About Belotero® Intense (+) Lidocaine

Before beginning your treatments, please review this important information.

GLOSSARY

Terms in the glossary are bold throughout the document.

Anesthetic – a medication (or “treatment”) that reduces pain.

BDDE – the ingredient used to crosslink the HA.

Cohesive Polydensified Matrix (CPM) gel – a **hyaluronic acid** gel produced using patented crosslinking technology, resulting in a **dermal filler** with different densities. These higher and lower density zones create an **HA** gel that flows easily into the skin for smooth, natural-looking and long-lasting results.

Crosslinking – a process in which **HA** chains are connected together to form a network.

Dermal filler – a material that is injected underneath the skin to smooth a wrinkle or restore volume to an area of skin.

Hyaluronic acid (HA) – a naturally occurring sugar, found in the body that gives the skin moisture, volume and elasticity.

Hyaluronidase – an enzyme that breaks down **hyaluronic acid**.

Lidocaine – a commonly used local **anesthetic** to decrease pain.

Topical – a cream or ointment applied to the top of the skin and affecting only the area to which it is applied.

Touch-up – an additional injection of **dermal filler** that is usually given a short time after the initial injection. Some patients may require a **touch-up** treatment to achieve the desired result.

PRODUCT DESCRIPTION

What is it?

Belotero® Intense (+) Lidocaine is a clear, colorless **hyaluronic acid (HA)** gel that contains a small quantity of local **anesthetic**. **HA** is a naturally occurring sugar found in the human body. The role of **HA** is to deliver nutrients and help the skin retain its moisture, volume and elasticity. Belotero® Intense (+) Lidocaine is **Cohesive Polydensified Matrix (CPM) gel** manufactured using dynamic crosslinking technology, during which **HA** is **crosslinked** with **BDDE**, an ingredient that helps form a network of **HA**, in two independent steps. This patented crosslinking technology results in a cohesive yet flexible gel filler that lasts longer at the treatment site.

How does it work?

Belotero® Intense (+) Lidocaine is injected directly into and around the lips using a small needle to temporarily plump the lips for lip enhancement in adults over the age of 21. The addition of **lidocaine** helps to improve comfort of the injection.

CONTRAINDICATIONS

Are there any reasons why I should not receive Belotero® Intense (+) Lidocaine?

Your doctor will ask you about your medical history and determine if you are an appropriate candidate for treatment. You will be asked questions about possible allergies to ensure that Belotero® Intense (+) Lidocaine can be safely administered. Tell your doctor about all your medical conditions, including if you:

- Have severe allergies with a history of severe reactions (anaphylaxis) or multiple severe allergies. Use of Belotero® Intense (+) Lidocaine may result in an allergic reaction.
- Are allergic to the **anesthetic lidocaine** or to any of the proteins used to make the **HA** in Belotero® Intense (+) Lidocaine (bacterial proteins). Use may result in an allergic reaction.

If you are not sure about your medical history concerning these allergies or other medical conditions you think might be relevant, please discuss further with your doctor.

WARNINGS

What warnings should my doctor advise me about?

To help you understand the treatment risks, your doctor should discuss the following:

- One of the risks with using this product is the 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, temporary or permanent blindness, stroke, temporary scabs, or permanent scarring of the skin.
- The use of Belotero® Intense (+) Lidocaine where skin sores, pimples, rashes, hives, cysts, or infections are present should be postponed until healing is complete. Use of Belotero® Intense (+) Lidocaine where these are present, could delay healing or make your skin problems worse.
- Do not use Belotero® Intense (+) Lidocaine if you have a history of developing big scars or keloids on your skin, scarring may occur after injection of Belotero® Intense (+) Lidocaine.

PRECAUTIONS

What precautions should my doctor discuss with me?

The following are important treatment considerations for you to discuss with your doctor and understand in order to help avoid unsatisfactory results and complications.

- You should discuss the potential treatment risks and benefits with your doctor.
- Belotero® Intense (+) Lidocaine is only to be used for adults over the age of 21.
- Tell your doctor if you are pregnant, planning to become pregnant, or breastfeeding. The safety of Belotero® Intense (+) Lidocaine has not been studied in women who are pregnant or breastfeeding.
- Tell your doctor if you are taking any medications used to decrease the body's natural defense system (immunosuppressants). Belotero® Intense (+) Lidocaine injections may then result in an increased risk of infection.
- Tell your doctor if you have a bleeding disorder or are taking any medication that can thin your blood or prolong bleeding, such as aspirin and warfarin. As with any injection procedure this may increase your risk of bruising or bleeding at the injection site.
- If you have had cold sores in the past, there is a risk that they will return after your procedure with Belotero® Intense (+) Lidocaine.
- Tell your doctor immediately if you experience any changes in your vision, signs of a stroke, white appearance of the skin, or unusual pain during or shortly after treatment. These could be signs of an unintentional intravascular injection and require immediate medical care to avoid permanent complications.
- Minimize exposure to excessive sun, heat, UV lamp exposure, Turkish bath, and extreme cold weather until any initial swelling and redness have gone away and needle entrance sites have healed.

