VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION REVIEW MEDICAL POLICY

POLICY: Inflammatory Conditions – Orencia Intravenous Utilization Review Medical Policy
- Orencia® (abatacept for intravenous infusion)

REVIEW DATE: 06/17/2020

OVERVIEW

Orencia intravenous, a selective T-cell costimulation modulator, is indicated for the following uses:

- **Rheumatoid arthritis**, for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely disease. In RA, Orencia intravenous may be used as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs) other than tumor necrosis factor inhibitors (TNFis).
- **Juvenile idiopathic arthritis**, for reducing signs and symptoms in pediatric patients ≥ 2 years of age with moderately to severely active polyarticular disease. In juvenile idiopathic arthritis, Orencia intravenous may be used alone or in combination with methotrexate (MTX).
- **Psoriatic arthritis**, in adults with active disease.

Orencia should not be administered concomitantly with TNFis and is not recommended for use concomitantly with other biologics for rheumatoid arthritis. Orencia is available as an intravenous infusion that is dosed on body weight. There is also a subcutaneous injection available in prefilled syringes (50 mg, 87.5 mg, and 125 mg per syringe) to allow for use in adults and weight-based dosing in pediatric patients. Some patients initiating therapy with Orencia subcutaneous will receive a single loading dose with Orencia intravenous.

Guidelines

Orencia is addressed in guidelines for treatment of various inflammatory conditions.

- **Rheumatoid Arthritis:** Guidelines from the American College of Rheumatology (ACR) [2015] have TNFis and non-TNF biologics such as Orencia, administered with or without methotrexate, equally positioned as a recommended therapy following a trial of a conventional synthetic DMARD (e.g., methotrexate, leflunomide, hydroxychloroquine, sulfasalazine).[2]
- **Juvenile Idiopathic Arthritis:** Guidelines (2019) list biologics among the treatment options for subsequent therapy in patients with polyarthritis.[3] Initial therapy with a biologic may be considered for patients with risk factors and involvement of high-risk joints (e.g., cervical spine, wrist, or hip), high disease activity, and/or those judged to be at high risk of disabling joint damage. In patients with active sacroiliitis or enthesitis despite nonsteroidal anti-inflammatory drug, a TNFi is recommended.
- **Psoriatic Arthritis:** Guidelines from ACR (2018) recommend TNFis over other biologics for use in treatment-naïve patients with PsA and in those who were previously treated with an oral therapy.[4] However, Orencia may be considered over other biologics in patients with recurrent or serious infections.

Safety

Orencia intravenous has Warnings concerning risks of serious infection.[1] Prior to initiating therapy with Orencia, patients should be evaluated for active tuberculosis infection. If a serious infection develops, treatment with Orencia should be discontinued.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Orencia intravenous. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist).

Because of the of the specialized skills required for evaluation and diagnosis of patients treated with Orencia intravenous as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Orencia intravenous to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

RECOMMENDED AUTHORIZATION CRITERIA

FDA-Approved Indications

1. **Rheumatoid Arthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets the following criteria (i and ii):
     - **i.** Patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months; AND
       Note: Examples of conventional synthetic DMARDs include methotrexate (oral or injectable), leflunomide, hydroxychloroquine, and sulfasalazine. An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already has a 3-month trial at least one biologic. Refer to Appendix for examples of biologics used for rheumatoid arthritis. These patients who have already tried a biologic are not required to "step back" and try a conventional synthetic DMARD.
     - **ii.** The agent is prescribed by or in consultation with a rheumatologist.
   - **B)** Patient is Currently Receiving Orencia (Intravenous or Subcutaneous). Approve for 1 year if the patient has had a response, as determined by the prescriber.
     Note: Examples of a response include less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values; reduced dosage of corticosteroids. The patient may not have a full response, but there should have been a recent or past response to Orencia.

   Dosing. Approve if dosing meets the following (A and B):
   - **A)** The dose is based on the patient's weight and meets ONE of the following (i, ii, or iii):
     - **i.** 500 mg if the patients weighs < 60 kg; OR
     - **ii.** 750 mg if the patient weighs 60 kg to 100 kg; OR
     - **iii.** 1,000 mg if the patient weighs > 100 kg; AND
   - **B)** The dose is administered at Weeks 0, 2, and 4, then every 4 weeks thereafter.

