as indicated in the criteria above, including but not limited to chart notes, applicable lab values and/or tests, adverse outcomes, treatment failures, or any other additional clinical information or clinical notes from the member's medical records supporting the diagnosis. Letters of support and/or explanation are often useful but are not sufficient documentation unless ALL specific information required by this MCP are included.

NOTE: Additional documentation, rationale, and/or supporting evidence may be requested for review as deemed necessary or appropriate by Molina Medical/Pharmacy staff.

REAUTHORIZATION /CONTINUATION OF THERAPY

Continuation of therapy with **Arcalyst (rilonacept)** may be authorized for members who meet **ALL** of the following criteria **[ALL]**

1. Initial Coverage Criteria

- ❑ Member continues to meet applicable initial coverage criteria

2. Compliance

- ❑ Compliance with therapy as verified by Prescriber and member's medication fill history (review medication fill history for compliance)
  - Therapy may be discontinued due to compliance issues or poor adherence upon agreement among treating physician, member, and Medical Director.

3. Labs/Reports/Documentation required [ALL]

For continuation of treatment after initial treatment authorization of **Arcalyst (by 4 weeks after initial therapy):**

- ❑ Positive response to treatment, including but not limited to:
  - ❍ Chart notes indicating sustained improvement in member's symptoms and disease stability
  - ❍ Clinical response indicated by normalization or improvement in laboratory test results for serum markers of inflammation
    - Erythrocyte sedimentation rate [ESR]
    - High-sensitivity C-reactive protein [hsCRP]
    - Serum amyloid A [SAA]
    - Interleukin-6 [IL-6]
  - ❍ Disease activity measures (i.e. daily diary reports of rash, joint pain and/or swelling, and fevers)
  - ❍ Health quality measures (Short Form 36 health survey questionnaire)
  - ❍ Functional impairment resulting in limitations of activities of daily living (ADLs)

4. Exclusion and Discontinuation of Treatment [ANY]

Member should be assessed for discontinuation of therapy if **ANY** of the following are applicable: **[ANY]**

- ❑ No response by 12 weeks after initial therapy
- ❑ Intolerable adverse effects or unacceptable toxicity from the drug (e.g. bronchitis, colitis, GI bleeding, Mycobacterium intracellulare infection, sinusitis, Streptococcus pneumoniae meningitis)
- ❑ Persistent and uncorrectable problems with adherence to treatment
- ❑ Poor response to treatment as evidenced by physical findings and/or clinical symptoms
- ❑ Contraindications/Exclusions to therapy
  - ❍ Active or chronic infections
  - ❍ Combination therapy with TNF-antagonists
  - ❍ Concurrent administration of live vaccines

ADMINISTRATION, QUANTITY LIMITATIONS, AND AUTHORIZATION PERIOD

Consult the manufacturer's labeling for more detailed information on dosage and administration of this drug, cautions, precautions, contraindications, potential drug interactions, laboratory test interferences, and monitoring.

1. Recommended Dosing Regimen [AS APPLICABLE]

Cryopyrin-Associated Periodic Syndromes

- ❑ Pediatric patients aged 12 to 17 years
  - ❍ Initial dosage: Loading dose of 4.4 mg/kg of body weight, up to a maximum of 320 mg (delivered as 1 or 2 subcutaneous injections with a maximum single-injection volume of 2 ml)
  - ❍ Maintenance dosage: Dose once-weekly (injection of 2.2 mg/kg) up to a maximum of 160 mg, administered as a single subcutaneous injection.

- ❑ Adult patients 18 years and older
  - ❍ Initial dosage: Loading dose of 320 mg delivered as two, 2-ml, subcutaneous injections of 160 mg on the same day at 2 different sites.
  - ❍ Maintenance dosage: Once-weekly injection of 160 mg administered as a single, 2-ml, subcutaneous injection.
    - ◆ *Maintenance doses greater than 160 mg weekly have not been clinically evaluated.*

2. Authorization Limit [ALL]

- ❑ Duration of treatment: May authorize up to 12 weeks for initial and continuation of treatment

- ❑ Quantity limit: **[ONE]**

  - ❍ Dose does not exceed a loading dose of 320 mg (as two injections) and once weekly dosing of 160 mg (as a single injection)

  - ❍ 5 vials for first month THEN 4 vials per month thereafter

3. Route of Administration [ALL]

- ❑ Arcalyst (rilonacept) weekly subcutaneous injections may be self-administered by the member

- ❑ If member meets all criteria and approval for therapy is granted, medication will be dispensed by a specialty pharmacy vendor at the discretion of Molina Healthcare.

