


PHARMACY / MEDICAL POLICY – 5.01.633

Intraarticular Corticosteroids

Effective Date:	Sept. 1, 2023	RELATED MEDICAL POLICIES:
Last Revised:	May 9, 2023	None
Replaces:	N/A	

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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
Zilretta (triamcinolone acetonide extended-release injectable suspension) Intra-articular	<p>Zilretta (triamcinolone acetonide extended-release injectable suspension) may be considered medically necessary for moderate to severe osteoarthritis pain of the knee in the adult individuals when the following criteria are met:</p> <ul style="list-style-type: none"> • Individual has a confirmed diagnosis of osteoarthritis of knee <p>AND</p> <ul style="list-style-type: none"> • Individual has not received a prior treatment with Zilretta in the requested knee <p>AND</p> <ul style="list-style-type: none"> • Individual has tried and had an inadequate response after 3-months of treatment or had intolerance to ALL of the following: <ul style="list-style-type: none"> ○ Oral nonsteroidal anti-inflammatory drugs (NSAIDs) ○ 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
Zilretta (triamcinolone acetonide extended-release injectable suspension)	Use of Zilretta for all other indications is considered investigational

Length of Approval	
Approval	Criteria
Initial authorization	Zilretta (triamcinolone acetonide extended-release injectable suspension) may be approved up to 1 month.



Length of Approval

Approval	Criteria
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

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:

- 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 December 2019.
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 May 2, 2023.
3. Osteoarthritis of the Knee. Osteoarthritis of the Knee | Arthritis Foundation. Accessed May 2, 2023.
4. Michael D, Abhishek A, et al. Clinical manifestations and diagnosis of osteoarthritis. Clinical manifestations and diagnosis of osteoarthritis - UpToDate. Accessed May 2, 2023.



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.

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). ©2023 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.



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Washington residents: You can also file a civil rights complaint with the Washington State Office of the Insurance Commissioner, electronically through the Office of the Insurance Commissioner Complaint Portal available at <https://www.insurance.wa.gov/file-complaint-or-check-your-complaint-status>, or by phone at 800-562-6900, 360-586-0241 (TDD). Complaint forms are available at <https://fortress.wa.gov/oic/online-services/cc/pub/complaintinformation.aspx>.

Alaska residents: Contact the Alaska Division of Insurance via email at insurance@alaska.gov, or by phone at 907-269-7900 or 1-800-INSURAK (in-state, outside Anchorage).

Language Assistance

ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 800-722-1471 (TTY: 711).

PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 800-722-1471 (TTY: 711).

注意: 如果您使用繁體中文，您可以免費獲得語言援助服務。請致電 800-722-1471 (TTY: 711)。

CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 800-722-1471 (TTY: 711).

주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 800-722-1471 (TTY: 711) 번으로 전화해 주십시오.

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MO LOU SILAFIA: Afai e te tautala Gagana fa'a Sāmoa, o loo iai auunaga fesoasoan, e fai fua e leai se totagi, mo oe, Telefoni mai: 800-722-1471 (TTY: 711).

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PAKDAAR: Nu saritaem ti Ilocano, ti serbisyo para ti baddang ti lengguahe nga awanan bayadna, ket sidadaan para kenyam. Awagan ti 800-722-1471 (TTY: 711).

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