MediNatura™

Reimbursement Guide

Traumeel®/Zeel® Injection Solution

For Moderate-to-Severe Pain
Associated with Osteoarthritis of the Knee

March 4, 2015

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Introduction

The Reimbursement Guide for MediNatura has been developed to help physicians obtain coding clarification and coverage for intra-articular (IA) injections of the Traumeel/Zeel injection solution to treat osteoarthritis (OA) of the knee.

The Guide provides background information to help explain to payers why the injection solution might be an appropriate alternative to conventional injections for OA of the knee. The processes for seeking a coding clarification and coverage are outlined, and the proper coding for self-pay patients is discussed as well.

MediNatura has made every effort to ensure that the information in this Guide is suitable and appropriate for describing and coding the services rendered in the care and management of patients undergoing IA injections for OA of the knee. MediNatura has developed this Guide as a service to its customers in an effort to facilitate the appropriate and effective use of coding conventions. The contents of the Guide are intended to supplement knowledge of the coding and coverage of IA injections already maintained by these providers. Ultimate responsibility for coding and billing lies with the provider of the services

While not all services or procedures are coded and included in this Guide, great care has been taken to ensure the suitability and accuracy of the codes and information provided. The codes are to be used to facilitate appropriate coding and are not to be construed as recommended guidelines in the establishment of policy, physician services or procedures, physician practice or standards of care.

Reimbursement support is provided by Comprehensive Reimbursement Solutions® (CRS). Please contact Bob Thompson at: 763.400.0987 or Bob.Thompson@CompReimSol.com.

Traumeel/Zeel injection solution

Traumeel injection solution, unlike NSAIDs and corticosteroids, is thought to enter the inflammation cascade well before the prostaglandin synthesis begins, thus modulating the inflammation as well as the pain associated with arthritis and other relevant conditions. The protective action of the prostaglandin synthesis remains intact and the healing and repair in joints continues.

Zeel injection solution's multi-targeted mechanism of action is not fully understood. It is thought that it addresses chronic inflammation, prevention of vascularization of the cartilage and endochondrium, remodeling and protection of cartilage, and alteration to cartilage mechanics. It has an excellent safety profile with very few reported adverse effects, few contraindications and no known drug interactions which makes it suitable for acute and longer-term treatment. It can be safely combined with other treatments but is effective as a mono-therapy as well.

Traumeel and Zeel injection solutions in combination are indicated for the treatment of inflammatory and degenerative conditions of the musculoskeletal system, such as arthrosis/osteoarthritis and/or rheumatic joint diseases, and for the relief of symptoms including pain, swelling, and joint stiffness.

The Traumeel/Zeel injection solution is comprised of a fixed formulation of ingredients. The composition of the Traumeel portion, including dilution, quantity and excipients, is shown below (per 2.2 ml ampule).

Ingredient Name	Potency	Quantity	Final Dilution
Aconitum napellus	2X	1.32 µl	5.22X
Arnica montana, radix	2X	2.20 µl	5.00X
Bellis perennis	2X	1.10 µl	5.30X
Belladonna	2X	2.20 µl	5.00X
Calendula officinalis	2X	2.20 µl	5.00X
Chamomilla	3X	2.20 µl	6.00X
Echinacea	2X	0.55 µl	5.60X
Echinacea purpurea	2X	0.55 µl	5.60X
Hamamelis virginiana	1X	0.22 µl	5.00X
Hepar sulphuris calcareum	6X	2.20 µl	9.00X
Hypericum perforatum	2X	0.66 µl	5.52X
Mercurius solubilis	6X	1.10 µl	9.30X
Millefolium	3X	2.20 µl	6.00X
Symphytum officinale	6X	2.20 µl	9.00X
Inactive Ingredients	Water for injection, Sodium chloride		

The composition of the Zeel portion, including dilution, quantity and excipients, is shown below (per 2.0 ml ampule).

Ingredient Name	Potency	Quantity	Final Dilution
a-Lipoicum acidum	8X	2.0 µl	10.99X
Arnica montana, radix	4X	200.0 µl	5.00X
Cartilago suis	6X	2.0 µl	9.00X
Coenzyme A	8X	2.0 µl	10.99X
Dulcamara	3X	10.0 µl	5.30X
Embryo totalis suis	6X	2.0 µl	9.00X
Funiculus umbilicalis suis	6X	2.0.µl	9.00X
Nadidum	8X	2.0 µl	10.99X
Natrum oxalaceticum	8X	2.0 µl	10.99X
Placenta suis	6X	2.0 µl	9.00X
Rhus toxicodendron	2X	10.0 µl	4.30X
Sanguinaria Canadensis	4X	3.0 µl	6.82X
Sulphur	6X	3.6 µl	8.74X
Symphytum officinale	6X	10.0 µl	8.30X
Inactive Ingredients	Water for injection, Sodium chloride		

Approved homeopathic drugs are those with monographs listed in the Homeopathic Pharmacopoeia of the United States (HPUS). The ingredients for Traumeel Injection Solution have all been listed in the HPUS since 1991 and the ingredients for Zeel Injection Solution since 2014. This type of approval is recognized by the Centers for Medicare and Medicaid Services for reimbursement purposes.

