DEAR PHYSICIAN: This letter is being provided as a sample to help you with your payor interactions concerning reimbursement for the administration of XIAFLEX® (collagenase clostridium histolyticum). Use of this document does not guarantee coverage or reimbursement. As a healthcare professional, you are solely responsible for providing accurate information to third-party payors. If there is any information in this document that does not accurately reflect your practices, it should be modified to appropriately represent your particular circumstances.

Indication

XIAFLEX® is indicated for the treatment of adult men with Peyronie’s disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy.

Important Safety Information for XIAFLEX®

| WARNING: CORPORAL RUPTURE (PENILE FRACTURE) OR OTHER SERIOUS PENILE INJURY IN THE TREATMENT OF PEYRONIE’S DISEASE |
|==================================================================================================================================|
| Corporal rupture (penile fracture) was reported as an adverse reaction in 5 of 1044 (0.5%) XIAFLEX®-treated patients in clinical studies. In other XIAFLEX®-treated patients (9 of 1044; 0.9%), a combination of penile ecchymoses or hematoma, sudden penile detumescence, and/or a penile “popping” sound or sensation was reported, and in these cases, a diagnosis of corporal rupture cannot be excluded. Severe penile hematoma was also reported as an adverse reaction in 39 of 1044 (3.7%) XIAFLEX®-treated patients. |
| Signs or symptoms that may reflect serious penile injury should be promptly evaluated to assess for corporal rupture or severe penile hematoma which may require surgical intervention. |
| Because of the risks of corporal rupture or other serious penile injury, XIAFLEX® is available for the treatment of Peyronie’s disease only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the XIAFLEX® REMS Program. |

- XIAFLEX® is contraindicated in the treatment of Peyronie’s plaques that involve the penile urethra due to potential risk to this structure and in patients with a history of hypersensitivity to XIAFLEX® or to collagenase used in any other therapeutic application or application method
- Injection of XIAFLEX® into collagen-containing structures such as the corpora cavernosa of the penis may result in damage to those structures and possible injury such as corporal rupture (penile fracture). Therefore, XIAFLEX® should be injected only into the Peyronie’s plaque and care should be taken to avoid injecting into the urethra, nerves, blood vessels, corpora cavernosa or other collagen-containing structures of the penis
- In the double-blind, placebo-controlled portions of the clinical trials in Peyronie’s disease, a greater proportion of XIAFLEX®-treated patients (4%) compared to placebo-treated patients (1%) had localized pruritus after up to 4 treatment cycles (involving up to 8 XIAFLEX® injection procedures). The incidence of XIAFLEX®-associated pruritus was similar after each injection regardless of the number of injections administered
- Because XIAFLEX® contains foreign proteins, severe allergic reactions to XIAFLEX® can occur. Anaphylaxis was reported in a post-marketing clinical trial in one patient who had previous exposure to XIAFLEX® for the treatment of Dupuytren’s contracture. Healthcare providers should be prepared to address severe allergic reactions following XIAFLEX® injections. The safety of more than one treatment course of XIAFLEX® is not known

Please see Important Safety Information continued on next page. Please click here for full Prescribing Information, including Boxed Warning and Medication Guide.
Important Safety Information for XIAFLEX® (collagenase clostridium histolyticum) (continued)

• In the XIAFLEX® controlled trials in Peyronie’s disease, 65.5% of XIAFLEX®-treated patients developed penile hematoma, and 14.5% developed penile ecchymosis. Patients with abnormal coagulation (except for patients taking low-dose aspirin, eg, up to 150 mg per day) were excluded from participating in these studies. Therefore, the efficacy and safety of XIAFLEX® in patients receiving anticoagulant medications (other than low-dose aspirin, eg, up to 150 mg per day) within 7 days prior to XIAFLEX® administration is not known. In addition, it is recommended to avoid use of XIAFLEX® in patients with coagulation disorders, including patients receiving concomitant anticoagulants (except for low-dose aspirin)

• In the XIAFLEX® clinical trials for Peyronie’s disease, the most frequently reported adverse drug reactions (≥25%) and at an incidence greater than placebo included: penile hematoma, penile swelling, and penile pain

Please click here for full Prescribing Information, including Boxed Warning and Medication Guide.

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December 2015 XP-04225a
Re: Letter of Medical Necessity for XIAFLEX® (collagenase clostridium histolyticum) for Peyronie’s disease

Patient name: [First and last name]
Patient date of birth: [XX/XX/XXXX]
Insurance ID #: [XXXXXXXXXXXXXXX]
Group #: [XXXXXXXXXXX]

Dear [Insurance contact name]:

[Patient’s first name] was diagnosed with Peyronie’s disease on [date]. The patient has [specify number of plaques and degree of penile curvature]. The curvature has resulted in [detail impact on patient]. By treating my patient with XIAFLEX®, I anticipate the following outcomes: [express your professional opinion about the potential to reach the anticipated outcome]. [If appropriate, provide any past clinical experiences you may have had with Peyronie’s disease, including previous treatments and clinical interventions.]

On December 6, 2013, XIAFLEX® was FDA-approved for the treatment of adult men with Peyronie’s disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy.

This letter is to provide clinical justification for [patient’s first and last name] to receive 2 injections of XIAFLEX® per treatment cycle, up to 4 treatment cycles (for a maximum of 8 injections over approximately 24 weeks). If the curvature deformity is less than 15 degrees after the first, second or third treatment cycle, or if I determine that further treatment is not clinically indicated, then the subsequent treatment cycles will not be administered. During the first visit, I will inject a pharmacological agent into the patient’s penis to induce an erection. This procedure reveals the location of the penile plaque at the point of maximum concavity and identifies the appropriate site for the injection of XIAFLEX®. After the penis has detumesced, I will inject an anesthetic agent into the penis, followed by an injection of XIAFLEX® into the penile plaque in accordance with the Prescribing Information. The patient will return to my office within 24 to 72 hours for a second injection of XIAFLEX®. He will return for a third visit 24 to 72 hours after the second injection for a modeling procedure. The interval between treatment cycles is approximately 6 weeks.

I will be using the following codes to bill for XIAFLEX® and related procedures:

**Product Code (J-code) designated by the Centers for Medicare & Medicaid Services**

J0775: collagenase clostridium histolyticum, 0.01 mg (single-use vial)

**Procedure Codes (CPT® codes) designated by the American Medical Association**

54200: Injection procedure for Peyronie’s disease

[If you used a pharmacologic agent to induce erection, submit:

54235: Injection of corpora cavernosa with pharmacologic agent(s) (eg, papaverine, phentolamine)]
If you have any questions regarding the material that I have provided, please do not hesitate to contact me. Thank you in advance for your prompt attention to this matter.

Sincerely,

[Physician’s name and credentials]
[Title]
[Name of practice]
[Street address]
[City, state, ZIP code]
[Phone number]

Enclosures:
[Patient medical records/chart notes]
[XIAFLEX® full Prescribing Information]
[FDA approval letter]