RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title: **Triamcinolone ER Injection (Zilretta™)**
Policy Number: **RxA.328**
Drug(s) Applied: **Triamcinolone ER Injection (Zilretta™)**
Last Review Date: **01/2020**
Line of Business: **Commercial, Medicaid, HIM-Medical Benefit**

Background

Triamcinolone acetonide extended-release injectable suspension (Zilretta™) is an extendedrelease synthetic corticosteroid. It is indicated as an intraarticular injection for the management of osteoarthritis pain of the knee.

Indication	Dosing Regimen	Maximum Dose
Osteoarthrits of the knee	32 mg (5 mL) as a single intra-articular extendedrelease injection	32 mg (5 mL)

Injectable suspension of microspheres (single-dose vial for reconstitution): 32 mg per 5 mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Osteoarthritis of the Knee (must meet all)**:**

1. Diagnosis of osteoarthritis of the knee;
2. Prescribed by or in consultation with a rheumatologist or an orthopedist;
3. Age 18 years of age or older;
4. Failure of ≥ 2 week trial of one of the following (a or b), unless contraindicated or clinically significant adverse effects are experienced:
    a. Oral nonsteroidal antiinflammatory drug (NSAID) at continuous therapeutic dosing (prescription strength);
    b. Topical NSAID* if member is ≥ 75 years old or unable to take an oral NSAID;
5. History of a positive but inadequate response to at least one other intraarticular glucocorticoid injection for the knee* (e.g., inadequate pain relief, frequent need of rescue medications such as NSAIDs or opioids, need to decrease or inability to increase activity levels, adequate pain relief but with steroid-induced hyperglycemia); **Prior authorization may be required.*
6. Dose does not exceed 32 mg as a single intraarticular injection into the knee.
   Approval duration: 3 months (one dose per knee)

II. Continued Therapy

A. Osteoarthritis of the Knee:

1. Zilretta is not indicated for repeat administration.

Approval duration: Not applicable

III. Appendices

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
NSAID: non-steroidal antiinflammatory drug
TA: triamcinolone acetonide

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Oral NSAIDs		
diclofenac (Voltaren®)	50 mg PO BID to TID	150 mg/day
etodolac (Lodine®)	400-500 mg PO BID	1200 mg/day
fenoprofen (Nalfon®)	400-600 mg PO TID to QID	3200 mg/day
ibuprofen (Motrin®)	400-800 mg PO TID to QID	3200 mg/day
indomethacin (Indocin®)	25-50 mg PO BID to TID	200 mg/day
indomethacin SR	75 mg PO QD to BID	150 mg/day
ketoprofen	25-75 mg PO TID to QID	300 mg/day
meloxicam (Mobic®)	7.5-15 mg PO QD	15 mg/day
naproxen (Naprosyn®)	250-500 mg PO BID	1500 mg/day
naproxen sodium (Anaprox®, Anaprox DS®)	275-550 mg PO BID	1650 mg/day
oxaprozin (Daypro®)	600-1200 mg PO QD	1800 mg/day
piroxicam (Feldene®)	10-20 mg PO QD	20 mg/day
salsalate (Disalcid®)	1500 mg PO BID or 1000 mg PO TID	3000 mg/day
sulindac	150 mg-200 mg PO BID	400 mg/day
Topical NSAIDs		
diclofenac 1.5% (Pennsaid®)	40 drops QID on each painful knee	160 drops/knee/day
Voltaren® Gel 1% (diclofenac)	2-4 g applied to affected area QID	32 g/day
Intraarticular Glucocorticoids		
triamcinolone acetonide (Kenalog®)	40 mg (1 mL) for large joints	80 mg/treatment
methylprednisolone acetate (Depo-Medrol®)	20-80 mg for large joints	80 mg/treatment

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): patients with hypersensitivity to triamcinolone acetonide or any component of the product.
- Boxed warning(s): none reported.

Appendix D: General Information

- Zilretta (extended-release triamcinolone acetonide [TA-ER]) is designed to deliver TA over 12 weeks using extended-release microsphere technology. In contrast, Bodick, et al., 2015, reports that, historically, immediate-release intraarticular glucocorticoids, while demonstrating a large initial analgesic effect, wane over one to four weeks.
- In an evaluation of TA-ER vs immediate-release triamcinolone acetonide (TA-IR) synovial and systemic pharmacokinetics, Krause, et al, 2017, reports that TA-ER demonstrated prolonged residency in the joint (through week 12) relative to TA-IR (through week 6), and consequently showed diminished peak plasma steroid levels relative to TA-IR through week 6. Russell, et al, 2017, reports that in patients with knee osteoarthritis and type-2 diabetes mellitus, TA-ER was associated with a significant and clinically relevant reduction in blood glucose elevation relative to TA-IR 72 hours postinjection.
- In the Zilretta pivotal trial, Conaghan, et al, 2018, reported superiority of TA-ER versus placebo to 12 weeks in average daily pain (ADP) scores (primary endpoint) and continuing TA-ER activity out to 24 weeks. While TA-ER did not show superior outcomes relative to TA-IR over 12 weeks in ADP scores (secondary endpoint), it was superior to TA-IR at week 12 when evaluated using the exploratory endpoints Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)-A/B/C and Knee injury and Osteoarthritis Outcome Score Quality of Life (KOOS QoL) subscales.
- Conaghan also reports that patients treated with TA-ER used significantly less rescue medication than those treated with TA-IR.
- Follow-up studies focusing on Zilretta efficacy duration and need for repeat dosing are currently underway.

References

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	01/2020	02/07/2020