Effective, Safe, And Affordable Osteoarthritis (OA) Knee Pain Relief That Keeps You Moving.
Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction to SUPARTZ FX</td>
<td>1</td>
</tr>
<tr>
<td>Ordering Information</td>
<td>2</td>
</tr>
<tr>
<td>Reimbursement Contact Information</td>
<td>3</td>
</tr>
<tr>
<td>Prior Authorization</td>
<td>4</td>
</tr>
<tr>
<td>Medicare and Medicaid Coverage</td>
<td>5</td>
</tr>
<tr>
<td>Coding and Billing</td>
<td>6</td>
</tr>
<tr>
<td>Examples of Completed Claims</td>
<td>7-10</td>
</tr>
<tr>
<td>Denied Claims and Appeals</td>
<td>11</td>
</tr>
<tr>
<td>SUPARTZ FX Prescribing Information</td>
<td>12-15</td>
</tr>
<tr>
<td>References</td>
<td>16</td>
</tr>
</tbody>
</table>
**Introduction**

SUPARTZ FX is the #1 prescribed viscosupplement worldwide.¹ Since the introduction of SUPARTZ FX, more than 300 million injections² have been prescribed globally.

**Indications and Usage**

SUPARTZ FX is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who:

- Have failed to adequately respond to conservative non-pharmacologic therapy, including physical therapy
- Have failed to respond to simple analgesics such as acetaminophen

**Directions for Use³**

SUPARTZ FX is approved for 5 weekly injections, but some patients may benefit from as few as 3 injections given at weekly intervals. These benefits have been noted in a study in which patients receiving 3 injections were followed for 90 days. Flexible dosing means patients only receive the number of shots that fits their needs.

**Sodium Hyaluronate Per Syringe**

25mg/2.5mL sodium hyaluronate per prefilled syringe.

**Contraindications to SUPARTZ FX**

One should not administer SUPARTZ FX to patients with known hypersensitivity or allergy to sodium hyaluronate preparations, and especially avian (bird) products (feathers or eggs). SUPARTZ FX should not be injected in the knees of patients with infections or skin diseases in the area of the injection site. Risks can include general knee pain, warmth and redness or pain at the injection site. Full prescribing information can be found on pages 12-15 of this brochure, at www.SupartzFX.com or by contacting Bioventus Customer Service by calling toll free: 1-800-836-4080.
Ordering Information

It’s easy to order SUPARTZ FX. You can order from the Bioventus sales representative or contact Bioventus Customer Service by calling toll-free: 1-800-396-4325.

SUPARTZ FX
Product Order Number: 7156-4444
Product NHRIC Number*: 89130-4444-1
Reimbursement J Code: J7321

Description: 1 pre-filled, plastic syringe with Luer-Lok™ needle attachment

Other Information: Shelf life of 42 months. Each syringe contains 1% sodium hyaluronate (25mg). In addition, SUPARTZ FX has 25% more active ingredient per syringe than other US 1% sodium hyaluronate products.

For more product and patient safety information, please visit SupartzFX.com.

SUPARTZ FX is approved for 5 injections. (Physician is responsible for confirming applicable insurance coverage requirements are met.) Some patients may benefit from as few as 3 injections.

*SUPARTZ FX is regulated as a medical device and is regulated using the NHRIC number. The NHRIC number serves a similar purpose as the NDC number used for pharmaceutical products. Luer-lok is a trademark of Medline Industries, Inc.
Reimbursement Contact Information

The cost of treatment with SUPARTZ FX is covered by Medicare, most Medicaid state agencies and private insurance companies. If you have questions about local coverage of the costs of treatment with SUPARTZ FX please call the following numbers for assistance with insurance verification:

BioLinx Reimbursement Hotline: 855-870-0920
BioLinx Reimbursement Verification Fax Line: 855-389-2239

Hotline Hours:
- 8:00 AM - 8:00 PM Eastern
- 7:00 AM - 7:00 PM Central
- 6:00 AM - 6:00 PM Mountain
- 5:00 AM - 5:00 PM Pacific

Services of the BioLinx Reimbursement Hotline

<table>
<thead>
<tr>
<th></th>
<th>Specialty Pharmacy</th>
<th>Buy &amp; Bill</th>
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</thead>
<tbody>
<tr>
<td><strong>PATIENT INTAKE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choice of online, fax, or phone patient intake</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Benefit investigation</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Coding support</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Integrated intake and HIPAA release form</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Satisfaction surveys</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><strong>SPECIALTY PHARMACY (SP) SUPPORT AND WORKFLOW MANAGEMENT</strong></td>
<td></td>
<td></td>
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<tr>
<td>Online office dashboard</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Automatic SP referral</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Automatic follow-up on &quot;stalled&quot; orders</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Acts as your liaison with specialty pharmacies</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Continuous patient status updates and customizable alerts</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Appeals support</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td><strong>OFFICE EFFICIENCY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handles patient follow-up for missing information and signatures</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Eliminates ordering/stocking/collections for SUPARTZ</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Eliminates SUPARTZ billing and collections risk</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Lightens the load of dealing with insurers</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Frees staff time for more valuable collections activities</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Input through customer satisfaction surveys</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

* Will inquire about additional forms; physician is responsible for submission of forms and follow-up

NHRIC: 89130-4444-1

Because SUPARTZ FX is regulated as a device, it is classified under an NHRIC number rather than an NDC number. An NHRIC number serves a similar purpose for devices as the NDC code serves for pharmaceuticals.

Note: Some health plans such as Medicaid will require that the NHRIC number be included on the claim form.

