BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

abatacept (Orencia®)

Policy # 00214
Original Effective Date: 09/20/2006
Current Effective Date: 11/16/2016

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Adult Rheumatoid Arthritis
Based on review of available data, the Company may consider abatacept (Orencia®)‡ for the treatment of adult rheumatoid arthritis (RA) to be **eligible for coverage**.

Patient Selection Criteria
Coverage eligibility for the use of abatacept (Orencia) for the treatment of rheumatoid arthritis (RA) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; and
- Patient has moderately to severely active rheumatoid arthritis (RA); and
- Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs); and (*Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met*)
- For Orencia SubQ requests or for Orencia intravenous loading dose requests prior to initiating Orencia SubQ therapy: Patient has failed treatment with adalimumab (Humira) AND etanercept (Enbrel) after at least two months of therapy with each product (unless there is clinical evidence or patient history that suggests that these products will be ineffective or cause an adverse reaction to the patient); and *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Orencia may be used alone or in combination with disease-modifying anti-rheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists or anakinra (Kineret); and
- Patient has a negative purified protein derivative (PPD) test prior to treatment.

Polyarticular Juvenile Idiopathic Arthritis
Based on review of available data, the Company may consider the use of abatacept (Orencia) for the treatment of moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA) to be **eligible for coverage**.

Patient Selection Criteria
Coverage eligibility for the use of abatacept (Orencia) for the treatment of polyarticular juvenile idiopathic arthritis (PJIA) will be considered when all of the following criteria met:

- Patient is 6 years of age or older; and
- Patient has moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA); and
- Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDS); and

abatacept (Orencia®)

Policy # 00214
Original Effective Date: 09/20/2006
Current Effective Date: 11/16/2016

*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- Orencia may be used as monotherapy or concomitantly with methotrexate (MTX) ; and
- Orencia should not be given concomitantly with tumor necrosis factor (TNF) antagonists or anakinra (Kineret); and
- Patient has a negative purified protein derivative (PPD) test prior to treatment.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of abatacept (Orencia) when patient selection criteria are not met to be **investigational*** (with the exception of those denoted above as not **medically necessary****).

Based on review of available data, the Company considers the use of abatacept (Orencia) for indications other than those listed above to be **investigational.***

When Services Are Considered Not Medically Necessary
Based on review on available data, the Company considers the use of abatacept (Orencia) when any of the following criteria for their respective disease state listed below (and denoted in the patient selection criteria above) are not met to be **not medically necessary**:**

- For adult rheumatoid arthritis:
  - Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs)
  - Patient has failed treatment with adalimumab (Humira) AND etanercept (Enbrel) after at least two months of therapy with each product. This criterion only applies to Orencia SubQ requests or Orencia intravenous loading dose requests prior to initiating Orencia SubQ therapy.
- For polyarticular juvenile idiopathic arthritis:
  - Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDS)

Background/Overview

Abatacept is an injectable synthetic protein produced by recombinant deoxyribonucleic acid (DNA) technology that is used for the treatment of RA. Abatacept is a selective costimulation modulator that binds to CD80 and CD86 to block the interaction with CD28 required for full T lymphocyte (T cell) activation. Activated T cells have been found in the synovium of patients with RA. These activated T cells multiply and release chemicals that cause destruction of tissues around the joints, and cause symptoms of rheumatoid arthritis.

Abatacept acts like an antibody and attaches to a protein on the surface of T-lymphocytes. This action prevents the activation of the T-lymphocytes and blocks the production of new T-lymphocytes and the production of the chemicals that destroy tissue and cause symptoms of arthritis. Abetacept comes as a lypophilized power for

abatacept (Orencia®)

Policy # 00214
Original Effective Date: 09/20/2006
Current Effective Date: 11/16/2016

intravenous infusion that provides 250mg of abatacept in a 15mL vial. Abetacept also comes in a 125mg/mL single dose prefilled syringe for subcutaneous use in patients with rheumatoid arthritis.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
The FDA has approved Orencia for second-line treatment of selected patients with RA. Orencia is a genetically engineered, first in class, selective T cell costimulation modulator. Its selective action allows other immune pathways to remain largely intact and ensures that T cell activation is modulated rather than completely blocked. A fully human soluble fusion protein, Orencia is typically administered as a 30-minute intravenous infusion on days one, 15, and 30, and once a month thereafter. It is approved by the FDA for reducing signs and symptoms, inducing major clinical response, slowing the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA who have had an inadequate response to one or more DMARDs, including methotrexate and TNF inhibitors. Orencia is indicated for use as monotherapy, as well as in combination with DMARDs other than TNF inhibitors.

The FDA has approved Orencia for reducing signs and symptoms in pediatric patients six years and older with moderately to severely active polyarticular juvenile idiopathic arthritis. Orencia may be used as monotherapy or concomitantly with methotrexate. Orencia should not be administered concomitantly with TNF antagonists and is not recommended for use concomitantly with other biologic rheumatoid arthritis therapy, such as anakinra. This new indication for Orencia provides significant evidence of its durable efficacy and long-term safety in pediatric patients, including those initiating biologic therapy for the first time. The safety and efficacy of Orencia in JIA were assessed in a three-part study through one year.

Rationale/Source

FDA approval of Orencia for adult rheumatoid arthritis is based on outcome data from three double blind, randomized, placebo-controlled trials that evaluated the biologic agent in adults with RA who had an unsuccessful response to other RA drugs. These trials include the Abatacept Trial in Treatment of Anti-TNF Inadequate responders (ATTAIN), Abatacept in Inadequate responders to Methotrexate (AIM), and Abatacept Study of Safety in Use with other RA therapies (ASSURE).