Clinical trial results

In a multi-center, double-blind, randomized, controlled trial, 232 patients with moderate-to-severe chronic knee OA were randomized to three weekly IA injections of either 2.2 mL Traumeel plus 2.0 mL Zeel or saline. The primary efficacy variable was change in knee pain from baseline to end-of-study (week 17) as measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) OA pain subscale. Secondary measures included total WOMAC and subscale scores for stiffness and physical function, change in pain following a 50-foot walk, as well as patient and physician global assessments.

By day 15, patients experienced significant reductions in pain, and secondary endpoints were directionally consistent. By week 17, changes in the WOMAC pain subscale score favored injection over placebo by a p-value of <0.05. The percent of subjects achieving a decrease in the WOMAC pain subscale score of > 32.6 mm from baseline also reached a p-value of <0.05 in favor of injection, as did mean changes from baseline in 50 foot walk pain.

Of note, the study does not report any related serious adverse events. Adverse events were generally mild and reported as unrelated to treatment.

The cost of the Traumeel/Zeel injection solution is similar to steroids, both being far less viscosupplementation.

Coding and payment

Because Traumeel/Zeel injection solution represents a new technology, payers may still be working on the appropriate coding. Some possible coding scenarios are listed below.

Diagnosis coding

ICD-9-CM diagnosis codes are used to describe why a procedure is being performed. The Traumeel/Zeel injection solution is indicated for the treatment of inflammatory and degenerative conditions of the musculoskeletal system, such as arthrosis/osteoarthritis and/or rheumatic joint diseases, and for the relief of symptoms including pain, swelling, and joint stiffness. When used for the knee, some applicable ICD-9-CM diagnosis codes might be:

Diagnosis Code	Code Description
715.16	Osteoarthrosis, localized, primary, lower leg
715.26	Osteoarthrosis, localized, secondary, lower leg
715.36	Osteoarthrosis, localized, not specified whether primary or secondary, lower leg
715.86	Osteoarthrosis involving or with mention of more than one site but not specified as generalized, lower leg
715.96	Osteoarthrosis, unspecified whether generalized or localized, lower leg
719.06	Effusion of joint, lower leg
719.46	Pain in joint, lower leg
719.56	Stiffness of joint, not elsewhere classified, lower leg

Physician procedure coding

When the solution is injected into the knee in the physician's office or in the hospital outpatient setting, the injection procedure has existing CPT® codes.[1] Two codes are available depending on whether ultrasound guidance was used.

CPT Code	Code Description	CY2015 Medicare National Average Payment*	
		Office Procedure	Hospital Outpatient Procedure
20610	Arthrodesis, aspiration, and/or injection, major joint or bursa (eg, shoulder, hip, knee joint, subacromial bursa), without ultrasound guidance	$61	$47
20611	Arthrodesis, aspiration, and/or injection, major joint or bursa (eg, shoulder, hip, knee joint, subacromial bursa), with ultrasound guidance, with permanent recording and reporting	$94	$64

*Subject to geographic variation

Note that code 20611 requires a permanent recording of the ultrasound. For that reason, the use of a handheld ultrasound device does not qualify.

Hospital outpatient coding

For hospital outpatient services, hospitals report the same CPT codes as physicians on their claims. For Medicare payment, the CPT codes are then grouped into Ambulatory Payment Classification (APC) categories, based on their clinical and resource similarities. Medicare uses median hospital costs (operating plus capital) for clinically similar procedures to determine the APC assignment. Each APC has a set payment amount.

Both 20610 and 20611 are assigned to the same APC. The 2015 hospital outpatient APC payment for the Traumeel/Zeel injection is:

[1] CPT Copyright 2014 American Medical Association (AMA). All rights reserved. CPT is a registered trademark of the American Medical Association. No fee schedules, basic units, relative values, or related listings are included in CPT. The AMA assumes no liability for the data contained herein. Applicable FARS/DFARS restrictions apply to government use.

