

PHARMACY / MEDICAL POLICY – 5.01.633


Intraarticular Corticosteroids

Effective Date: May 1, 2025
Last Revised: Apr. 21, 2025
Replaces: N/A

RELATED MEDICAL POLICIES:
None

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Introduction

Intraarticular refers to the inside of the joints. Corticosteroids are a group of steroids produced in the adrenal cortex or made synthetically and include glucocorticoids and mineralocorticoids. Corticosteroids regulate cellular functions including development, homeostasis, metabolism, cognition, and inflammation. They are used to treat inflammatory and autoimmune diseases, such as asthma, allergies, rheumatoid arthritis, osteoarthritis, inflammatory bowel disease, and multiple sclerosis. Corticosteroids have anti-inflammatory and immunosuppressive effects by interrupting the inflammatory and immune cascade at various levels, preventing the synthesis and secretion of inflammatory mediators like prostaglandin and leukotrienes. The clinical benefits of these actions include a decrease in erythema, swelling, tenderness in the inflamed joints, and increase in relative viscosity due to an increase in hyaluronic acid (HA) concentration.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

| Drug | Medical Necessity |
|---|---|
| <p>Zilretta (triamcinolone acetonide extended-release injectable suspension) Intra-articular</p> | <p>Zilretta (triamcinolone acetonide extended-release injectable suspension) may be considered medically necessary for moderate to severe osteoarthritis pain of the knee when the following criteria are met:</p> <ul style="list-style-type: none"> • The individual is aged 18 years or older <p>AND</p> <ul style="list-style-type: none"> • Has a confirmed diagnosis of osteoarthritis of knee <p>AND</p> <ul style="list-style-type: none"> • Has not received prior treatment with Zilretta in the requested knee <p>AND</p> <ul style="list-style-type: none"> • Has tried and had an inadequate response after 3-months of treatment or had intolerance to ALL the following: <ul style="list-style-type: none"> ○ Oral nonsteroidal anti-inflammatory drugs (NSAIDs) <p>AND</p> <ul style="list-style-type: none"> ○ At least TWO of following intra-articular corticosteroid injections in the requested knee: methylprednisolone acetate, triamcinolone, betamethasone, and dexamethasone <p>AND</p> <ul style="list-style-type: none"> • Dose is limited to a single-dose intra-articular extended-release injection (32 mg) of Zilretta <p>Zilretta may only be approved for one intra-articular injection per knee per lifetime.</p> |

| Drug | Investigational |
|---|--|
| <p>Zilretta (triamcinolone acetonide extended-release injectable suspension)</p> | <p>Use of Zilretta for all other indications is considered investigational.</p> <p>The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.</p> |



| Length of Approval | |
|----------------------------------|--|
| Approval | Criteria |
| Initial authorization | <p>Non-formulary exception reviews for Zilretta (triamcinolone acetonide extended-release injectable suspension) may be approved up to 12 months</p> <p>All other reviews for Zilretta (triamcinolone acetonide extended-release injectable suspension) may be approved up to 1 month.</p> |
| Re-authorization criteria | Future re-authorization of Zilretta (triamcinolone acetonide extended-release injectable suspension) following the administration of one injection is considered investigational. |

| Documentation Requirements |
|---|
| <p>The individual’s medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:</p> <ul style="list-style-type: none"> • Office visit notes that contain the diagnosis, relevant history, medication history, imaging history and physical evaluation |

Coding

| Code | Description |
|--------------|---|
| HCPCS | |
| J3304 | Injection, triamcinolone acetonide, preservative-free, extended-release, microsphere formulation (Zilretta), 1 mg |

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Related Information



Definition of Terms

Mild knee osteoarthritis: Individuals with mild knee osteoarthritis have low or intermittent level of knee pain with mostly well-preserved joint function and quality of life.

Moderate/severe knee osteoarthritis: Individuals with moderate/severe knee osteoarthritis have constant pain which significantly impairs functionality, daily activity, and quality of life.