In the AIM study, which was a one year placebo controlled Phase III trial using a fixed dose of abatacept in patients with active RA despite MTX treatment. This study showed that abatacept plus MTX inhibits radiographic progression of joint damage significantly better than placebo plus MTX.

The purpose of the ASSURE trial is to assess the safety of combination therapy with abatacept and approved biologic and non-biologic DMARDs in patients with active RA. This study showed that abatacept and placebo have a similar safety profile when added to DMARD therapy in patients with active RA and co-morbidities. However, abatacept added with biologic therapy showed the least favorable profile with increased incidences of adverse events and infections.

The ATTAIN study is a randomized, double blind, phase III trial that evaluated the efficacy of abatacept in patients with active RA and an inadequate response to anti-TNF-alpha therapy. In both phase III studies (AIM and ATTAIN), Orencia demonstrated significant improvement in the signs and symptoms of RA as measured by

abatacept (Orencia®)

Policy # 00214
Original Effective Date: 09/20/2006
Current Effective Date: 11/16/2016

the American College of Rheumatology (ACR). Significant improvements in physical function were noted as compared to placebo. These improvements were maintained up to three years in a Phase II trial of patients with inadequate response to MTX.

FDA approval of Orencia for juvenile idiopathic arthritis was assessed in a three part study in patients 6-17 years of age. The ACR scores were assessed in these patients at the end of the first part of the study and the pediatric ACR 30/50/70 responses were 65%, 50%, and 28%, respectively. Period B included a withdrawal phase and patients on abetacept had fewer disease flares than those patients treated with placebo. The last part of the trial was an open label extension.

References

1. http://www.orencia.com/orencia/home/index.jsp?BV_UseBVCookie=Yes .
2. U.S. Food and Drug Administration. (2009 August) Center for Drug Evaluation and Research. FDA Labeling Information. Orencia (Abatacept). http://www.fda.gov.
3. Orencia (abatacept) Package insert. 12/2013.

Policy History

Original Effective Date: 09/20/2006
Current Effective Date: 11/16/2016

09/06/2006	Medical Director review
09/20/2006	Medical Policy Committee review
09/05/2007	Medical Director review
09/19/2007	Medical Policy Committee review. Rheumatology criterion removed for patient selection criteria. Policy statements added for not medically necessary, not covered and investigational.
05/07/2008	Medical Director review
05/21/2008	Medical Policy Committee approval. Added new FDA indication for juvenile idiopathic arthritis.
04/02/2009	Medical Director review.
04/15/2009	Medical Policy Committee approval. “Must not be on a live vaccine concurrently with abatacept or within three months of its discontinuation” added as a criteria bullet for adult rheumatoid arthritis.
07/02/2009	Medical Director review.
07/22/2009	Medical Policy Committee approval. Added the criteria bullet: • May be used alone or in combination with Disease Modifying Antirheumatic Drugs (DMARDs) other than TNF antagonists. The When Services Are Not Covered section was deleted from the policy. Added that when patient selection criteria are not met, or if abatacept is used for non-FDA approved indications, to deny investigational.
07/01/2010	Medical Policy Committee approval.
07/21/2010	Medical Policy Implementation Committee approval. No change to coverage.
07/07/2011	Medical Policy Committee approval.
07/20/2011	Medical Policy Implementation Committee approval. No change to coverage.
06/28/2012	Medical Policy Committee approval.
07/27/2012	Medical Policy Implementation Committee approval. Added a not medically necessary denial section to deny step therapy in absence of inadequate clinical response to one or more therapies specific to the condition such as Disease Modifying Antirheumatic Drugs (DMARDs) or tumor necrosis factor (TNF) antagonists. Juvenile rheumatoid arthritis was removed from list of investigational conditions.
06/27/2013	Medical Policy Committee review

abatacept (Orencia®)

Policy # 00214
Original Effective Date: 09/20/2006
Current Effective Date: 11/16/2016

07/17/2013	Medical Policy Implementation Committee approval. Removed requirement regarding vaccines. Clarified that PPD is required. Changed wording of criteria to match policy wording for similar drugs. Moved notes into the patient selection criteria section. Reworded and simplified the investigational and not medically necessary sections.
10/10/2013	Medical Policy Committee review
10/16/2013	Medical Policy Implementation Committee approval. Added criteria that requires Humira AND Enbrel be tried prior to use of Orencia for Rheumatoid Arthritis. Modified the not medically necessary section to reflect changes.
10/02/2014	Medical Policy Committee review
10/15/2014	Medical Policy Implementation Committee approval. No change to coverage.
11/21/2014	Medical Policy Implementation Committee approval. "For Orencia SubQ requests or for Orencia intravenous loading dose requests prior to initiating Orencia SubQ therapy" was added to eligibility criteria, and "This criterion only applies to Orencia SubQ requests or Orencia intravenous loading dose requests prior to initiating Orencia SubQ therapy" was added under the not medically necessary section for adult rheumatoid arthritis section.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/29/2015	Medical Policy Committee review
11/16/2015	Medical Policy Implementation Committee approval. No change to coverage.
11/03/2016	Medical Policy Committee review
11/16/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes

Next Scheduled Review Date: 11/2017

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2015 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. *Applicable FARS/DFARS apply.*

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0129
ICD-10 Diagnosis	D89.810-D89.813 G35 L40.0-L40.9 M05.00-M05.9

abatacept (Orencia®)

Policy # 00214
Original Effective Date: 09/20/2006
Current Effective Date: 11/16/2016

	M06.00-M06.9	M08.00-M08.99	M32.0-M32.9	T86.00-T86.99

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.