- ❑ Refer to MHI Policy & Procedure (P&P): Specialty Medication Administration Site of Care Policy: MHI Pharm 11

COVERAGE EXCLUSIONS

All other uses of Arcalyst (rilonacept) that are not an FDA-approved indication or not included in the 'Coverage Criteria' section of this policy is considered experimental/investigational or not a covered benefit of this policy. This subject to change based on research and medical literature, or at the discretion of Molina Healthcare. The following list is not all-inclusive:

- ❒ Dosage other than FDA approved dosing regimen, i.e. rilonacept injections given more than once a week
- ❒ Concurrent use of any other biologic DMARD [eg. IL-1 inhibitor Kineret (anakinra); TNF-α blocking agents [Enbrel (etanercept), Remicade (infliximab), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
- ❒ Atherosclerotic coronary artery disease
- ❒ Diabetes Mellitus Type 1
- ❒ Familial Mediterranean Fever (FMF)
- ❒ Gout/gouty arthritis
- ❒ Neonatal-onset multi-systemic inflammatory disease
- ❒ Rheumatoid arthritis (RA)

BACKGROUND/SUMMARY

Cryopyrin-associated periodic syndromes (CAPS) is a term used to encompass three rare auto-inflammatory disorders: familial cold auto inflammatory syndrome (FCAS), Muckle–Wells syndrome (MWS) and neonatal-onset multisystem inflammatory disorder (NOMID). CAPS consists of three phenotypically related disorders all associated with mutations in the CIAS-1 gene.

- Familial Cold Auto-inflammatory Syndrome (FCAS)
- Muckle-Wells Syndrome (MWS)
- Neonatal-Onset Multisystem Inflammatory Disease (NOMID)/Chronic Infantile Neurologic Cutaneous Articular Syndrome (CINCA)

The incidence of CAPS has been reported to be approximately 1 to 2 per 1,000,000 people in the United States. Symptoms include urticaria-like rash, fever and/or chills, as well as inflammation of the joints and eyes caused by a variety of triggers. Symptoms can be present at birth or early infancy and occur daily throughout life.

Symptoms occur when alterations in the cryopyrin protein lead to over-production of interleukin-1 (IL-1), resulting in an inflammatory response. These related diseases have been associated with mutations in the *NLRP3* (*CIAS1*) gene leading to aberrant regulation of the interleukin-1 (IL-1) pathway and hypersecretion of active pro-inflammatory IL-1β. Inhibitors of IL-1β signaling such as rilonacept and canakinumab have demonstrated high efficacy in treating these conditions, supporting the fundamental role of IL-1 in disease pathogenesis.

Familial Cold Auto-inflammatory Syndrome (FCAS)

FCAS, the most common form of CAPS, is characterized by recurrent episodes of urticaria-like rash, fever, chills, and joint pain precipitated by generalized cold exposure. Attacks are also characterized by conjunctivitis, sweating, drowsiness, headache, extreme thirst, and nausea. Symptoms usually develop 1-2 hours after exposure, peak approximately 6-8 hours Patients with FCAS develop symptoms when they are exposed to even a mild degree of cold. Exposures might include a cool breeze, air conditioning, or a light mist. Following cold exposure, a systemic inflammatory response usually ensues within a few hours. Signs and symptoms include recurrent rash, fever/chills, joint pain, fatigue, and eye pain/redness. FCAS patients also can experience headache, muscle pain, excessive thirst, and nausea. These symptoms generally last for up to 24 hours.

Laboratory markers of systemic inflammation [C-reactive protein (CRP) and Serum Amyloid A (SAA) levels] are elevated. A small percent of FCAS patients may develop renal consequences due to secondary amyloidosis.

Muckle-Wells Syndrome
MWS shares many of the same inflammatory signs and symptoms of FCAS, but they are often more chronic and patients have multiple unknown triggers for symptoms onset. Cold exposure may, however, exacerbate inflammation. In addition to episodes of rash, fever/chills, joint pain, fatigue, and eye pain/redness, which can last from 2 to 3 days, MWS also is associated with synovitis and sensorineural deafness. Secondary amyloidosis may occur in as many as 25 percent of patients with MWS, often resulting in renal failure.