2. **Juvenile Idiopathic Arthritis (JIA) [or Juvenile Rheumatoid Arthritis] (regardless of type of onset).** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets BOTH of the following criteria (i and ii):
     - **i.** Patient meets one of the following conditions (a, b, c, or d):
       - **a)** Patient has tried one other agent for this condition; OR
         Note: Examples of therapies which could have been tried include methotrexate, sulfasalazine, or leflunomide, and a nonsteroidal anti-inflammatory drug (NSAID). A biologic also counts as a trial of one agent for JIA. Refer to Appendix for examples of biologics used for JIA.
       - **b)** Patient will be starting on therapy concurrently with methotrexate, sulfasalazine, or leflunomide; OR
       - **c)** Patient has an absolute contraindication to methotrexate, sulfasalazine, or leflunomide; OR
         Note: Examples of absolute contraindications to methotrexate include pregnancy, breast feeding, alcoholic liver disease, immunodeficiency syndrome, blood dyscrasias.
       - **d)** Patient has aggressive disease, as determined by the prescriber; AND
     - **ii.** The agent is prescribed by or in consultation with a rheumatologist.
   - **B)** Patient is Currently Receiving Orencia (Intravenous or Subcutaneous). Approve for 1 year if the patient has had a response, as determined by the prescriber.
     Note: Examples of a response include improvement in limitation of motion; less joint pain or tenderness; improved function or activities of daily living; decreased duration of morning stiffness or fatigue; reduced dosage of corticosteroids; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values. The patient may not have a full response, but there should have been a recent or past response to Orencia.

   Dosing. Approve if dosing meets the following (A, B, and C):
   - **A)** The weight-based dose meets ONE of the following (i or ii):
     - **i.** Patient weighs < 75 kg: the dose is 10 mg/kg; OR
     - **ii.** Patient weighs ≥ 75 kg:
       - **a)** 750 mg if the patient weighs ≤ 100 kg; OR
       - **b)** 1,000 mg if the patient weighs > 100 kg; AND
   - **B)** The maximum dose is 1,000 mg per infusion; AND
   - **C)** The dose is administered at Weeks 0, 2, and 4, then every 4 weeks thereafter.

3. **Psoriatic Arthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if prescribed by or in consultation with a rheumatologist or a dermatologist.
   - **B)** Patient is Currently Receiving Orencia (Intravenous or Subcutaneous). Approve for 1 year if the patient has responded, as determined by the prescriber.
     Note: Examples of a response include less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improvements in acute phase reactants (for example, C-reactive protein). The patient may not have a full response, but there should have been a recent or past response to Orencia.

   Dosing. Approve if dosing meets the following (A and B):

A) The dose is based on the patient's weight and meets ONE of the following (i, ii, or iii):
- **i.** 500 mg if the patients weighs < 60 kg; OR
- **ii.** 750 mg if the patient weighs 60 kg to 100 kg; OR
- **iii.** 1,000 mg if the patient weighs > 100 kg; AND

B) The dose is administered at Weeks 0, 2, and 4, then every 4 weeks thereafter.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Orencia intravenous is not recommended in the following situations:

1. **Ankylosing Spondylitis.** In an open-label Phase II trial, Orencia was administered by IV infusion on Days 1, 15, 29, and every 28 days thereafter to patients with active AS.[5] Patients received a fixed dosage of Orencia of approximately 10 mg/kg based on body weight. The primary endpoint was a 40% improvement in disease activity at Week 24 in the Assessment of SpondyloArthritis international Society criteria (ASAS 40). At Week 24, the ASAS 40 was 13.3% (n = 2/15) in TNF blocker-naïve patients compared with no responses in patients who had previously failed TNF blockers (n = 15). ASAS 20 response was 26.7% (n = 4/15) in TNF blocker-naïve patients compared with 20% (n = 3/15) in those who had previously failed TNF blockers. A major response was not shown with treatment to Orencia.

2. **Concurrent Use with a Biologic or with a Targeted Synthetic DMARD.** Orencia IV should not be administered in combination with another biologic or with a targeted synthetic DMARD used for an inflammatory condition (see Appendix for examples). Combination therapy is generally not recommended due to a higher rate of AEs with combinations and lack of data supportive of additional efficacy.[6-7] Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Orencia IV.

3. **Inflammatory Bowel Disease (i.e., Crohn's Disease, Ulcerative Colitis).** In placebo-controlled trials evaluating the efficacy of Orencia IV for induction and maintenance in adults with active, moderate to severe Crohn's disease (n = 451) and ulcerative colitis (n = 490), Orencia was no more effective than placebo.[8] Patients were randomized to Orencia 30, 10, or 3 mg/kg IV (according to body weight) or placebo and dosed at Weeks 0, 2, 4, and 8. A total of 90 patients with Crohn's disease and 131 patients with ulcerative colitis who responded to Orencia IV induction were then randomized to Orencia 10 mg/kg IV or placebo every 4 weeks through Week 52. When used for induction of Crohn's disease, 17.2%, 10.2%, and 15.5% of patients receiving Orencia 30 mg, 10 mg, and 3 mg/kg IV achieved a clinical response at Weeks 8 and 12 compared with 14.4% of patients receiving placebo (P = not significant [NS] for all comparisons). In patients with Crohn's disease, response and remission at Week 52 was not significantly different between the Orencia IV and placebo treatment groups. When used as induction therapy in ulcerative colitis, 21.4%, 19.0%, and 20.3% of patients receiving Orencia 30 mg, 10 mg, and 3 mg/kg IV achieved a clinical response at Week 12 compared with 29.5% of patients receiving placebo (P = 0.043 for 10 mg/kg vs. placebo; other comparisons NS). At Week 52, 12.5% (n = 8/64) and 14.1% (n = 9/64) of patients with ulcerative colitis were in remission (P = NS) and 17.2% of patients in each treatment group (n = 11/64 for each group) had achieved a response.