Prior Authorization

Private Payers

This step is recommended for privately insured patients. The patient should be specifically preauthorized for their SUPARTZ FX (sodium hyaluronate) 25mg injection series (HCPCS code J7321). The BioLinx reimbursement hotline is available for insurance verification and prior authorization support. If you choose not to use BioLinx, your staff will need to inquire whether the payer requires prior authorization and/or use of a specific Specialty Pharmacy. Payers may not volunteer Specialty Pharmacy requirements, so you must ask! When a payer requires that SUPARTZ FX be ordered through a Specialty Pharmacy, please contact that entity to obtain the product. If the payer states that no preauthorization is necessary, verify that sodium hyaluronate injections are a covered benefit under the patient’s plan.

Each private payer varies in administration of benefits, reimbursement and policy coverage. Some private payers may follow Medicare’s coverage policies, while others may have less restrictive criteria. Refer to specific payer guidelines and provider fee schedules for more information.

Document Everything

In speaking with a payer, note the date and time and ask the payer representative for his/her name along with a call reference number. This information will help the payer trace your inquiry in its archives.

Is Retreatment Covered?

Even though most payers do cover more than one series of SUPARTZ FX injections, some payers may not cover it. In these instances, prior authorization is critical. When the payer does cover retreatment, be certain that the patient’s progress notes show a benefit from the first series of injections. Refer to the payer policy/guidelines for more details. Inform your sales representative if you find a payer who does not cover retreatment.
Medicare and Medicaid Coverage

Medicare

The physician's office must buy and bill SUPARTZ FX for Medicare fee-for-service patients. Medicare fee-for-service does not require prior authorization; however, Medicare requires documented improvement from the first series for patients to receive a second series of treatment. Medicare contractors referred to as Medicare Administrative Contractors (MACs) generally develop Local Coverage Determinations (LCDs) for specific codes or services. LCDs are specific to a MAC’s jurisdiction. In other words, specific coverage criteria for a product and coding requirements may vary by Medicare contractor. Refer to the appropriate Medicare MAC policy/guidelines for more details on initial treatment and retreatment criteria.

Note: The process for Medicare Advantage plans varies by payer. We recommend utilizing BioLinx for assistance or verify benefits and plan requirements before providing SUPARTZ FX.

Medicare Reimbursement

The reimbursement rate for SUPARTZ FX administered in a physician’s office is based on the CMS formula of adding 4.3% to the Average Sales Price issued quarterly by the CMS. In addition, professional services for administering an intraarticular injection (CPT code 20610) that are associated with the drug/product code are reimbursed based on the physician fee schedule provided by the specific Medicare Administrative Contractor (MAC).

Note: After a deductible has been met, Medicare pays 80% of the allowed amount of the drug/product and service. The Medicare beneficiary is responsible for 20% of the allowed amount. Secondary coverage can be used to offset the beneficiary’s remaining financial responsibility.

Medicaid

The reimbursement rate for the drug/product and services administered in a physician’s office for Medicaid fee-for-service programs varies by state. Please check the local Medicaid fee schedule and guidelines for coverage criteria and contact the area Medicaid representative if needed.

Some Medicaid managed care plans may have restrictions such as requiring a prior authorization, and coverage criteria can vary by plan. BioLinx is available for insurance verification and prior authorization support. BioLinx does not complete the prior authorization submission but will provide guidance on what needs to be done as a next step.
Coding and Billing

Include proper ICD-9-CM diagnosis codes for SUPARTZ FX. Each payer may have its own specific coding requirements for joint fluid therapy. For example, some managed care plans require ICD-9 code 719.46, pain in joint, lower leg in your initial patient evaluation. Some payers may require additional documentation as well. Contact your provider relations representative or payer website to confirm the requirements.

Example diagnosis codes (ICD-9)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>715.16</td>
<td>Osteoarthrosis, localized, primary, involving lower leg</td>
</tr>
<tr>
<td>715.26</td>
<td>Osteoarthrosis, localized, secondary, involving lower leg</td>
</tr>
<tr>
<td>715.36</td>
<td>Osteoarthrosis, localized, not specified whether primary or secondary, involving lower leg</td>
</tr>
<tr>
<td>715.96</td>
<td>Osteoarthrosis, not specified whether generalized or localized, involving lower leg</td>
</tr>
</tbody>
</table>

Example diagnosis codes (ICD-10)

ICD-10 codes are effective beginning October 1, 2015

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M17.10</td>
<td>Unilateral primary osteoarthritis, unspecified knee</td>
</tr>
<tr>
<td>M17.5</td>
<td>Other unilateral secondary osteoarthritis of the knee</td>
</tr>
<tr>
<td>M17.9</td>
<td>Osteoarthritis of the knee, unspecified</td>
</tr>
</tbody>
</table>

Always check with the specific managed care plan to confirm that you are using the correct ICD-10 code.
SUPARTZ FX injections are billed using a HCPCS code for SUPARTZ FX and a CPT code for administration of the injections.

**Example billing codes and modifiers**

<table>
<thead>
<tr>
<th>(AMA CPT) 99213 Established patient, expanded problem focused examination</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>24 Modifier</strong> indicates an unrelated evaluation and management (E/M) service performed by the same physician during a postoperative period.</td>
</tr>
<tr>
<td><strong>25 Modifier</strong> indicates an unrelated E/M service performed by the same physician on the same day as the minor operation.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(AMA CPT) 20610 Arthrocentesis, aspiration and/or injection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LT Modifier</strong> is an anatomic modifier indicating the procedure was performed on the left knee.</td>
</tr>
<tr>
<td><strong>RT Modifier</strong> is an anatomic modifier indicating the procedure was performed on the right knee.</td>
</tr>
<tr>
<td><strong>50 Modifier</strong> is an anatomic modifier indicating the procedure was performed on both knees.</td>
</tr>
<tr>
<td><strong>59 Modifier</strong> indicates that a procedure was distinct or independent of another service performed on the same day. This is used to indicate a second injection in a different anatomical site.</td>
</tr>
<tr>
<td><strong>79 Modifier</strong> indicates that an unrelated procedure or service was provided by the same physician during the postoperative period. Should be used if SUPARTZ FX is given during a global period for an unrelated surgical procedure.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(HCPCS) J7321 SUPARTZ FX (sodium hyaluronate) per 25mg dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LT Modifier</strong> is an anatomic modifier indicating the material was injected into the left knee.</td>
</tr>
<tr>
<td><strong>RT Modifier</strong> is an anatomic modifier indicating the material was injected into the right knee.</td>
</tr>
</tbody>
</table>
Examples of Completed Claims