Chronic Infantile Neurological Cutaneous Articular Syndrome (CINCA) or Neonatal-Onset Multisystem Inflammatory Disorder (NOMID)
NOMID/CINCA is the most severe and debilitating form of CAPS with symptoms manifesting shortly after birth. Beyond those symptoms manifested in FCAS and MWS, NOMID patients also present with significant disabilities, including optic nerve abnormalities (papilledema), chronic aseptic meningitis, mental retardation, facial malformation, and arthropathy with aberrant ossification (especially in the knees and elbows).

There are currently no approved therapies for the treatment of NOMID.

Rilonacept is a targeted inhibitor of interleukin-1 (IL-1), the key driver of inflammation in cryopyrin-associated periodic syndromes (CAPS). Rilonacept acts as a decoy receptor that binds IL-1 beta and the blocks IL-1 beta signaling, thereby preventing its interaction with cell surface receptors. It also binds IL-1 alpha and IL-1 receptor antagonist with reduced affinity.

The FDA's approval of Arcalyst was based on a phase III clinical trial by Hoffman et al. (2008)

One randomized, controlled study compared rilonacept to placebo in 47 patients randomized to receive either rilonacept (n=23) or placebo (n=24) in a blinded fashion for six weeks. Of 47 patients who enrolled in the 24-week, multiphase, sequential, Phase III pivotal trials of rilonacept, 44 entered into the open-label treatment phase in 22 centers in the United States. All patients were tested and found to be positive for the CIAS1 mutation. At the end of six weeks, patients receiving placebo received active drug, while patients randomized to rilonacept continued with treatment in a single blinded fashion and were enrolled in 2 consecutive studies.

A two-part double-blind, placebo-controlled, randomized trial was conducted to determine the efficacy of rilonacept in patients with FCAS and MWS.

Study 1 entailed a 6-week randomized double-blind comparison of weekly subcutaneous injections of rilonacept (160 mg) versus placebo. Study 2 consisted of a 9-week single-blind treatment with rilonacept (part A), followed by a 9-week, randomized, double-blind, placebo-controlled withdrawal procedure (part B). Primary effectiveness was evaluated using a validated composite key symptom score. A total of 44 patients completed both studies.

- In Study 1, rilonacept therapy reduced the group mean composite symptom score by 84%, compared with 13% with placebo therapy (primary end point; $p < 0.0001$ versus placebo). Rilonacept also significantly improved all other effectiveness end points in Study 1 (numbers of multi-symptom and single-symptom disease flare days, single-symptom scores, physician's and patient's global assessments of disease activity, limitations in daily activities, as well as hsCRP and SAA levels).

- In Study 2-part B, rilonacept was superior to placebo for maintaining the improvements seen with rilonacept therapy, as shown by all effectiveness parameters (primary end point; $p < 0.0001$ versus placebo). Rilonacept was generally well-tolerated. The authors concluded that treatment with weekly rilonacept provided marked and lasting improvement in the clinical signs and symptoms of CAPS, and normalized the levels of SAA from those associated with risk of developing amyloidosis. Rilonacept exhibited a generally favorable safety and tolerability profile.

The main outcome measure was the change from baseline in patient-rated mean symptom scores. Symptoms assessed were joint pain, fatigue, rash, eye redness/pain, and fever or chills. The rilonacept group reported a statistically greater decrease in symptom score from baseline (-2.4) compared to placebo (-0.5, $p < 0.0001$) during the first part of the trial. In the second part (n = 45), all patients were treated with rilonacept for 9 weeks, followed by 9 more weeks of rilonacept or withdrawal with placebo. Mean symptom scores increased more in patients who were switched to placebo from rilonacept (0.9) compared to those who remained on rilonacept (0.1, 95% CI -1.3 to -0.4).

