Before beginning your treatments, please review this important information.

Glossary of terms
(Nota that terms in the glossary are bold throughout this document.)

Abscess—a swollen lump filled with pus
Anaphylaxis—severe allergic reaction
Anesthetic—a substance that reduces sensitivity to pain
Anticoagulants—a substance that prevents or reduces blood clots
Arnica—an herbal ointment that is commonly used to treat pain, bruising, and swelling
Bovine-based collagen—a dermal filler created from cowhides
Compensatory—free, at no cost
Cushioning agent—absorbs shock
Duration—length of time
Epinephrine—a medication used in emergencies to treat serious allergic reactions
Expressed a preference—subjects liked better
Gram-positive bacterial proteins—remnants of protein from the bacteria that produce the hyaluronic acid used in JUVÉDERM® Ultra Plus XC
Hyaluronidase—an enzyme that breaks down hyaluronic acid
Hypertrophic scarring—a thick, hard scar that grows over the injured area
Inflammatory reaction—a localized response to injury, typically including pain, heat, redness, and swelling
Injection-site responses—side effects from treatment
Keloid formation—a thick, hard scar that grows outside the injured area
Nasolabial folds (NLFs)—the lines or wrinkles that run from the corners of the nose downward toward the corners of the mouth
Necrosis—death of living tissue (skin)
NSAIDs—nonsteroidal anti-inflammatory drug, such as aspirin or ibuprofen
Optimal—the best possible outcome
Pigmentation disorders—a lightening or darkening of an area of the skin
Repeat treatment vs repeat injection—an additional treatment with dermal filler that is given after the effects of the initial treatment have worn off, in order to maintain the desired result
Topical—cream or ointment applied to a certain area of the skin and affecting only the area to which it is applied
Touch-up injection—an additional injection of a small amount of dermal filler usually given about 2 weeks to 1 month after the initial injection. A touch-up injection may be necessary to achieve the desired result
Vasodilators—medicines that open blood vessels

What is it?
JUVÉDERM® Ultra Plus XC injectable gel is a colorless hyaluronic acid gel that contains a small quantity of local anesthetic (lidocaine) and is injected into facial tissue to smooth wrinkles and folds, especially around the nose and mouth. Hyaluronic acid is a naturally occurring sugar found in the human body. The role of hyaluronic acid in the skin is to deliver nutrients, hydrate the skin by holding in water, and to act as a cushioning agent. The role of lidocaine is to reduce the pain associated with injections into the skin.

What does it do?
JUVÉDERM® Ultra Plus XC temporarily adds volume to facial tissue and restores a smoother appearance to the face. The lidocaine in the gel improves the comfort of the injection.

How is it used?
JUVÉDERM® Ultra Plus XC is injected into areas of facial tissue where moderate to severe facial wrinkles and folds occur. It temporarily adds volume to the skin and may give the appearance of a smoother surface.

What will it accomplish?
JUVÉDERM® Ultra Plus XC injectable gel will help to smooth moderate to severe facial wrinkles and folds. Most patients need 1 treatment to achieve optimal wrinkle smoothing, and the results last about 1 year.

What are possible side effects?
Most side effects are mild or moderate in nature, and their duration is short lasting (7 days or less). The most common side effects include, but are not limited to, temporary injection-site responses such as: redness, pain/tenderness, firmness, swelling, lumps/bumps, bruising, itching, and discoloration.

As with all skin injection procedures, there is a risk of infection. One of the risks with using this product is unintentional injection into a blood vessel. The chances of this happening are very small, but if it does happen, the complications can be serious, and may be permanent. These complications, which have been reported for facial injections, can include vision abnormalities, blindness, stroke, temporary scabs, or permanent scarring of the skin.

Are there any reasons why I should not receive JUVÉDERM® Ultra Plus XC (contraindications)?
Your physician will ask about your medical history to determine if you are an appropriate candidate for treatment. The product should not be used in patients who have:

- Severe allergies marked by a history of anaphylaxis or history or presence of multiple severe allergies
- A history of allergies to lidocaine or Gram-positive bacterial proteins
- History of keloid formation or hypertrophic scarring

What should my physician warn me about?
The safety and effectiveness for the treatment of areas other than facial wrinkles and folds (such as lips) have not been established in controlled clinical studies.

What precautions should my physician advise me about?
The following are important treatment considerations for you to discuss with your physician and understand in order to help avoid unsatisfactory results and complications.

- Patients who are using substances that can prolong bleeding, such as aspirin or ibuprofen, as with any injection, may experience increased bruising or bleeding at injection site. You should inform your physician before treatment if you are using these types of substances
- If laser treatment, chemical peeling, or any other procedure based on active dermal response is considered after treatment with JUVÉDERM® Ultra Plus XC, there is a possible risk of an inflammatory reaction at the treatment site
- JUVÉDERM® Ultra Plus XC injectable gel should be used with caution in patients on immunosuppressive therapy, or therapy used to decrease the body’s immune response, as there may be an increased risk of infection
- The safety for use during pregnancy, in breast-feeding females, or in patients under 18 years has not been established
- The safety in patients with a history of excessive scarring (eg, hypertrophic scarring and keloid formations) and pigmentation disorders has not been studied

What did the clinical study show?
In the primary US clinical study to establish safety and effectiveness, 144 subjects were followed for 24 weeks after injection with JUVÉDERM® Ultra Plus (without lidocaine) in 1 nasolabial fold (NLF) and ZYPLAST® dermal filler (bovine-based collagen) in the other. The percentage of subjects who reported common injection-site responses are presented in the table below.

