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Triamcinolone Acetonide Extended-Release Injectable Suspension (Zilretta®)

Table of Contents
Coverage
Policy Guidelines
Description
Rationale
Coding
References
Policy History

Related Policies (if applicable)
None

Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of care developed by: nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan**

description or contract will govern.

Coverage

Triamcinolone acetonide extended-release injectable suspension (Zilretta®) **may be considered medically necessary** when the following criteria are met:

- Radiologic evidence confirms individual has osteoarthritis of the knee; AND
- Individual has tried at least one intraarticular corticosteroid injection in the knee to be treated; AND
- Individual is not receiving re-treatment of knee(s) previously treated with triamcinolone acetonide extended-release injectable suspension (Zilretta®).

Triamcinolone acetonide extended-release injectable suspension (Zilretta®) **is considered experimental, investigational and/or unproven** for all other non-Food and Drug Administration approved indications, including but not limited to:

- Injection in small joints such as the hand;
- Management of osteoarthritis of the shoulder or hip as efficacy and safety have not been evaluated;
- Administration by the following routes: epidural, intrathecal, intravenous, intraocular, intramuscular, intradermal, subcutaneous;
- Repeat administration of Zilretta® as the efficacy and safety have not been demonstrated.

Policy Guidelines

Per the prescribing information for Zilretta®,

- Zilretta is administered as a single intra-articular extended-release injection of triamcinolone acetonide, to deliver 32 mg (5 mL).
- The efficacy and safety of repeat administration have not been demonstrated.
- Zilretta is for intra-articular use only.
- It is not to be administered by the following routes: epidural, intrathecal, intravenous, intraocular, intramuscular, intradermal, subcutaneous.
- Zilretta is not suitable for use in small joints, such as the hand.
- The efficacy and safety of Zilretta for management of osteoarthritis pain of shoulder and hip have not been evaluated.
- Zilretta is NOT substitutable with other formulations of injectable triamcinolone acetonide. (1)

Description

Osteoarthritis is the most common form of arthritis, affecting an estimated 32.5 million adults in the United States according to the Centers for Disease Control (CDC) (2), and 302 million people worldwide and is a leading cause of disability among older adults. (3) The knees, hips, and hands are the most commonly affected appendicular joints. OA is characterized by pathology involving the whole joint, including cartilage degradation, bone remodeling, osteophyte formation, and synovial inflammation, leading to pain, stiffness, swelling, and loss of normal joint function. (2, 3)

The knee is a frequent site for OA]. The prevalence of knee osteoarthritis (KOA) in men over 60 years is 5% - 15%, while in women aged 60 years and over, it is 10% - 25%. Risk factors for KOA include age, gender, obesity, joint injuries (work/sports activities), and geographic region. KOA can cause joint pain, muscle weakness, physical disability, and decreased quality of life. In contrast, chronic pain can cause anxiety, depression, and cognitive dysfunction, impacting daily life socially and economically. (4)

Classification of knee OA is divided into primary and secondary, depending on the cause. Primary knee OA results from articular cartilage degeneration, the exact cause of which is still unknown, presumably due to increasing age. Secondary knee OA results from articular cartilage degeneration with known causes, including post-traumatic, congenital, or limb malformations, malposition (varus/valgus), scoliosis, rachitis, Wilson's disease, gout, pseudogout, rheumatoid arthritis, hemophilia, and Paget's disease. (4)

Management of OA in terms of reducing pain includes physiotherapy (exercise, biomechanical intervention, electrotherapy, diathermy), pharmacology, intra-articular (IA) injections (corticosteroids, hyaluronic acid, geniculate nerve blocks), extra-articular injections, and radiofrequency. IA corticosteroid injections are often conditionally advised in KOA above other IA injections. The injection technique can be blinded or guided by ultrasound. The ultrasound injection site injects steroids into the suprapatellar recess or bursae. Glucocorticoid injections are far more effective than other medications. Corticoids exert their immunosuppressive and anti-inflammatory effects by acting directly on nuclear receptors, disrupting the inflammatory cascade. They decrease the activity and generation of interleukin-1, prostaglandin, leukotriene, MMP9, and MMP-11, which are thought to promote joint mobility in KOA and are a component of the process of pain alleviation. Several corticosteroids, including methylprednisolone acetate, triamcinolone acetate, triamcinolone hexacetonide, betamethasone acetate, betamethasone sodium phosphate, and dexamethasone, are now approved by the Food and Drug Administration for IA treatment. (4)

Regulatory Status

The U.S. Food and Drug Administration approved triamcinolone acetonide extended-release injectable suspension (Zilretta®) for intra-articular injection for the management of osteoarthritis pain of the knee in 2024. The efficacy and safety of repeat administration of Zilretta have not been demonstrated for the prescribing information.