Consideration of Age

Zilretta: The safety and efficacy has not been evaluated in individuals under the age of 18 years.

Benefit Application

Medical Benefit

Zilretta (triamcinolone)

Evidence Review

Background

Osteoarthritis of the knee

Osteoarthritis (OA) was once thought to be merely a “wear and tear” process, but it involves inflammation of the bone, as “osteo” means bone and “Arthritis” means inflammation. Osteoarthritis is a degenerative joint disease that can impact any joint, but usually affects the hands, knees, hips, lower back, and neck. The causes of OA are multifactorial and include age, obesity, joint injury, genetics, environmental factors, gender, and musculoskeletal abnormalities. Symptoms of OA include joint stiffness, clicking or popping sound during joint movement, joint swelling, joint pain, and joint instability. Diagnosis of knee OA is typically based on medical history, physical examination, and lab tests.

The treatment of knee OA is based on clinical presentation. Mild knee OA treatment includes nonpharmacological management and pharmacological management, such as topical



Nonsteroidal anti-inflammatory drugs (NSAID) or capsaicin. For moderate to severe knee OA, nonpharmacological and pharmacological management such as oral NSAIDs or oral duloxetine are used. If persistent or progressive symptoms persist despite these treatments, intra-articular glucocorticoid injections may provide short-term pain relief, with other intra-articular therapies available, such as hyaluronan and platelet-rich plasma.

Summary of Evidence

Zilretta (triamcinolone)

Zilretta is an extended-release formulation of triamcinolone acetonide, a corticosteroid with anti-inflammatory and immunomodulatory effects. The mechanism of action of triamcinolone acetonide involves activating the glucocorticoid receptor, resulting in the stimulation of anti-inflammatory transcription factors, such as lipoproteins, and inhibiting the inflammatory transduction pathway by blocking the release of arachidonic acid, thereby preventing the synthesis of prostaglandins and leukotrienes.

Zilretta Evidence of Support

The efficacy and safety of Zilretta was studied in a multi-center, international, randomized, double-blind, parallel-arm, placebo-and active-controlled study. A total of 484 individuals with osteoarthritis pain of the knee was randomized to receive Zilretta 32mg (n = 161), placebo (n = 162) and active control (a crystalline suspension, immediate-release formulation of triamcinolone acetonide 40mg) (n = 161) and were monitored for up to 24 weeks. The primary efficacy endpoint was a change in the weekly mean of the Average Daily Pain intensity scores (ADP) as measured by 0-12 Numeric Rating Scale (NRS) from baseline to week 12 in each arm. Compared to the placebo arm, Zilretta demonstrated a statistically significant reduction in pain intensity. The least square mean reduction in pain intensity was -3.12 in the Zilretta group and -2.14 in the placebo group with $p < 0.0001$.

References

1. Zilretta (triamcinolone acetonide extended-release injectable suspension) [package insert]. Burlington, MA; Flexion Therapeutics, Inc. Revised May 2024.



2. Sivapriya R, John C, et al. Corticosteroids: Mechanisms of Action in Health and Disease. Corticosteroids: Mechanisms of Action in Health and Disease - PubMed (nih.gov). Accessed April 6, 2025.
3. Osteoarthritis of the Knee. Osteoarthritis of the Knee | Arthritis Foundation. Accessed April 6, 2025.
4. Michael D, Abhishek A, et al. Clinical manifestations and diagnosis of osteoarthritis. Clinical manifestations and diagnosis of osteoarthritis - UpToDate. Accessed April 6, 2025.

History

| Date | Comments |
|----------|--|
| 06/01/23 | New policy, approved May 9, 2023, effective for dates of service on or after September 1, 2023, following 90-day provider notification. Add to Prescription Drug section. Added new coverage criteria for Zilretta for the adult individuals with moderate to severe osteoarthritis pain of the knee. Added HCPCS code J3304 for Zilretta. |
| 08/01/24 | Annual Review, approved July 8, 2024. No changes to policy statements. |
| 05/01/25 | Annual Review, approved April 21, 2025. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. |

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2025 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.