Table 1. Injection-Site Side Effects (Nasolabial Folds)\(^1\) N = 144

<table>
<thead>
<tr>
<th>Injection-Site Responses</th>
<th>JUVÉDERM® Ultra Plus</th>
<th>ZYPLAST®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Redness</td>
<td>129</td>
<td>128</td>
</tr>
<tr>
<td>Pain/Tenderness</td>
<td>129</td>
<td>90%</td>
</tr>
<tr>
<td>Firmness</td>
<td>127</td>
<td>88%</td>
</tr>
<tr>
<td>Swelling</td>
<td>124</td>
<td>86%</td>
</tr>
<tr>
<td>Lumps/Bumps</td>
<td>120</td>
<td>83%</td>
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<tr>
<td>Bruising</td>
<td>87</td>
<td>60%</td>
</tr>
<tr>
<td>Itching</td>
<td>49</td>
<td>34%</td>
</tr>
<tr>
<td>Discoloration</td>
<td>49</td>
<td>34%</td>
</tr>
</tbody>
</table>

\(^1\) Occurring in > 5% of subjects.

\(^2\) Number of subject NLFs with each specific injection-site response.

Injection-site responses were similar in duration and frequency for the JUVÉDERM® Ultra Plus injectable gel and ZYPLAST® treated sides, were usually mild or moderate in severity, did not require intervention, and lasted 7 days or less.

JUVÉDERM® Ultra Plus was found to provide a more persistent wrinkle correction than ZYPLAST® dermal filler over the 24-week course of the study. The percentage of subjects who maintained improvement with JUVÉDERM® Ultra Plus at 24 weeks was 90% compared to 40% with ZYPLAST®. At the conclusion of the study, 123 (84%) of 146 subjects expressed a preference for JUVÉDERM® Ultra Plus injectable gel, while only 15 (10%) expressed a preference for ZYPLAST® and 8 (5%) had no preference.

![Figure 1. Subject Preference](chart)

Subjects who completed the 24-week study were invited to return for a complimentary repeat treatment. Subjects returned at their (or their physician’s) convenience. Of the 146 subjects, 111 (76%) returned for repeat treatment, on average at 9 months after their last injection. Forty-seven (47) subjects returned more than 36 weeks (9 months) after their last injection; the percentage of those subjects who had maintained improvement with JUVÉDERM® Ultra Plus was 81%. Of the twenty-three (23) subjects who returned more than 48 weeks (1 year) after their last injection, 78% had maintained improvement.

(Continued on reverse side.)
The most commonly reported adverse events were swelling, redness, bruising, and pain.

Additionally there have been reports of nodules, infection, inflammation, allergic reaction, and blood vessel blockade.

- Nodules generally occurred from immediately to 6 months after injection. Treatment included NSAIDs, antibiotics, steroids, and hyaluronidase. In most cases, nodules went away within one month
- Infection generally occurred from immediately to 1 month after injection. Treatment included antibiotics, pain killers, antifungals, and antibacterial medicines
- Inflammation generally occurred from the day of treatment to 2 months after injection. Treatment included antibiotics, steroids, and needle aspiration. Resolution of symptoms has been reported within 4 days
- Allergic reaction generally occurred from immediately to 1 day after injection. Treatment included steroids and antihistamines
- Blood vessel blockage generally occurred from immediately to 2 days after injection. Treatment included anticoagulants, epinephrine, NSAIDs, vasodilators, hyaluronidase, surgery, and warm compress. Outcomes have ranged from completely resolved to ongoing at time of last contact

Other adverse events that were reported included: blister, skin rash, bleeding at the injection site, necrosis at the injection site, abscess at the injection site, increase or decrease in sensation, skin discoloration, device migration, dry skin, headache, flu-like symptoms, vision abnormalities, herpes, anxiety, scarring, dizziness, nausea, depression, lack or loss of correction, unsatisfactory result, overcorrection, varied injuries, discomfort, drainage, product coming back out, acne, shortness of breath, passing out, cardiac complication, deeper wrinkle, spider vein, collection of blood outside of a blood vessel, swelling from reactive blood vessels, calcification, severe life-threatening allergic reaction, tissue hardening, and cyst.

Delayed-onset inflammation near the site of dermal filler injections is one of the known adverse events associated with dermal fillers. Cases of delayed-onset inflammation have been reported to occur at the dermal filler treatment site following viral or bacterial illnesses or infections, vaccinations, or dental procedures. Typically, the reported inflammation was responsive to treatment or resolved on its own.

What side effects have been reported through voluntary postmarket surveillance of JUVÉDERM® Ultra and JUVÉDERM® Ultra Plus (without lidocaine) use in and outside of the United States?

The most commonly reported adverse events were swelling, redness, bruising, and pain.

- Swelling, redness, and pain generally occurred from immediately to 2 months after injection.
  - The treatment prescribed included NSAIDs, antihistamines, antibiotics, steroids, arnica, and hyaluronidase. In most cases, these went away within a few days to 5 weeks
- Bruising generally occurred from immediately to 1 day after injection. Treatment included NSAIDs, antihistamines, antibiotics, steroids, arnica, and hyaluronidase. In most cases, it went away within a few days to 6 weeks