Example of claim submission for submitting the first of five unilateral injections

A. Enter SUPARTZ FX (sodium hyaluronate) 25mg per dose
B. ICD-9 Diagnosis Code or ICD-10 Diagnosis Code (starting October 1, 2015)
C. Established patient, expanded problem focused examination
D. Modifier 25 indicates E/M on same day*
E. X-ray code
F. Arthrocentesis, aspiration and/or injection into a knee, without ultrasound guidance
G. J7321 SUPARTZ FX (sodium hyaluronate) 25mg dose
H. Anatomic modifier RT or LT is required

*An office visit code can only be billed when the physician also provided significant, separately identifiable (E/M) services beyond the usual preoperative and postoperative services associated with the procedure. In such a case, be certain to include the modifier 25.
Example of claim submission for the second through fifth unilateral injections

| A. Enter SUPARTZ FX (sodium hyaluronate) 25mg dose |
| B. Enter ICD-9 Diagnosis Code or ICD-10 Diagnosis Code (starting October 1, 2015) |
| C. Arthrocentesis, aspiration and/or injection into a knee, without ultrasound guidance |
| D. J7321 SUPARTZ FX (sodium hyaluronate) 25mg dose* |
| E. Anatomic modifier RT or LT is required |

*An office visit code can only be billed when the physician also provided significant, separately identifiable (E/M) services beyond the usual preoperative and postoperative services associated with the procedure. In such a case, be certain to include the modifier 25.
Example of claim submission for the first of five bilateral injections

| A. Enter SUPARTZ FX (sodium hyaluronate) 25mg dose |
| B. Enter ICD-9 Diagnosis Code or ICD-10 Diagnosis Code (starting October 1, 2015) |
| C. Established patient, expanded problem focused examination |
| D. Modifier 25 indicates E/M on same day* |
| E. X-ray code |
| F. Arthrocentesis, aspiration and/or injection into knees, without ultrasound guidance |
| G. Enter the modifier 50 |
| H. J7321 SUPARTZ FX (Sodium Hyaluronate) 25mg |
| I. Each code must be modified with an LT or RT |

*An office visit code can only be billed when the physician also provided significant, separately identifiable (E/M) services beyond the usual preoperative and postoperative services associated with the procedure. In such a case, be certain to include the modifier 25. Some carriers require entering the single modifier 50 for the bilateral procedure. Others use individual anatomic modifiers for clarity. Contact the carrier for clarification.
Example of claim submission for the second through fifth bilateral injections

| A. | Enter SUPARTZ FX (sodium hyaluronate) 25mg |
| B. | Enter ICD-9 Diagnosis Code or ICD-10 Diagnosis Code (starting October 1, 2015) |
| C. | Arthrocentesis, aspiration and/or injection into knees, without ultrasound guidance |
| D. | J7321 SUPARTZ FX (sodium hyaluronate) 25mg |
| E. | Enter the modifier 50 |
| F. | Each code must be modified with an LT or RT |
Denied Claims and Appeals

Handling Denials

• Compare the rejected HCFA (CMS) 1500 form to the most appropriate example in this reimbursement guide. Check that all necessary codes and/or modifiers are included and accurate.

• Review the explanation of benefits (EOB) sent by the payer to identify rationale for denial.
  - Claims often are denied as a result of simple errors, such as missing the number of units, member identification numbers, patient names, or coding.

• Resubmit the corrected claim form after changing any errors.

When should you submit a Letter of Medical Necessity (LOMN)?

If the denial did not result from claim errors, a LOMN and/or supporting documentation is recommended to resubmit with the claim. Refer to specific payer guidelines for coverage criteria and documentation requirements.

Appealing Denials

If the payer denies the claim again, the provider or patient has the option to file a grievance or an appeal. Refer to specific plan criteria for filing grievances and appeals.
CAUTION
Federal law restricts this device to sale by or on the order of a physician (or a properly licensed practitioner).

DESCRIPTION
SUPARTZ FX is a sterile, viscoelastic non-
pyrogenic solution of purified, high molecular
weight (620,000-1,170,000 daltons) sodium
hyaluronate (hyaluronan) having a pH of 6.8-7.8.
Each one mL of SUPARTZ FX contains 10 mg
of sodium hyaluronate hydrate and 13.4 mg
of sodium phosphate dodecahydrate.

PRECAUTIONS
• Do not administer to patients with known
hypersensitivity (allergy) to sodium hyaluronate.

CONTRAINdications
• Do not inject this product in the knees of patients
with infections or skin diseases in the area of the
injection site.

WARNINGS
• Do not concomitantly use disinfectants containing
Quaternary ammonium salts for skin preparation
because sodium hyaluronate can precipitate in
their presence.