- Tell your doctor if you are planning laser treatments, chemical peels, or other procedures performed on your skin after treatment with Belotero® Intense (+) Lidocaine, as there may be an increased risk that you will have a reaction at the injection site.
- Belotero® Intense (+) Lidocaine should only be used by a health care professional trained in the correct procedure to inject dermal fillers and who completely understands the entire package insert and physician label.

If you have any additional questions about any topic in this section, please discuss further with your doctor. See below for when you should contact your doctor immediately after treatment.

Clinical Studies

How was Belotero® Intense (+) Lidocaine studied?

Belotero® Intense (+) Lidocaine was tested in a clinical study comparing it to another **dermal filler** to ensure it worked properly (was effective) and was safe. The study included 220 participants, (96% female and 4% male) who were randomly selected to receive treatment with Belotero® Intense (+) Lidocaine or another similar **dermal filler** (comparator). The product was randomly assigned to each participant so that 165 received Belotero® Intense (+) Lidocaine and 55 received the comparator product. To achieve participants' desired results, a **touch-up** treatment was allowed 4 weeks later with the same product as used at the initial treatment.

The Belotero® Intense (+) Lidocaine treatment group included participants with multiple skin tones (pale to dark skin). Each of these participants expressed a desire to improve the fullness of their lips. The amount of Belotero® Intense (+) Lidocaine used in the clinical study to achieve optimal outcomes varied and was based on their individual need.

To objectively measure improvements in lip fullness, each participant was evaluated by a doctor other than the one who had performed the treatment. Participants also evaluated themselves. To measure side effects following the procedure, each participant kept a diary for 28 days to record side effects. These were then shared with the doctors. Side effects were also reported by doctors based on office visits with each participant. These office visits included discussing any symptoms or complaints with the participants and assessing their appearance.

After 48 weeks, participants in the Belotero® Intense (+) Lidocaine treatment group could receive an optional repeat treatment. Participants that received repeat treatment were monitored for another 12 weeks for effectiveness and safety.

BENEFITS

What will it accomplish?

Belotero® Intense (+) Lidocaine will temporarily add volume and improve lip fullness.

What did the clinical study show?

Belotero® Intense (+) Lidocaine was found to safely and effectively increase lip fullness. The clinical study showed that benefits of Belotero® Intense (+) Lidocaine last up to 48 weeks for participants receiving a single treatment with or without touch-up and up to 60 weeks in the majority of participants with repeat treatment.

- Belotero® Intense (+) Lidocaine and the comparator **dermal filler** have similar abilities in adding volume to your lips and increasing lip fullness 8 weeks after treatment.
- Based on in-person live assessment by the doctor using the 5-point photonumeric Merz Lip Fullness Assessment Scale, 91% of participants had at least a 1-point improvement in their lips 8 weeks after treatment.
- Based on the in-person assessment by the doctor and participant using the 5-point Global Aesthetics Improvement Scale, 100% of participants were 'improved', 'much improved' or 'very much improved' in lip fullness 8 weeks after treatment. 92% of participants according to a doctor's assessment as well as 90% of participants self-reported that aesthetic improvement lasted up to 48 weeks.
- The majority of participants reported improvement in the softness, smoothness, attractiveness, look and feel of their lips throughout the study and up to 60 weeks after treatment.
- 92% of participants were satisfied with Belotero® Intense (+) Lidocaine treatment.
- Most participants surveyed reported being 'extremely likely' to receive future Belotero® Intense (+) Lidocaine treatment.
- Participants self-reported reported improvements on the FACE Q Psychological Function module, which measured how confident, attractive or happy the participants felt after Belotero® Intense (+) Lidocaine treatment. These improvements were maintained throughout the study.

RISKS

What are possible side effects?

During the study of Belotero® Intense (+) Lidocaine to improve lip fullness, participants reported side effects in 28-day daily diaries. If these side effects lasted longer than 28 days, they were reported as adverse events. Most participants reported the following side effects at the site where they received the injection:

- Swelling
- Lumps / Bumps
- Bruising
- Soreness
- Redness

- Pain/Tenderness
- Firmness / Hardness

Other side effects reported in the study included discoloration, burning/stinging, and itching at the injection site. These temporary reactions were typically mild or moderate and usually disappeared within 2-4 weeks.

Adverse events were any side effects that lasted longer than 28 days (the duration of the daily diary) or were reported by doctors at any time throughout the study). The reported adverse events included injection site lumps/bumps, tissue firmness/hardening, swelling, pain, discoloration, redness, and cold sores. Most of these adverse events were mild and resolved on their own in an average of 44 days.

As with all skin injection procedures, there is a risk of infection that can occur with **dermal filler** injections.