APC	Code Description	CY2015 Medicare National Average Payment*
0204	Level I Nerve Injections	$211

*Subject to geographic variation

The payment includes the cost of the drug. If the injection is the highest-paying procedure or the only procedure performed, payment is made at 100%. If the injection is performed along with another procedure that pays more, it is paid at 50% of the above rate due to the multiple-procedures rule. The multiple-procedures rule factors in the economies of performing multiple procedures, on the same patient, for example, excluding the cost of prepping the patient for injection who is already prepped from another procedure.

Drug coding, coding clarification

Drug codes, called J-codes, are permanent codes used to report injectable drugs that ordinarily cannot be self-administered. There are currently no existing J-codes for homeopathic injection solutions. When an existing code is unavailable, an unlisted J-code, with no specified price, must be used. An unlisted J-code that *may* be suitable for Traumeel/Zeel injection solution is:

Drug Code	Code Description	CY2015 Payment
J3490	Unclassified drugs	Carrier priced

However, the use of code J3490 is not specifically recommended for homeopathic drugs by the Medicare Workgroup that creates J codes. Consequently, each third party payer, Medicare or private, must be asked for instructions on how to code and bill Traumeel/Zeel injection solution, prior to its use.

To request clarification regarding the use of code J3490 for Traumeel/Zeel injection solution, please review the template letter in Appendix A. The purpose of the letter is to provide all the information necessary for the payer, Medicare or private, to make a decision regarding the use of the code. Being a template, it will need to be modified to fit your actual situation and sent to the patient's payer. This is different from a prior authorization because the focus is on a coding clarification rather than coverage. The process will need to be repeated for each payer until all clarifications are obtained.

Billing instructions

If a payer allows the use of a listed J-code for the Traumeel/Zeel injection solution, the billing is performed similarly to injectable steroids or viscosupplements. If an unlisted J-code is needed, billing is performed differently.

Unlisted codes require additional paperwork on the part of the physician and manual review by the payer. Because unlisted codes have no set payment, the physician must provide additional information, usually by attaching the invoice. Since claims are submitted electronically, an indication is needed stating that supporting documentation will be provided separately. To do this, providers can indicate "See attachment" in Item 19 of the CMS-1500 and submit the supporting documentation on paper, unless otherwise specified by the payer.

In addition to the invoice, a cover letter should be included identifying the claim and stating that having researched the current HCPCs II Manual, there is no specific J-code that adequately describes the drug being used. Therefore, following the instructions provided by their organization in the attached letter from _____ dated __/__/___we have been asked to: for example, submit the unlisted J-code J3490 and provide pricing information.

Self-pay patients

For self-pay patients, no part of the cost of the service is billed to the payer. This includes billing only the injection procedure, which is not separately billable from the drug.

Coverage

Coverage is the decision of whether or not to include a procedure as a benefit under a health insurance plan. Be aware that inquiries regarding coding clarification may cause payers to question coverage. When this happens, please contact CRS before modifying the coverage template letter in Appendix B. Without coverage, no part of the Traumeel/Zeel intra-articular injection is billable.

Appendix A: Template Coding Clarification Letter

Date

Medical Director
Address

Dear Dr. **_____**

My name is **_____** and I'm a licensed **_____** practicing in your catchment area. As a **_____** I often treat patients for chronic pain associated with osteoarthritis of the knee.

I practice conservative medicine proceeding from the less to more invasive/expensive treatments, based on the patient's condition. When treating knee pain through intra-articular injections, I have used steroids and viscosupplementation. However, based on the results of a recent randomized, controlled trial, I would like to add a homeopathic injection to this portion of the continuum of care. The drug, Traumeel/Zeel injection solution, is indicated for the treatment of inflammatory and degenerative conditions of the musculoskeletal system, such as arthrosis/osteoarthritis and/or rheumatic joint diseases, and for the relief of symptoms including pain, swelling, and joint stiffness. It has an excellent safety profile and showed statistically significant results[1]. The cost of the Traumeel/Zeel injection solution is similar to steroids, both being far less expensive than viscosupplementation.

Approved homeopathic drugs are those with monographs listed in the Homeopathic Pharmacopoeia of the United States. The ingredients for Traumeel Injection Solution and Zeel Injection Solution are listed in the HPUS. This type of approval is recognized by the Centers for Medicare and Medicaid Services for reimbursement purposes.

My questions involve correct coding and billing. There is currently not an existing J-code for homeopathic injectable solutions. An unlisted J-code that may be suitable is J3490, unclassified drugs. Is this the appropriate J-code for Traumeel/Zeel or you would like me to use another? If an unlisted code is required, I plan to bill electronically with the text "See attachment" in Item 19. The invoice for the drug would then be sent on paper with a cover letter linking it to the claim. Are these your preferred billing instructions?