PRECAUTIONS
General
• The effectiveness of a single treatment cycle
of less than 3 injections has not been established.
• Strict aseptic administration technique must be
followed.
• Remove joint effusion, if present, before injecting
SUPARTZ FX.
• The safety and effectiveness of the use of
SUPARTZ FX in joints other than the knee have
not been established.
• The safety and effectiveness of the use of
SUPARTZ FX concomitantly with other intra-
articular injectables have not been established.
• Use caution when injecting SUPARTZ FX into
patients who are allergic to avian proteins,
feathers and egg products.
• STEREIL CONTENTS. The prefilled syringe is
intended for single use. The contents of the
syringe must be used immediately once the
container has been opened. Discard any unused
SUPARTZ FX.
• Do not use SUPARTZ FX if the package is
opened or damaged. Store in the original
packaging below 77°F (25°C). DO NOT FREEZE.
Do not use after expiration date indicated on
package. Shelf life is 42 months.

INFORMATION FOR PATIENTS
• Provide patients with a copy of the Patients’
Information prior to use.
• Transient pain and/or swelling of the injected
joint may occur after intra-articular injection of
SUPARTZ FX.
• As with any invasive joint procedure, it is
recommended that the patient avoid any strenuous
activities or prolonged (i.e., more than 1 hour)
weight-bearing activities such as jogging or
tennis within the 48 hours that follow the intra-
articular injection.

• The effectiveness of repeat treatment cycles of
SUPARTZ FX has not been established.

Use in Specific Populations
• Pregnancy: The safety and effectiveness of
SUPARTZ FX have not been established in
pregnant women.
• Nursing Mothers: It is not known if SUPARTZ FX
is excreted in human milk. Excretion has been
seen in rat milk. The safety and effectiveness of
SUPARTZ FX have not been established in
lactating women.
• Pediatrics: The safety and effectiveness of
SUPARTZ FX have not been demonstrated in
children.

ADVERSE EVENTS
The evaluable safety population included all
patients receiving at least one injection (532
SUPARTZ FX 5; 87 SUPARTZ FX 3; 53 control
injection) in five well controlled clinical trials.
The most common adverse events occurring in SUPARTZ FX-treated patients were:
• Joint pain with no evidence of inflammation, arthropathy/
arthrosis/arthritis, defined as joint pain with evidence of
inflammation, back pain, pain (non-specific),
• Injection site reaction, headache, and injection site
pain (See Table 1). There were no statistically
significant differences in the occurrence rates of
these adverse events between treatment groups.
Five (5) allergic reactions were reported in the
SUPARTZ FX group. All five events were
classified as mild to moderate. These were:
• hayfever (2), reaction on face and neck, cutaneous
reactions, and asthma (1), and an undefined mild allergy
reaction. No anaphylactic reactions were observed in
any study patients. Other adverse events occurring in
4% or less but not less than 1% of the SUPARTZ FX
tried patients included upper respiratory tract
infection, influenza-like symptoms, nausea, sinusitis,
urinary tract infection, bronchitis, abdominal pain,
diarrhea, infected injury, leg pain, discomfort in legs,
dyspepsia, dizziness, rhinitis, and fall.
SUPARTZ FX (ARTZ) has been in use in Japan
since 1987. A prospective post-market surveillance
study conducted from 1987 to 1993 evaluated
safety on 7404 knees treated from a total of 675
medical institutions. A subset of 7155 knees was
treated with 3 or more consecutive injections. There
were 58 cases of adverse reactions in 37 knees (3.4%)
injected (UK study) in five well controlled clinical trials. The
difference in reduction in total Lequesne scores
between the SUPARTZ FX treated group and the
control group is 0.68, which is statistically significant
anesthetic may be recommended prior to injection.
The most common adverse reactions included:
Injection site reactions (pain / swelling / effusion /
redness / warmth). Rare cases of severe
reactions have been reported.
• Other adverse reactions include: Itching; swelling
of the face, eyelids, mouth and/or extremities;
• Rash; hives; redness in face; nausea; vomiting
and fever. Anaphylactic/anaphylactoid reactions
accompanied by transient hypotension (sudden
drop in blood pressure), have been rarely reported,
all of which resolved either spontaneously or after
conservative treatment.

CLINICAL STUDIES
Study Design
The safety and effectiveness of SUPARTZ FX was
based on an integrated analysis of five randomized,
multicenter, blinded, "placebo controlled" clinical
trials. Entry criteria are described for all studies
(See Table 2). The treatment regimen consisted of
5 weekly injections in all studies. All patients in
these studies (including those injected with the
coposite received arthritis treatment). Prior to an
injection to an injection of SUPARTZ FX or vehicle
(phosphate buffered saline) or, in the German
study only, a dilute (1%) form of the SUPARTZ FX
formulation. The French study included an
additional treatment arm: 3 SUPARTZ FX injections
followed by 2 injection (of the control arm). Table 3
describes the study design and the treatment
and follow-up schedules.

Measures of Effectiveness
Table 3 provides details of the primary and
secondary effectiveness parameters used in each
study. The Lequesne Index, although a primary
measure of effectiveness in only three studies
(France, Germany, and Sweden) was common to
all five studies. It was used for the integrated
analysis of effectiveness across all five studies.
The primary measure used in the other two studies
was the WOMAC Index in Australia1, and VAS pain
ratings in the United Kingdom.
Results
Patient Population and Demographics
The demographics of study participants were
comparable across treatment groups with respect
to age, sex, mean body mass index, and baseline
scores, with the exception of gender in the
German study (see Table 4).
Individual Study Results
Medication use results are presented in Table 5.
The results for the Australian study for the protocol-
specific primary analysis are presented in Table 6A.
The results for all studies of analysis of the
Lequesne score performed with analysis of
covariance (ANCOVA) of mean reduction from
baseline over all visits at or following the 5 week
visit are presented in table 6B. Other analyses are
as follows: The results for the German study of the
parameter of consumption performed as a non-
parametric ranking procedure (stratified Wilcoxon
rank-sum test), over weeks 1-5, are SUPARTZ FX
= 0.85 and Control = 0.89 (p > 0.05). The results
for the Swedish and UK studies for the protocol-
specific primary analysis = VAS ratings as analysis
of covariance (ANOVA) at weeks 1-5, 1 (and 3
describes the study design and the treatment
and follow-up schedules.)