In the clinical study, some participants experienced delayed-onset reactions that occurred more than 21 days after receiving Belotero® Intense (+) treatment. These delayed-onset reactions included: injection site bumps, tissue firmness/hardening, pain, redness, and skin discoloration. Delayed-onset reactions were mild and resolved on their own within 3 weeks. 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.

Although most side effects will resolve with time, your doctor may choose to treat them with medications, such as antibiotics, drugs to reduce inflammation (corticosteroids), drugs to relieve pain (analgesics), drugs to relieve allergy symptoms (antihistamines), surgical procedure (removal or drainage) or **hyaluronidase** (an enzyme that breaks down **HA**).

If you have any questions concerning possible side effects, please discuss further with your doctor. You should always tell your doctor if you experience anything unusual at the site of treatment. See below for additional information on when you should contact your doctor immediately.

BEFORE PROCEDURE INFORMATION

What happens in the office before the injection?

Note that each doctor may have a unique process for treating patients.

The following is an example of what your doctor may do before the injection procedure. Before the injection procedure, your document will ask you questions about your medical history as well as

your treatment goal. Your doctor will discuss whether you are an appropriate candidate for Belotero® Intense (+) Lidocaine is the right treatment for you.

- Review what you should expect during and after the procedure.
- Let you know of any possible side effects that you may experience, and what to do if you experience these.
- Take photos of the area of your face that will be treated.

Your doctor may also have additional ways of evaluating patients and preparing them for a procedure.

PROCEDURE DESCRIPTION

What happens during the procedure?

Your doctor may do the following during your procedure:

- Your skin will be cleansed prior to treatment.
- Your doctor may use a cream or ointment called a topical anesthetic to numb the area where you will receive your injection.
- Your doctor will begin the procedure by giving you the first injection, then pausing to allow the anesthetic that is part of Belotero® Intense (+) Lidocaine to continue to numb the area around your injection. The anesthetic part of Belotero® Intense (+) Lidocaine has been shown to significantly reduce the pain and discomfort that may occur with a dermal filler gel injection.
- Your doctor will continue the injection of Belotero® Intense (+) Lidocaine until the area being treated shows the desired results.
- After the injection is completed, your doctor may gently massage the area that was treated to ensure the **dermal filler** gel is distributed evenly and looks natural.

AFTER PROCEDURE INFORMATION

What should I do after receiving treatment?

- Avoid touching the treated area within six hours following treatment so you do not accidentally injure your skin while the area is numb. After that, the area can be gently washed with soap and water.
- For the first 24 hours, you should avoid or minimize hard (strenuous) exercise. You should also avoid or minimize exposure to extensive sun or extreme temperatures. Exposure to

any of these may cause the area where you were treated to temporarily become red, swell and/or itch. If you experience any of these, an ice pack can be applied for relief.

- Avoid taking aspirin, NSAID, St. John's Wort, blood thinners, and high doses of Vitamin E supplements for one week after treatment. These agents may increase bruising and bleeding at the injection site.

Will I need more than one treatment to achieve my desired result?

You should discuss your treatment goals and plan with your doctor. In the clinical study, 60% of participants received a touch-up treatment 4 weeks after initial treatment in order to achieve the desired result.

Does the improvement last forever?

No. While individual results may vary, in the clinical study, the results lasted up to 48 weeks in many participants; with repeat treatment, the improvements lasted even longer (up to 60 weeks). Repeat treatments are usually needed to maintain your desired result.

ALTERNATIVE PROCEDURES

What other treatments are available to me?

There are other **dermal filler** gels in the United States that are available to you for treatment. Additionally, there are alternative treatments such as surgical procedures, implants, or fat injections. You can discuss these treatments with your doctor to determine which one is right for you.

WHEN TO CALL YOUR DOCTOR

When should I call my doctor?

You should call your doctor immediately if you have:

- Changes in your vision.
- Signs of a stroke (including sudden difficulty speaking, numbness or weakness in your face, arms, or legs, difficulty walking, face drooping, severe headache, dizziness, or confusion) (http://www.nlm.nih.gov/medlineplus/stroke.html).
- White appearance of the skin.
- Unusual pain during or shortly after treatment.

Be sure to call your doctor if you have:

- Injection site reactions that continue more than two weeks after treatment. Most side effects such as bruising, swelling, pain, tenderness, redness, and itching will usually go away within one to two weeks.
- Blisters or skin sores that recur, which may signal the presence of a herpes infection.
- Any signs of infection such as fever, redness that spreads to surrounding areas, drainage, increasing tenderness or increasing pain that does not go away.
- Significant pain away from the injection site.
- Any side effect that occurs weeks or months after treatment.
- Any other symptoms that cause you concern.

ADDITIONAL INFORMATION

What if I experience a problem?

If you believe that you have experienced a serious problem related to Belotero® Intense (+) Lidocaine, you should call your doctor. You may also contact Merz North America, Inc. at 1-844-469-6379 or email AxUS-adverse.events@merz.com to report any side effects.

For further information please call Merz North America at (844) 469-6379.

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