Children's Hospital and Health System
Chorus Community Health Plans
Policy and Procedure

This policy applies to the following entity(s):

☐ CHW – Milwaukee	☐ CHW - Fox Valley
☐ CHHS Foundation	☐ CHW - Surgicenter
☐ CHW – Community Services Division	☒ Chorus Community Health Plans
☐ Children's Medical Group - Primary Care	☐ Children's Specialty Group
☐ Children's Medical Group - Urgent Care	☐ CHHS Corporate Departments

Medical Utilization Management Policy

SUBJECT: EXTENDED-RELEASE INTRA-ARTICULAR GLUCOCORTICOIDS

INCLUDED PRODUCT(S):

Medicaid	**Individual and Family**
☒ BadgerCare Plus	☒ Commercial
☒ Care4Kids Program	☒ Marketplace

PURPOSE OR DESCRIPTION:
The purpose of this policy is to define criteria for the medically necessary use of extended-release intra-articular glucocorticoids (e.g. Zilretta).

FDA Approved Indication:
Triamcinolone acetonide ER (Zilretta) is an extended-release synthetic intra-articular corticosteroid injection indicated for management of osteoarthritis pain of the knee.

Limitation of Use: The efficacy and safety of repeat administration of triamcinolone acetonide ER (Zilretta) have not been demonstrated.

POLICY:
Extended-release intra-articular glucocorticoids may be indicated for the following:

1. Diagnosis of osteoarthritis of the knee and **ALL** of the following:
    a. Prescribed by an appropriate specialist (e.g. orthopedics, rheumatology, sports medicine, etc.)

b. History of trial and failure, intolerance, or contraindication to **ALL** of the following:
    i. **ONE** non-pharmacologic treatment (e.g. brace, DME, exercise, occupational therapy, physical therapy, weight loss, etc.)
    ii. **ONE** pharmacologic treatment (e.g. acetaminophen, oral NSAID, topical NSAID, tramadol, etc.)
    iii. **ONE** immediate-release intra-articular glucocorticoid injection in the knee (e.g. betamethasone, dexamethasone, methylprednisolone, triamcinolone)
c. Documented rationale for why an extended-release intra-articular glucocorticoid injection is expected to be safe and effective despite failure/intolerance to immediate-release intra-articular glucocorticoid injection
d. Patient is 18 years of age or older
e. Patient has not been previously treated with triamcinolone acetonide ER (Zilretta) in the requested knee

Authorization is intended for a one-time approval per knee. Triamcinolone acetonide ER (Zilretta) is not eligible for reauthorization in the same knee.

For all other uses, CCHP considers triamcinolone acetonide ER (Zilretta) NOT medically necessary.

Quantity Limits
Zilretta 32 mg/5mL injection: One Injection (32 mg/5mL) per knee per lifetime

Applicable Codes:
HPCS Code: J3304

Diagnosis Codes:
- M17.10
- M17.11
- M17.12
- M17.2
- M17.30
- M17.31
- M17.32
- M17.4
- M17.5
- M17.9

Background:
Triamcinolone acetonide ER (Zilretta) is a first in class extended-release intra-articular glucocorticoid that is approved for the treatment of osteoarthritis knee pain. This product is a novel formulation composed of triamcinolone acetonide embedded in a biodegradable PLGA matrix that extends residence time in the joint. Quantifiable concentrations of triamcinolone in the synovial fluid are detected out to 12 weeks.[1]
In a phase-3, multicenter, double-blinded, randomized clinical trial, triamcinolone acetonide ER (Zilretta) provided significant, clinically meaningful pain reduction compared with saline-solution placebo at week 12 based on a patient reported numerical rating scale ($p<0.0001$).[2] No significant difference was found for average daily pain improvement at 12 weeks compared to triamcinolone 40 mg immediate-release based on a patient reported numerical rating scale ($p=0.383$).[2] It should be noted that exploratory end points using WOMAC-A (pain), WOMAC-B

(stiffness), and WOMAC-C (physical function) trended favorably toward triamcinolone acetonide ER (Zilretta) compared to immediate-release triamcinolone injections, but statistical significance cannot be determined.[2] Results from an open-label, phase 3b case series showed that repeat administration of Zilretta for osteoarthritis knee pain was generally safe and well tolerated, with x-ray data at week 52 showing no negative impact on cartilage or joint structure.[3] Per FDA approved product labeling, statistical significance of this data was not assessed, and the safety and efficacy of repeat triamcinolone acetonide ER (Zilretta) injections has not been demonstrated.

The American Academy of Orthopaedic Surgeons (AAOS) 2021 Management of Osteoarthritis of the Knee (3rd edition) guideline provides a moderate recommendation that intra-articular corticosteroids could provide short-term relief for patients with symptomatic knee osteoarthritis. The AAOS guidelines further state that when immediate release intra-articular corticosteroids were compared to extended-release intra-articular corticosteroids, extended release IA steroids can be used over immediate release to improve patient outcomes (moderate recommendation).[4] This recommendation was based on one high quality and two moderate quality studies.

The 2019 American College of Rheumatology clinical practice guidelines for the management of the osteoarthritis of the hand, hip, and knee state that “Intra-articular glucocorticoid injections are strongly recommended for patients with knee and/or hip osteoarthritis.” The recommendation notes insufficient data to judge the choice of short-acting over long-acting preparations or the use of low rather than high doses.[5]

REFERENCES

1. Zilretta Prescribing Information. Burlington, MA: Flexion Therapeutics, Inc.; March 2022. Available at: http://www.zilrettalabel.com/PI. Accessed April 19, 2022
2. Conaghan PG, Hunter DJ, Cohen SB, et al. Effects of a single intra-articular injection of a microsphere formulation of triamcinolone acetonide on knee osteoarthritis pain: a double-blinded, randomized, placebo-controlled, multinational study. J Bone Joint Surg Am. 2018;100(8):666-677. doi:10.2106/JBJS.17.00154
3. Spitzer AI, Richmond JC, Kraus VB, et al. Safety and efficacy of repeat administration of triamcinolone acetonide extended-release in osteoarthritis of the knee: a phase 3b, open-label study. Rheumatol Ther. 2019;6(1):109-124. doi:10.1007/s40744-019-0140-z
4. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline (3rd Edition). https://www.aaos.org/oak3cpg Published August 31, 2021. Accessed April 19, 2022
5. American College of Rheumatology (ACR). Clinical Practice Guideline: Osteoarthritis. Available at: http://www.rheumatology.org. Accessed April 19, 2022.
6. Hayes Health Technology Assessment, Zilretta, July 2021 , Copyright © 2022 Hayes, LLC