Integrated Analysis
An integrated longitudinal analysis was conducted
to examine results across all five studies. See
Table 6C. This method of analyzing data with
repeated measures takes into account the
correlation structure of the repeated measurements
and examines the effects of treatment over time.
The integrated longitudinal analysis showed a
reduction in the total Lequesne score of 2.68 in
the SUPARTZ FX treatment groups compared to a
Reduction in the total Lequesne score of 2.68 in
the control groups (p=0.0026). The 95% confidence
interval for the difference of the reduction in total

Lequesne score between SUPARTZ FX and control is (0.56, 0.79).

Summary of Results
The difference in reduction in total Lequesne scores between SUPARTZ FX treated group and the control group is 0.68, which is statistically significant in the integrated analysis (p=0.0026). Additionally, the Australian study shows a significant difference between SUPARTZ FX and control in both the WOMAC pain (p=0.045) and stiffness (p=0.024) scores, and Lequesne total scores (p=0.0114).

DETAILED DEVICE DESCRIPTION
Each 2.5 mL prefilled syringe of SUPARTZ FX contains:
- Sodium Hyaluronate (hyaluronic) 25.0 mg
- Sodium Chloride 21.25 mg
- Dibasic Sodium Phosphate Dodecahydrate 1.343 mg
- Sodium Dihydrogen Phosphate Dihydrate 0.04 mg
- Water for Injection q.s.

HOW SUPPLIED
SUPARTZ FX is supplied as a sterile, non-pyrogenic solution in 2.5 mL prefilled syringe.

DIRECTIONS FOR USE
SUPARTZ FX is administered by intra-articular injection once a week (1 week apart) for a total of 5 injections. Some patients may experience benefit with 3 injections given at weekly intervals. This has been noted in a study in which patients treated with three injections were followed for 90 days1. Injection of subcutaneous lidocaine or similar local anesthetic may be recommended prior to injection of SUPARTZ FX.

Warning: Do not concomitantly use disinfectants containing quaternary ammonium salts for skin preparation because sodium hyaluronate can precipitate in their presence.

Precaution: Do not use SUPARTZ FX if the package is opened or damaged. Store in the original packaging below 77°F (25°C). DO NOT FREEZE. Do not use after expiration date indicated on package. Shelf life is 42 months.

Precaution: Strict aseptic administration technique must be followed.

Precaution: Remove joint effusion, if present, before injection of SUPARTZ FX.

Take care to remove the tip cap of the syringe and needle aseptically. Inject SUPARTZ FX into the joint through a 22-23 gauge needle.

Inject the full 2.5 mL in one knee only. If treatment is bilateral, a separate syringe should be used for each knee.

Precaution: The prefilled syringe is intended for single use. The content of the syringe must be used immediately once the container has been opened. Discard any unused SUPARTZ FX.

Table 1: Adverse Events Occurring in > 4% of SUPARTZ FX-treated Patients

<table>
<thead>
<tr>
<th>Integrated Safety Database</th>
<th>SUPARTZ FX (n=619)</th>
<th>Control (n=537)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthralgia</td>
<td>110 (17.8%)</td>
<td>95 (17.7%)</td>
</tr>
<tr>
<td>Arthropathy/Arthritis</td>
<td>68 (11.0%)</td>
<td>57 (10.6%)</td>
</tr>
<tr>
<td>Back Pain</td>
<td>40 (6.5%)</td>
<td>26 (4.8%)</td>
</tr>
<tr>
<td>Pain (non-specific)</td>
<td>37 (6.0%)</td>
<td>26 (4.8%)</td>
</tr>
<tr>
<td>Injection Site Reaction*</td>
<td>35 (5.7%)</td>
<td>18 (3.4%)</td>
</tr>
<tr>
<td>Headache</td>
<td>27 (4.4%)</td>
<td>23 (4.3%)</td>
</tr>
<tr>
<td>Injection Site Pain</td>
<td>26 (4.2%)</td>
<td>22 (4.1%)</td>
</tr>
</tbody>
</table>

*Includes application/injection site reaction, injection site inflammation, and purpura injection site.

Table 1A: Adverse Events Occurring in 3-Injection SUPARTZ FX-treated Patients

<table>
<thead>
<tr>
<th>Adverse Event Type</th>
<th>Number (%) of Patients Receiving Control Injections (N=80)</th>
<th>Number (%) of Patients Receiving SUPARTZ FX-3 (N=87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthralgia</td>
<td>12(15.0%)</td>
<td>11(12.6%)</td>
</tr>
<tr>
<td>Arthropathy, Arthritis or Arthritis</td>
<td>3(3.8%)</td>
<td>1(1.1%)</td>
</tr>
<tr>
<td>Back Pain</td>
<td>10(12.5%)</td>
<td>10(11.5%)</td>
</tr>
<tr>
<td>Pain</td>
<td>16(20.0%)</td>
<td>16(18.4%)</td>
</tr>
<tr>
<td>Injection Site Reaction*</td>
<td>0(0.0%)</td>
<td>1(1.1%)</td>
</tr>
<tr>
<td>Headache</td>
<td>4(5.0%)</td>
<td>3(3.4%)</td>
</tr>
<tr>
<td>Injection Site Pain</td>
<td>4(5.0%)</td>
<td>3(3.4%)</td>
</tr>
</tbody>
</table>

*Includes application/injection site reaction, injection site inflammation, and purpura injection site.

