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 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.

- **Contraindications:** 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
- **Corporal Rupture or Other Serious Injury to the Penis:** 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. Cases of localized skin and soft tissue necrosis occuring as sequelae of penile hematoma, some requiring surgical intervention, have been reported post-marketing
- **Hypersensitivity Reactions, Including Anaphylaxis:** 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
- **Risk of Bleeding in Patients with Abnormal Coagulation:** 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)

Please see additional Important Safety Information on next page.

Click for full Prescribing Information, including Boxed Warning and Medication Guide.

IMPORTANT SAFETY INFORMATION FOR XIAFLEX (collagenase clostridium histolyticum) (cont)

- **Acute Post-Injection Back Pain Reactions:** Post-marketing reports of acute lower back pain reactions, sometimes accompanied by radiation to the lower extremities, chest and arms, muscle spasms, chest pain, paresthesias, headache, and dyspnea, have been received by patients treated with XIAFLEX for Peyronie's disease. These events can be mild to severe in intensity. The events typically lasted for 15 minutes and typically did not require intervention. Administer the smallest number of treatment cycles necessary to treat the patient's curvature deformity
- **Syncope and Presyncope:** Most, but not all cases of syncope and presyncope in patients with Peyronie's disease, occurred in association with post-injection penile pain and hematoma, penile pain with spontaneous erections, and pain during micturition. These potential triggers suggest a vasovagal mechanism. Make patients aware of the potential symptoms that could trigger syncope and presyncope after treatment with XIAFLEX.
  If presyncopal symptoms occur, patients should remain recumbent until symptoms resolve. Syncope may be associated with bodily injuries, including concussion, head abrasion, and other accidental injuries

Adverse Reactions

Clinical trials

- 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.

Post-marketing experience

- Acute post-injection lower back pain reactions have occurred in close temporal proximity to XIAFLEX treatments
- Cases of localized skin and soft tissue necrosis events as sequelae of penile hematoma, some of which required surgical intervention
- Syncope and presyncope have been reported in men treated with XIAFLEX for Peyronie's disease. Most, but not all cases occurred in the immediate treatment period or within 1-2 days following injection. Bodily injuries associated with the syncopal events have been reported

Click for full Prescribing Information, including Boxed Warning and Medication Guide.

Insurance payor coverage criteria and restrictions may vary. Please check your local payor's coverage policy for more information.

MM-05783/August 2022 www.xiaflex.com 1-800-462-ENDO (3636)

[Date]

[Insurance contact name]
[Insurance contact title]
[Name of insurance company]
[Insurance street address]
[City, state, ZIP code]

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 #: **[XXXXXXXXXX]**

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.

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]