Thank you for your consideration. If you have any questions, please call me at **(phone number)** or **(e-mail address)**. If I have not heard from you in two weeks, I will follow-up to discuss my request in further detail along with any questions you have.

Sincerely,

_____, MD

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[1]Lozada, Carlos et al. A Multi-Center Double-Blind, Randomized, Controlled Trial (db-RCT) to Evaluate the Effectiveness and Safety of Co-Administered Traumeel® (Tr14) and Zeel® (Ze14) Intra-articular (IA) Injections Versus IA Placebo in Patients with Moderate-to-Severe Pain Associated with OA of the Knee. Arthritis & Rheumatology 2014; 66, Number 11:S1266

Appendix B: Template Coverage Request Letter

Date

Medical Director
Address

Dear Dr. _____

My name is _____ and I'm a licensed _____ practicing in your catchment area. As a _____ I often treat patients for chronic pain associated with osteoarthritis of the knee. I practice conservative medicine proceeding from the less to more invasive/ expensive treatments, based on the patient's condition.

When treating knee pain through intra-articular injections, I have used steroids and viscosupplementation. However, based on the results of a recent randomized controlled trial, I would like to add a homeopathic injection to this portion of the continuum of care. The drug, Traumeel/Zeel injection solution, is indicated for the treatment of inflammatory and degenerative conditions of the musculoskeletal system, such as arthrosis/osteoarthritis and/or rheumatic joint diseases, and for the relief of symptoms including pain, swelling, and joint stiffness. It has an excellent safety profile and showed statistically significant results. The cost of the Traumeel/Zeel injection solution is similar to steroids, both being far less expensive than viscosupplementation.

Approved homeopathic drugs are those with monographs listed in the Homeopathic Pharmacopoeia of the United States. The ingredients for Traumeel Injection Solution and Zeel Injection Solution are listed in the HPUS. This type of approval is recognized by the Centers for Medicare and Medicaid Services for reimbursement purposes.

My purpose in writing is to request a coverage determination for the use of the Traumeel/Zeel injection solution for chronic pain due to osteoarthritis of the knee. My patient has **(documented current findings)**, and has undergone **(documented treatment history)**. He/she is now a candidate for the Injection solution because **(clinical rationale)**.

I request confirmation that an intra-articular injection of Traumeel/Zeel is covered based on the medical necessity documented for this patient. A copy of the published clinical trial abstract is enclosed.

Thank you for your consideration. If you have any questions, please call me at (phone number) or (e-mail address). If I have not heard from you in two weeks, I will follow-up to discuss my request in further detail along with any questions you have.

Sincerely,

_____, MD

A Multi-Center Double-Blind, Randomized, Controlled Trial (db-RCT) to Evaluate the Effectiveness and Safety of Co-Administered Traumeel® (Tr14) and Zeel® (Ze14) Intra-articular (IA) Injections Versus IA Placebo in Patients with Moderate-to-Severe Pain Associated with OA of the Knee.

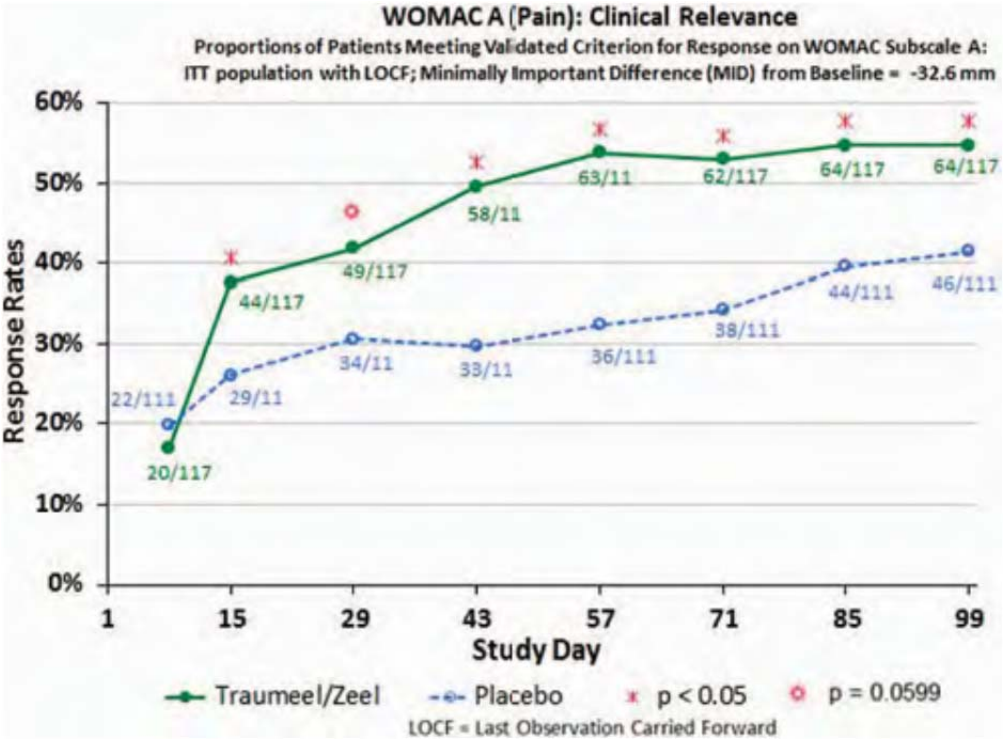
Carlos Lozada1, Eve del Rio2, Donald Reitberg3, Robert Smith3, Charles Kahn4 and Roland W. Moskowitz5. 1University of Miami Miller School of Medicine, Miami, FL, Miami, FL, 2Rio Pharmaceutical Services, LLC, Bridgewater, Afghanistan, 3Rio Pharmaceutical Services, LLC, Bridgewater, NJ, 4South Florida Rheumatology, Hollywood, FL, 5University Hospitals
Case Medical Center, Cleveland, OH.