Table 2: Entry Criteria

<table>
<thead>
<tr>
<th>Study</th>
<th>Baseline pain level</th>
<th>Duration of pain prior to study entry</th>
<th>Unilateral versus bilateral</th>
<th>Radiologic criteria</th>
<th>Effusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>Not specified</td>
<td>≥ 3 months</td>
<td>Unilateral or predominantly unilateral**</td>
<td>Evidence of one or more of the following features in an x-ray taken during the previous 6 months: femorotibial osteophytes, osteosclerosis of the femoral or tibial endplates, or joint space narrowing</td>
<td>&gt; 50 mL</td>
</tr>
<tr>
<td>France</td>
<td>Lequesne total score = 4 - 12</td>
<td>≥ 3 months</td>
<td>Unilateral or predominantly unilateral**</td>
<td>Narrowing of femorotibial space &gt; 20% and &lt; 90% in at least 1 of the appropriate angles and/or OA and/or osteocondensation, and/or geode(s)</td>
<td>Severe (tight, distending effusion)</td>
</tr>
<tr>
<td>Germany</td>
<td>Moderate to medium*</td>
<td>Not specified</td>
<td>Unilateral or bilateral</td>
<td>Osteophytes</td>
<td>&gt; 100 mL</td>
</tr>
<tr>
<td>Sweden</td>
<td>Not specified</td>
<td>Not specified</td>
<td>Unilateral</td>
<td>Knee flexion angle of 10 - 15°; 50 - 100% obliteration (&gt; 400 mm) of the joint space (standing radiographs) without any bone erosion</td>
<td>Not specified</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Moderate*</td>
<td>&gt; 3 months</td>
<td>Unilateral or predominantly unilateral**</td>
<td>Femorotibial osteophytes</td>
<td>&gt; 50 mL</td>
</tr>
</tbody>
</table>

* Definition not specified in protocol.
** Predominantly unilateral means that even in the case of bilateral disease it is possible for the patient to identify one predominant knee that is affected, as reported by the investigator.

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Durham, NC 27703 USA
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Reference
CAUTION

Federal law restricts this device to sale by or on the order of a physician (or a properly licensed practitioner).

DESCRIPTION

SUPARTZ FX is a sterile, viscoelastic non-
pyrogenic solution of purified, high molecular weight (620,000-1,170,000 daltons) sodium hyaluronate (hyaluronan) having a pH of 6.8-7.8. Each ounce (30 mL) of SUPARTZ FX contains 10 mg of sodium hyaluronate (hyaluronan) dissolved in a physiological saline (1.0% solution). The sodium hyaluronate (hyaluronan) is extracted from chicken combs. Sodium hyaluronate (hyaluronan) is a polysaccharide containing repeating disaccharide units of glucuronic acid and N-acetylglucosamine.

INDICATIONS AND USAGE

SUPARTZ FX is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics, e.g., acetaminophen.

CONTRAINdications

Do not administer to patients with known hypersensitivity (allergy) to sodium hyaluronate preparations.

Do not inject this product in the knees of patients with infections or skin diseases in the area of the injection site.

WARNINGS

Do not concomitantly use disinfectants containing quaternary ammonium salts for skin preparation because sodium hyaluronate can precipitate in their presence.

PRECAUTIONS

General

• The effectiveness of a single treatment cycle of less than 3 injections has not been established.

• Strict aseptic administration technique must be followed.

• Remove joint effusion, if present, before injecting SUPARTZ FX.

• The safety and effectiveness of the use of SUPARTZ FX in joints other than the knee have not been established.

• The safety and effectiveness of the use of SUPARTZ FX concomitantly with other intra-articular injectables have not been established.

• Use caution when injecting SUPARTZ FX into patients who are allergic to avian proteins, feathers and egg products.

STERILE CONTENTS. The prefilled syringe is intended for single use. The contents of the syringes must be used immediately once the container has been opened. Discard any unused SUPARTZ FX.

Do not use SUPARTZ FX if the package is opened or damaged. Store in the original packaging below 77°F (25°C). DO NOT FREEZE. Do not use after expiration date indicated on package. Shelf life is 42 months.

INFORMATION FOR PATIENTS

• Provide patients with a copy of the Patients’ Information prior to use.

• Transient pain and/or swelling of the injected joint may occur after intra-articular injection of SUPARTZ FX.

As with any invasive joint procedure, it is recommended that the patient avoid any strenuous activities or prolonged (i.e., more than 1 hour) weight-bearing activities such as jogging or tennis within the 48 hours that follow the intra-articular injection.

• The effectiveness of repeat treatment cycles of SUPARTZ FX has not been established.

Use in Specific Populations

• Pregnancy: The safety and effectiveness of SUPARTZ FX have not been established in pregnant women.

• Nursing Mothers: It is not known if SUPARTZ FX is excreted in human milk. Excretion has been seen in rat milk. The safety and effectiveness of SUPARTZ FX have not been established in lactating women.

• Pediatrics: The safety and effectiveness of SUPARTZ FX have not been demonstrated in children.

