



Louisiana

triamcinolone extended release intra-articular injection (Zilretta™)

Policy # 00612

Original Effective Date: 03/21/2018

Current Effective Date: 01/11/2021

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.*

Based on review of available data, the Company may consider triamcinolone extended release intra-articular injection (Zilretta™)† for the management of osteoarthritis of the knee to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for triamcinolone extended release intra-articular injection (Zilretta) will be considered when the following criteria are met:

- Patient has knee pain and a documented diagnosis of osteoarthritis of the knee with x-ray (radiologic) confirmation of Kellgren-Lawrence Scale score of grade 2 or greater; AND
- Zilretta is dosed at 32 mg PER KNEE as a one-time intra-articular injection; AND
- Patient has NOT received a previous dose of Zilretta in the requested knee(s); AND
- Patient does NOT have a contraindication to intra-articular steroid injections (e.g., septic arthritis, periarticular infections, joint instability); AND
- Patient is 18 years of age or older; AND
- Patient has failed a sufficient trial with (e.g., intolerance or inadequate response) TWO of the following:
 - Cardiovascular (aerobic) activity, such as: walking, biking, stationary bike, aquatic exercise; OR
 - Resistance exercise; OR
 - Weight reduction (for persons who are overweight); OR

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- Participation in self-management programs; OR
- Wear of medially directed patellar taping; OR
- Wear of wedged insoles; OR
- Thermal agents; OR
- Walking aids; OR
- Physical therapy; OR
- Occupational therapy; AND

*(Note: This specific patient criterion requiring the failure of non-pharmacologic therapy is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Patient has failed (e.g., intolerance or inadequate response) TWO or more of the following:
 - acetaminophen; OR
 - Oral non-steroidal anti-inflammatory drugs (NSAIDs); OR
 - Topical NSAIDs; OR
 - tramadol; AND

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

- Patient has failed (e.g., intolerance or inadequate response) TWO (different ingredients) immediate release intra-articular steroid injections (e.g., triamcinolone, methylprednisolone, betamethasone, dexamethasone) in the requested knee(s) for treatment in which efficacy lasted less than 8 weeks for BOTH pre-requisite immediate release intra-articular steroid injections.

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

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of triamcinolone extended release intra-articular injection (Zilretta) when other therapies have NOT been tried and failed (e.g., both pharmacologic and non-pharmacologic therapy) to be **not medically necessary.****

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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 triamcinolone extended release intra-articular injection (Zilretta) when any of the following are NOT met to be **investigational***:

- Patient has knee pain and a documented diagnosis of osteoarthritis of the knee with x-ray (radiologic) confirmation of Kellgren-Lawrence Scale score of grade 2 or greater
- Zilretta is dosed at 32 mg PER KNEE as a one-time intra-articular injection
- Patient has NOT received a previous dose of Zilretta in the requested knee(s)
- Patient does NOT have a contraindication to intra-articular steroid injections (e.g. septic arthritis, periarticular infections, joint instability)
- Patient is 18 years of age or older

Based on review of available data, the Company considers the use of triamcinolone extended release intra-articular injection (Zilretta) for non-FDA approved indications to be **investigational***.

Background/Overview

Zilretta is an extended release triamcinolone injectable that is indicated as an intra-articular injection for the management of osteoarthritis pain of the knee. It is the first extended release intra-articular extended release product. The package insert states that Zilretta is NOT intended for repeat administration. Zilretta is given as a 32 mg intra-articular injection in the knee.

Osteoarthritis is the most common form of arthritis and presents with joint pain, stiffness, and locomotor restriction. Symptoms typically present in just one or a few joints. Osteoarthritis is confirmed by radiographic evidence and is classified via the Kellgren-Lawrence Radiographic Criteria for Assessment of Osteoarthritis. The scale ranges from grade 0 to grade 4, with the higher number representing worsening disease. Grade 0 includes no radiographic features of osteoarthritis. Grade 1 represents doubtful narrowing of joint space with possible osteophytic lipping. Grade 2 represents possible narrowing of joint space with definite osteophytes. Grade 3 represents definite narrowing of joint space, moderate multiple osteophytes, some subchondral sclerosis, and possible

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deformity of bone contour. Grade 4 represents marked narrowing of joint space, large osteophytes, severe subchondral sclerosis, and definite deformity of bone contour.

Typical pathways for treatment include use of non-pharmacologic therapy, such as those mentioned in the patient selection criteria (e.g., cardiovascular activity, weight reduction, resistance exercise, etc). If those have failed, then therapy would include pharmacologic agents such as acetaminophen, non-steroidal products (oral and/or topical), and tramadol. If pain persists, intra-articular injectable options include hyaluronic acid products (e.g., Synvisc/One[®]†, Euflexxa[®]†, etc.) as well as intra-articular corticosteroid products (e.g., triamcinolone, methylprednisolone, betamethasone, dexamethasone). Zilretta is the only extended release intra-articular corticosteroid that is FDA approved. It should be noted that in a secondary exploratory analysis, statistical significance was NOT demonstrated between Zilretta and the active control (immediate-release triamcinolone acetonide) treatment group (see rationale/source below). It should also be noted that Zilretta should only be given once per knee per lifetime.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Zilretta was approved in October of 2017 for the management of osteoarthritis pain of the knee.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Zilretta was demonstrated in a multi-center, international, randomized, double-blind, parallel-arm, placebo- and active-controlled study in patients with osteoarthritis pain of the knee. A total of 484 patients (Zilretta 32 mg, N=161; placebo [saline], N=162; active control [a crystalline suspension, immediate-release formulation of triamcinolone acetonide 40 mg], N=161) were treated and followed for up to 24 weeks. Twenty-five percent (25%) of patients had received at least one prior corticosteroid intra-articular injection more than 3 months prior to treatment. A total of 470

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patients (97%) completed follow-up to Week 12, the time point for primary efficacy determination, and 443 (91.5%) completed to Week 24.

The primary efficacy endpoint comparing Zilretta to placebo was change from baseline at Week 12 in the weekly mean of the Average Daily Pain intensity scores (ADP) as assessed by a 0-10 Numeric Rating Scale (NRS). Zilretta demonstrated a statistically significant reduction in pain intensity at the primary endpoint vs placebo. Zilretta also demonstrated a reduction in pain intensity scores each week from Weeks 1 through 12.

In a secondary exploratory analysis, statistical significance was not demonstrated between the Zilretta and the active control (immediate-release triamcinolone acetonide) treatment groups for the change from baseline at Week 12 in weekly mean ADP.

References

1. Zilretta [package insert]. Flexion Therapeutics, Inc. Burlington, Massachusetts. Updated October 2017.
2. Management of moderate to severe knee osteoarthritis. UpToDate. Updated January 2018.
3. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthritis. *Ann Rheum Dis*. 1957 Dec; 16(4): 494-502.

Policy History

Original Effective Date: 03/21/2018

Current Effective Date: 01/11/2021

03/01/2018 Medical Policy Committee review

03/21/2018 Medical Policy Implementation Committee approval. New policy.

07/01/2018 Coding update

01/01/2019 Coding update

12/05/2019 Medical Policy Committee review

12/11/2019 Medical Policy Implementation Committee approval. Clarified coverage of osteoarthritis with the Kellgren-Lawrence Scale. Updated background information to include Kellgren-Lawrence Scale.

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12/03/2020 Medical Policy Committee review

12/09/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 12/2021

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 2019 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.

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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	C9399, J3304, J3490

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ICD-10 Diagnosis	M17.0-M17.9, M19.90-M19.93
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*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. Food and Drug Administration (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.

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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.

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NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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.

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