Background/Purpose: Tr14 & Ze14 is a combination of dilute biological and mineral extracts administered IA for painful knee OA. In response to clinician impressions of positive outcomes, a db-RCT to assess efficacy and safety compared to IA saline was deployed in the US.

Methods: Pts with moderate-to-severe chronic knee OA were randomized to 3 weekly IA injections of either Tr14 & Ze14 or saline by clinical investigators experienced with use of the IA injection route. The primary efficacy variable was change in knee pain from Baseline to End-of-Study (Week 17) as measured by the WOMAC OA Pain Subscale (Section A, 1–5) 100 mm VAS. Secondary measures included Total WOMAC and sub scores for stiffness (B), and physical function (C), change in pain following a 50 ft walk (100 mm VAS), patient and physician global assessments. Clinical relevance was assessed by comparing proportions of patients with reductions from baseline in WOMAC A scores greater than a validated benchmark Minimal Clinically Important Difference (MCID). This was chosen as _32.6 mm (the most conservative value) based on a study of outpatients with knee or hip OA where WOMAC VAS MCIDs ranged from_7.9mm to_32.6mm [see reference 59 Tauback et al., *Ann Rheum Dis.* 2005; 64(1):29–33 in the description of the WOMAC index published by ACR]. Safety was assessed by monitoring of vital signs, physical examinations of the target knee, adverse events and concomitant medications.

Results: 232 patients were randomized and treated (All Tr14 & Ze14, n_119, All Placebo, n_113; Intention-to-Treat (ITT) Tr14 & Ze14, n_117, Placebo, n_ 111). Treatment arms were well balanced across demographic and baseline characteristics. Tr14 & Ze14 did not discriminate for WOMAC A Pain as expected after only 1 of 3 injections on Day 8 (p_0.3715), but subsequently was significantly different (p_0.05) on Days 15, 43, 57, 71, 85 and 99 (primary endpoint day), and approached significance on Day 29 (p_0.0686). Logistic regressions showed the proportion of MCID responders was not significant on Day 8. As this was an expected finding, it served as a no-effect internal-model-validation. Tr14 & Ze14 was significantly different (p_0.05) on all subsequent days except Day 29 (approached significance, p_0.0599, Figure 1). 50' walk pain was similarly discriminating as was the physician global assessment. Total WOMAC and subscores B&C were directionally consistent with WOMAC A. There were no related SAEs. AEs were generally mild and unrelated to treatment. Local knee-related AEs, lab assessments, ECGs and vital signs were unremarkable and similar between

treatments.



Conclusion: Tr14 & Ze14 provided statistically significant and clinically relevant pain relief on days 15 to 99 in comparison to placebo. In this double-blind, randomized, controlled trial, a biological/mineral multi-extract combination was shown to be a safe and effective treatment for pain in moderate-to-severe knee OA.

Disclosure: C. Lozada, Rio Pharmaceutical Services, 5, Heel USA, 5; **E. del Rio**, Biologische Heilmittel Heel GmbH, 5; **D. Reitberg**, Rio Pharmaceutical Services, LLC, 5; **R. Smith**, Rio Pharmaceutical Services, LLC, 5; **C. Kahn**, Biologische Heilmittel Heel GmbH, 5; **R. W. Moskowitz**, Rio Pharmaceutical Services, LLC, 5, Heel USA, 5.

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