ADVERSE EVENTS

The evaluable for safety population included all patients receiving at least one injection (532 SUPARTZ FX; 277 placebo for the German study; 537 concomitant injection) in five well controlled clinical trials. The most common adverse events occurring in SUPARTZ FX-treated patients were arthropgia, defined as joint pain with no evidence of inflammation, arthropathy/ arthritis/arthrosis, defined as joint pain with evidence of inflammation, back pain, pain (specific), injection site reaction, headache, and injection site pain (See Table 1). There were no statistically significant differences in the incidence rates of these adverse events between treatment groups. Five (5) allergic reactions were reported in the SUPARTZ FX group. All five events were classified as mild to moderate. These were: hay fever, reaction on face and neck, cutaneous reaction forearms and knees, and an undefined mild allergy reaction. No anaphylactic reactions were observed in any study patients. Other adverse events occurring in 4% or less but not less than 1% of the SUPARTZ FX treated patients included upper respiratory tract infection, influenza-like symptoms, nausea, sinusitis, urinary tract infection, bronchitis, abdominal pain, diarrhea, infected injury, leg pain, discomfort in legs, dyspepsia, dizziness, rhinitis, and faint. SUPARTZ FX (ARTZ) has been in use in Japan since 1987. A prospective post-market surveillance study1 conducted from 1987 to 1993 evaluated safety on 7404 knees treated from a total of 675 medical institutions. A subset of 7155 knees was treated with 3 or more consecutive injections. There were 58 cases of adverse reactions in 37 knees (0.50%, -37/7404). The most frequently observed were 29 cases of pain at the injection site, 16 cases of swelling, and 3 cases of redness. Other adverse reactions were 3 cases of rash, 3 cases of increased serum GPT, 2 cases of increased serum GGT, 1 case of itching, and 1 case of increased A-P. The incidence of adverse reactions was not related to the number of injections. There was no increase in adverse events in patients requiring 3 or more injections.

Adverse experience data from the literature contain no evidence of increased safety risk relating to retreatment with SUPARTZ FX. The frequency and severity of adverse events occurring during repeat treatment cycles did not increase over that reported for a single treatment cycle.

Post-market experience: The following possible adverse reactions have been reported worldwide.

• The most common adverse reactions include: Injection site reactions (pain/swelling), effusion, redness, or warmth (rare). Rare cases of severe reactions have been reported.

• Other adverse reactions include: Itching; swelling of the face, eyelids, mouth and/or extremities; rash; hives; redness in face; nausea; vomiting and fever. Anaphylactic/anaphylactoid reactions accompanied by transient hypotension (sudden drop in blood pressure), have been rarely reported, all of which resolved either spontaneously or after conservative treatment.

CLINICAL STUDIES

Study Design

The safety and effectiveness of SUPARTZ FX was based on an integrated analysis of five randomized, multi-center, blinded, “placebo controlled” clinical trials. Entry criteria are described for all studies (See Table 2). The treatment regimen consisted of 5 weekly injections in all studies. All patients in these studies (including those injected with the control) received arthrocentesis of the knee prior to an injection of SUPARTZ FX or vehicle (phosphate buffered saline) or, in the German study only, a dilute (1%) form of the SUPARTZ FX formulation. The French study included an additional treatment arm: 3 SUPARTZ FX injections followed by 2 injections of the control per patient. (Table 3 describes the study design and the treatment and follow-up schedules.)

Measures of Effectiveness

Table 3 provides details of the primary and secondary effectiveness parameters used in each study. The Lequesne Index, although a primary measure of effectiveness in only three studies (France, Germany, and Sweden) was common to all five studies. It was used for the integrated analysis of effectiveness across all five studies. The primary measure used in the other two studies was the WOMAC index in Australia, and VAS pain ratings in the United Kingdom.

Results

Patient Population and Demographics

The demographics of study participants were comparable across treatment groups with respect to age, sex, mean body mass index, and baseline scores, with the exception of gender in the German study (see Table 4).

Individual Study Results

Medication use results are presented in Table 5. The results for the Australian study for the protocol-specific primary analysis are presented in Table 4A. The results for all studies of analysis of the Lequesne score as repeated measures analysis of covariance (ANCOVA) of mean reduction from baseline over all visits at or following the 5 week entry were 27 (68.0% of patients) in the SUPARTZ FX group. Additionally, there were significant differences in the incidence rates of WOMAC pain (p=0.045) and stiffness (p=0.024) when compared to the control (p>0.05). The results for the Swedish and UK studies for the protocol-specific primary analysis as VAS ratings as analysis of covariance (ANCOVA) at weeks 1, 5, 13 and 20 (Swedish study), and repeated measures analysis of variance (ANOVA), over weeks 10, 14, and 18, (UK study) are the following: SUPARTZ FX = 10.11 and Control = 0.89 (p > 0.05). The results for the Swedish and UK studies for the protocol-specific primary analysis as VAS ratings as analysis of covariance (ANCOVA) at weeks 1, 5, 13 and 20 (Swedish study), and repeated measures analysis of variance (ANOVA), over weeks 10, 14, and 18, (UK study) are the following: SUPARTZ FX = 10.11 and Control = 9.76 for the Swedish study (p > 0.05); and SUPARTZ FX = 13.47 and Control = 12.89 for the UK study (p = 0.05).

Integrated Analysis

An integrated longitudinal analysis was conducted to examine results across all five studies. See Table 6C. This method of analyzing data with repeated measurements takes into account the correlation structure of the repeated measurements and examines the effects of treatment over time. The integrated longitudinal analysis showed a significant reduction in the total Lequesne score of 2.68 in the SUPARTZ FX treatment groups compared to a reduction in the total Lequesne score of 2.00 in the control groups (p=0.0026). The 95% confidence interval for the difference of the reduction in total
Lequesne score between SUPARTZ FX and control is (0.56, 0.79).

**Summary of Results**

The difference in reduction in total Lequesne scores between the SUPARTZ FX treated group and the control group is 0.68, which is statistically significant in the integrated analysis (p<0.0026). Additionally, the Australian study shows a significant difference between SUPARTZ FX and control in both the WOMAC pain (p=0.045) and stiffness (p=0.024) scores and Lequesne total scores (p=0.0114).