4. **Psoriasis**. (Note: Patients with concomitant plaque psoriasis and psoriatic arthritis may be reviewed under the psoriatic arthritis criteria above.) In a multicenter, Phase I, 26-week, open-label dose-escalation study, 43 patients with stable plaque psoriasis (10% to 49% body surface area involvement) received four doses of Orencia given as a 1-hour IV infusion on Days 1, 3, 16 and 29.[9] The starting dose was 0.5 mg/kg. Four to six patients were accrued to each of eight dose levels: 0.5, 1, 2, 4, 8, 16, 25 and 50 mg/kg. A parallel control group was matched for age and overall disease severity. In all, 46% of patients on Orencia for IV infusion achieved a 50% or greater sustained improvement in clinical disease activity (Physician's Global Assessment of disease activity) compared with baseline psoriasis evaluation. Progressively greater effects were observed with the highest doses. Further studies are needed to establish safety and efficacy in plaque psoriasis.

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Orencia® for injection [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; March 2019.
2. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol.* 2016;68(1):1-26.
3. Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for non-systemic polyarthritis, sacroiliitis, and enthesitis. *Arthritis Rheumatol. Arthritis Rheumatol.* 2019;71(6):717-734.
4. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. *Arthritis Care Res (Hoboken).* 2019;71(1):2-29.
5. Song IH, Heldmann F, Rudwaleit M, et al. Treatment of active ankylosing spondylitis with abatacept: an open-label, 24-week pilot study. *Ann Rheum Dis*. 2011;70(6):1108-1110.
6. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2011. *Ann Rheum Dis*. 2012;71 Suppl 2:i2-i45.
7. Xeljanz® tablets [prescribing information]. New York, NY: Pfizer Inc; December 2017.
8. Sandborn WJ, Colombel JF, Sands BE, et al. Abatacept for Crohn's disease and ulcerative colitis. *Gastroenterology.* 2012;143(1):62-69.e4.
9. Abrams JR, Lebwohl MG, Guzzo CA, et al. CTLA4Ig-mediated blockade of T-cell costimulation in patients with psoriasis vulgaris. *J Clin Invest.* 1999;103:1243-1252.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual revision	Throughout the policy, references to Humira, Enbrel, and Rituxan were reworded as adalimumab, etanercept, and rituximab products, respectively, with the innovator names listed as examples of these products. Renflexis and Erelzi were also added as respective examples of infliximab and etanercept products. Remove criterion for patients established on Orencia IV or SC for ≥ 90 days. This requirement was moved to the criteria section of the policy and now applies to patients currently receiving Orencia IV or SC for any duration of time, if the patient has responded to therapy.	05/09/2018
Annual revision	**Rheumatoid Arthritis:** Truxima was added as an example of a rituximab product. **Juvenile Idiopathic Arthritis:** Actemra SC was added as an example of an agent which may have been previously tried. In the dosing section, remove age restrictions from the policy.	06/05/2019
Annual revision	**Rheumatoid Arthritis:** Examples of conventional synthetic disease-modifying antirheumatic drugs were moved to a Note (previously listed as examples within the criteria). Examples of biologics for Rheumatoid Arthritis were moved to be included in the Appendix (previously listed in a Note in the criteria section). Examples of a response to therapy were moved to a Note (previously listed as examples within the criteria). **Juvenile Idiopathic Arthritis:** Examples of therapies that could have been tried prior to Orencia were moved to a Note (previously listed as examples within the criteria). Examples of biologics were moved to be included in the Appendix (previously listed in a Note in the criteria section). Examples of a response to therapy were moved to a Note (previously listed as examples within the criteria). For the exception applying to patients with aggressive disease, wording was updated to more generally allow this determination by the prescriber (criteria previously specified this was according to the prescribing physician). **Psoriatic Arthritis:** Examples of a response to therapy were moved to a Note (previously listed as examples within the criteria).	06/17/2020

APPENDIX

Products	Mechanism of Action	Examples of Inflammatory Indications for Products*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, PJIA, PsO, PsA, RA, SJIA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: PJIA, PSA, RA
		IV formulation: PJIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Ilaris (canakinumab SC injection**)**	Inhibition of IL-1β	SJIA
Kineret® (anakinra SC injection)	Inhibition of IL-1	RA, SJIA^
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx™ (secukinumab SC injection)	Inhibition of IL-17A	AS, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpa, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi™ (risankizumab-rzza SC injection)	Inhibition of IL-23	PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of the JAK pathways	RA
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indication (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AS – Ankylosing spondylitis; CD – Crohn's disease; PJIA – Polyarticular juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; SJIA – Systemic juvenile idiopathic arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; ^ Off-label use of SJIA supported in guidelines.