Rationale

This policy is based on the U.S. Food and Drug Administration labeled indications for ZILRETTA® (triamcinolone acetonide extended-release injectable suspension) and a review of relevant professional guidelines and position statements.

ZILRETTA® (triamcinolone acetonide extended-release injectable suspension) (1)

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. Patients had a mean age of 62 (range 40 to 85 years); baseline demographics and disease characteristics were balanced across treatment arms. 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 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 a 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.

Practice Guidelines and Position Statements

American Academy of Orthopaedic Surgeons (5)

The 2021 American Academy of Orthopaedic Surgeons Evidence-Based Clinical Practice Guideline on Management of Osteoarthritis of the Knee (Non-Arthroplasty) provides the following recommendation for the use of intra-articular (IA) corticosteroid injections in the management of OA of the knee.

- Intra-articular (IA) corticosteroids could provide short-term relief for patients with symptomatic osteoarthritis of the knee. Strength of Recommendation: Moderate.

American College of Rheumatology/Arthritis Foundation (3)

The 2019 American College of Rheumatology/Arthritis Foundation Guidelines for the Management of Osteoarthritis of the Hand, Hip and Knee states:

- Intraarticular glucocorticoid injections are strongly recommended for patients with knee and/or hip OA and conditionally recommended for patients with hand OA.

They provide the following rationale for the recommendation:

“Trials of intraarticular glucocorticoid injections have demonstrated short-term efficacy in knee OA. Intraarticular glucocorticoid injection is conditionally, rather than strongly, recommended for hand OA given the lack of evidence specific to this anatomic location. There are insufficient data to judge the choice of short-acting over long-acting preparations or the use of low rather than high doses. A recent report raised the possibility that specific steroid preparations or a certain frequency of steroid injections may contribute to cartilage loss, but the Voting Panel was uncertain of the clinical significance of this finding, particularly since change in cartilage thickness was not associated with a worsening in pain, functioning, or other radiographic features.”

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member’s benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J3304

*Current Procedural Terminology (CPT®) ©2025 American Medical Association: Chicago, IL.

References

1. Prescribing Label: Zilretta® (triamcinolone acetonide extended-release injectable suspension). November 2024. Available at accessdata.fda.gov/scripts/cder/daf/index.cfm (accessed Aug. 4, 2026).
2. Arthritis Foundation. Osteoarthritis. Available at [arthritis.org](https://www.arthritis.org) (accessed Aug. 20, 2026).
3. Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of

the Hand, Hip, and Knee. Arthritis Care Res (Hoboken). 2020 February; 2(2): 149–162. PMID 31908149

4. Mintarjo JA, Poerwanto, E, Tedyanto EH. Current Non-surgical Management of Knee Osteoarthritis. Cureus. 2023 Jun 26;15(6):e40966. PMID 37503484
5. American Academy of Orthopaedic Surgeons (AAOS) Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. (Aug. 32, 2021). Available at www.aaos.org (accessed Aug. 19, 2026).

Centers for Medicare & Medicaid Services

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare & Medicaid Services does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at cms.hhs.gov.

Policy History/Revision

Date	Description of Change
9/15/2026	New medical document. Triamcinolone acetonide extended-release injectable suspension (Zilretta®) may be considered medically necessary when the following criteria are met: Radiologic evidence confirms individual has osteoarthritis of the knee; AND Individual has tried at least one intraarticular corticosteroid injection in the knee to be treated; AND Individual is not receiving re-treatment of knee(s) previously treated with triamcinolone acetonide extended-release injectable suspension (Zilretta®). Triamcinolone acetonide extended-release injectable suspension (Zilretta®) is considered experimental, investigational and/or unproven for all other non-Food and Drug Administration approved indications, including but not limited to: Injection in small joints such as the hand; Management of osteoarthritis of the shoulder or hip as efficacy and safety have not been evaluated; Administration by the following routes: epidural, intrathecal, intravenous, intraocular, intramuscular, intradermal, subcutaneous; Repeat administration of Zilretta® as the efficacy and safety have not been demonstrated.