**DETAILED DEVICE DESCRIPTION**

Each 2.5 mL prefilled syringe of SUPARTZ FX contains:

- Sodium Hyaluronate (hyaluronan) 25.0 mg
- Sodium Chloride 21.25 mg
- Dibasic Sodium Phosphate Dodecahydrate 1.343 mg
- Sodium Dihydrogen Phosphate Dihydrate 0.04 mg
- Water for Injection q.s.

**HOW SUPPLIED**

SUPARTZ FX is supplied as a sterile, non-pyrogenic solution in 2.5 mL pre-filled syringe.

**DIRECTIONS FOR USE**

SUPARTZ FX is administered by intra-articular injection once a week (1 week apart) for a total of 5 injections. Some patients may experience benefit with 3 injections given at weekly intervals. This has been noted in a study in which patients treated with three injections were followed for 90 days.

**Injection of subcutaneous lidocaine or similar local anesthetic may be recommended prior to injection of SUPARTZ FX.**

**Warning:** Do not concomitantly use disinfectants containing quaternary ammonium salts for skin preparation because sodium hyaluronate can precipitate in their presence.

**Precaution:** Do not use SUPARTZ FX if the package is opened or damaged. Store in the original packaging below 77°F (25°C). DO NOT FREEZE. Do not use after expiration date indicated on package. Shelf life is 42 months.

**Precaution:** Strict aseptic administration technique must be followed.

**Precaution:** Remove joint effusion, if present, before injection of SUPARTZ FX.

**Precaution:** Take care to remove the tip cap of the syringe and needle aseptically. Inject SUPARTZ FX into the joint through a 22-23 gauge needle. Inject the full 2.5 mL in one knee only. If treatment is bilateral, a separate syringe should be used for each knee.

**Precaution:** The prefilled syringe is intended for single use. The content of the syringe must be used immediately once the container has been opened. Discard any unused SUPARTZ FX.

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**Reference**


---

**Table 1: Adverse Events Occurring in > 4% of SUPARTZ FX-treated Patients**

<table>
<thead>
<tr>
<th>Adverse Event Type</th>
<th>Number (%) of Patients Receiving Control Injections (N=537)</th>
<th>Number (%) of Patients Receiving SUPARTZ FX (N=619)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arthralgia</strong></td>
<td>12(15.0%)</td>
<td>11(12.6%)</td>
</tr>
<tr>
<td><strong>Arthropathy, Arthritis or Arthritis</strong></td>
<td>3(3.8%)</td>
<td>1(1.1%)</td>
</tr>
<tr>
<td><strong>Back Pain</strong></td>
<td>10(12.5%)</td>
<td>10(11.5%)</td>
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<tr>
<td><strong>Injection Site Reaction</strong></td>
<td>16(20.0%)</td>
<td>16(18.4%)</td>
</tr>
<tr>
<td><strong>Headache</strong></td>
<td>4(5.0%)</td>
<td>3(3.4%)</td>
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<tr>
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<td>4(5.0%)</td>
<td>3(3.4%)</td>
</tr>
</tbody>
</table>

**Table 1A: Adverse Events Occurring in 3-Injection SUPARTZ FX-treated Patients**

<table>
<thead>
<tr>
<th>French Study</th>
<th>Number (%) of Patients Receiving Control Injections (N=80)</th>
<th>Number (%) of Patients Receiving SUPARTZ FX (N=87)</th>
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</tbody>
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*Includes application/injection site reaction, injection site inflammation, and purpura injection site.

**Table 2: Entry Criteria**

<table>
<thead>
<tr>
<th>Study</th>
<th>Baseline pain level</th>
<th>Duration of pain prior to study entry</th>
<th>Unilateral versus bilateral</th>
<th>Radiologic criteria</th>
<th>Effusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Australia</strong></td>
<td>Not specified</td>
<td>≥ 3 months</td>
<td>Unilateral or predominantly unilateral**</td>
<td>Evidence of one or more of the following features in an x-ray taken during the previous 6 months: femorotibial osteophytes, osteosclerosis of the femoral or tibial epiphyses, or joint space narrowing</td>
<td>&gt; 50 mL</td>
</tr>
<tr>
<td><strong>France</strong></td>
<td>Lequesne total score = 4 - 12 Global pain ≥ 35 mm on VAS</td>
<td>≥ 3 months</td>
<td>Unilateral or Predominantly unilateral**</td>
<td>Narrowing of femorotibial space &gt; 20% and &lt; 90% in at least 1 of the appropriate angles and/or OA and/or osteocondensation, and/or geode(s)</td>
<td>Severe (tight, distending effusion)</td>
</tr>
<tr>
<td><strong>Germany</strong></td>
<td>Moderate to medium*</td>
<td>Not specified</td>
<td>Unilateral or bilateral</td>
<td>Osteophytes</td>
<td>&gt; 100 mL</td>
</tr>
<tr>
<td><strong>Sweden</strong></td>
<td>Not specified</td>
<td>Not specified</td>
<td>Unilateral</td>
<td>Knee flexion angle of 10 - 15°: 50 - 100% obliteration (= 400 mm) of the joint space (standing radiographs) without any bone erosion</td>
<td>Not specified</td>
</tr>
<tr>
<td><strong>United Kingdom</strong></td>
<td>Moderate*</td>
<td>&gt; 3 months</td>
<td>Unilateral or predominantly unilateral**</td>
<td>Femorotibial osteophytes</td>
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* Definition not specified in protocol.

**Predominantly unilateral means that even in the case of bilateral disease it is possible for the patient to identify one predominant knee that is affected, as reported by the investigator.
References:


Disclaimer: The Reimbursement Guide is intended solely as a tool to assist physician offices with reimbursement issues. Bioventus does not recommend or endorse the billing of any particular diagnosis or procedure code(s) nor does Bioventus determine how claims will be reimbursed. Any determination on how to seek reimbursement should be made by the physician and staff.

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