Conclusion:

- The results of 2 pivotal, sequential, placebo-controlled, Phase III studies have shown that subcutaneous rilonacept 160 mg weekly provides marked and lasting improvement in the clinical signs and symptoms associated with CAPS, with a generally favorable safety and tolerability profile.
- Treatment of patients with FCAS or MWS with rilonacept resulted in a significant (84%) improvement in a composite symptom score and normalized elevated SAA and hs-CRP levels. Unlike previous studies of therapies for CAPS, these 2 studies were multicenter, large (n=47) relative to the total population of patients with CAPS in North America, and used a validated instrument for CAPS symptom self-assessment to demonstrate the efficacy of rilonacept in adults.1

⌘ 72-week open-label extension: Case series of 101 patients with familial cold autoinflammatory syndrome or Muckle-Wells syndrome treated with rilonacept 160 mg subcutaneously weekly

- 44 adults from the above study received 72 additional weeks of treatment and 57 newly enrolled patients aged 12-80 years received treatment for 72-96 weeks
- among all 101 patients, rilonacept associated with significant reductions in physician assessed disease activity score, mean serum amyloid A, and mean C-reactive protein at 24 weeks compared to baseline
- Reference: Clinical Therapeutics, Volume 34, Issue 10, 2091 - 2103

CODING INFORMATION: THE CODES LISTED IN THIS CLINICAL POLICY ARE FOR INFORMATIONAL PURPOSES ONLY. LISTING OF A SERVICE OR DEVICE CODE IN THIS POLICY DOES NOT IMPLY THAT THE SERVICE DESCRIBED BY THIS CODE IS A COVERED OR NON COVERED. COVERAGE IS DETERMINED BY THE BENEFIT DOCUMENT. THIS LIST OF CODES MAY NOT BE ALL INCLUSIVE AND INCLUSION OR EXCLUSION OF ANY CODES DOES NOT GUARANTEE COVERAGE. PROVIDERS SHOULD REFERENCE THE MOST UP TO DATE SOURCES OF PROFESSIONAL CODING GUIDANCE PRIOR TO THE SUBMISSION OF CLAIMS FOR REIMBURSEMENT OF COVERED SERVICES.

CPT	Description
96372	Therapeutic, prophylactic or diagnostic injection (specify substance or drug), subcutaneous or intramuscular

HCPCS	Description
J2793	Injection, rilonacept, 1 mg (Arcalyst)

*CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

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Policy History	Approval
Policy Developed Peer Review. Practicing Physician. Board certified in Rheumatology. Date completed: 4/9/2009	MCP 2/2007
Revision* Peer Review. Board certified in Pediatrics, Pediatric Rheumatology. Date completed: 5/17/2012	MCP 6/29/2012
Revision* Peer Review. Practicing Physician. Board certified in Internal Medicine, Rheumatology. Date completed: 9/4/2019	P&T Q4 2019
Annual Review* No coverage criteria changes with this annual review. Minor revisions, including clarification and addition of language, however no change to intent. Notable updates: • Addition to 'Exclusions' criteria (#5) in Initial Treatment section to include: "Active or chronic infections, Combination therapy with TNF-antagonists, Concurrent administration of live vaccines." No change to intent as the added exclusions correlate to existing criteria in Initial Treatment section. • Revised Continuation of Treatment section (#4) to include: Intolerable adverse effects or unacceptable toxicity from the drug (e.g. bronchitis, colitis, GI bleeding, Mycobacterium intracellulare infection, sinusitis, Streptococcus pneumoniae meningitis); Persistent and uncorrectable problems with adherence to treatment; Poor response to treatment as evidenced by physical findings and/or clinical symptoms; Contraindications/Exclusions to therapy	P&T Q3 2020
• Previous MCP-110 'Cryopyrin-Associated Periodic Syndromes (CAPS) IL-1 Antagonists' included Arcalyst (rilonacept) and Ilaris (canakinumab): 2/2007 • Review Date(s): 12/16/2015, 6/15/2016, 3/21/2017, 3/8/2018 • MCP converted to PA criteria and MCP retired: 2018 • MCP re-developed: 2019	

*Policy Revisions and Annual Reviews: All content, clinical evidence, coverage criteria, practice guidelines, appendices and reference sections were reviewed and revised with the most recent medical literature and available evidence for both 'Annual Reviews' and 'Revisions.' Revisions include notable content updates or revisions that which may have affected criteria or requires review by a practicing specialist, Peer Reviewer. The revisions noted below but may not be all-inclusive of all revised criteria and content in each policy; refer to MCP for all revisions and complete context.