

# Belotero Balance® (+) Patient Information Guide

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This guide will help you decide whether treatment with Belotero Balance® (+) Lidocaine (herein after referred to as Belotero Balance® (+)) is right for you. This information does not take the place of a discussion with your doctor. This guide will answer some questions you may have about Belotero Balance® (+) treatment.

- Only you and your doctor can decide whether Belotero Balance® (+) is right for you. Other treatments are available to correct volume loss under the eyes and you may discuss these treatment options with your doctor.
- Please read all the information in this guide and discuss any questions with your doctor before you are treated with Belotero Balance® (+).

Please keep this information. You may want to read it again.

## 1. GLOSSARY

Note: the terms in the glossary are underlined throughout this document.

<b>Adverse event</b>	Undesirable side effects
<b>Allergic Reaction</b>	<u>Allergic reactions</u> occur when a person's immune system (needed to fight infections) overreacts to substances that are harmless in most people. Symptoms can include a rash, sneezing, itching, congestion, or difficulty breathing
<b>Anaphylactic Shock</b>	A severe allergic reaction with lip swelling and difficulty breathing; this is a medical emergency
<b>Anesthetic</b>	A substance that blocks the sensation of pain
<b>BDDE</b>	1,4-butanediol diglycidyl ether is a compound that is added to crosslink the hyaluronic acid
<b>Cannula</b>	A thin metal tube with a blunt tip
<b>Dermal Filler</b>	A substance that is injected in the skin to create a smoother and/or fuller appearance in the face
<b>Edema</b>	Swelling
<b>Erythema</b>	Redness
<b>Granuloma</b>	Small lump under the skin due to an immune response
<b>Hematoma</b>	Collection of blood under the skin
<b>Hyaluronic Acid (HA)</b>	A naturally occurring substance in the skin that forms some of its structure
<b>Hyaluronidase</b>	A substance that breaks down hyaluronic acid (HA)
<b>Induration</b>	Firmness of the skin from swelling or inflammation
<b>Injection Site Reactions</b>	Reactions that occur at the site of an injection. For dermal fillers, this can include bruising, change in skin color, change in firmness, itching, lumps, pain or tenderness, redness, and swelling.
<b>Keloid</b>	A thick scar that is larger than the injury that caused it
<b>Lidocaine</b>	A type of anesthetic drug that can be used to block the sensation of pain
<b>Necrosis</b>	Local death of the skin
<b>Nodules</b>	Lumps under the skin (e.g cyst-like) that can be felt with the fingers
<b>Quincke's edema</b>	Swelling of the skin or mucous membranes, similar to an allergic reaction or hives
<b>Pustule</b>	A small skin bump with pus

<b><i>Streptococcus equi</i></b>	A type of bacterium that is used to make hyaluronic acid
<b>Touch-up</b>	An additional injection, performed 2 to 4 weeks after the initial injection. Some patients may require a <u>touch-up</u> treatment to achieve the desired aesthetic results.
<b>Topical</b>	Any drug or product that is applied to the outside of the skin.
<b>Tyndall effect</b>	Bluish skin discoloration in the area of treatment
<b>Undereye Hollows</b>	Depressed, sunken, or hollow area under the eye
<b>Vascular occlusion</b>	Blockage of a blood vessel
<b>Vascular compromise</b>	A situation in which an area does not receive sufficient blood flow.

## 2. ABOUT BELOTERO BALANCE® (+)

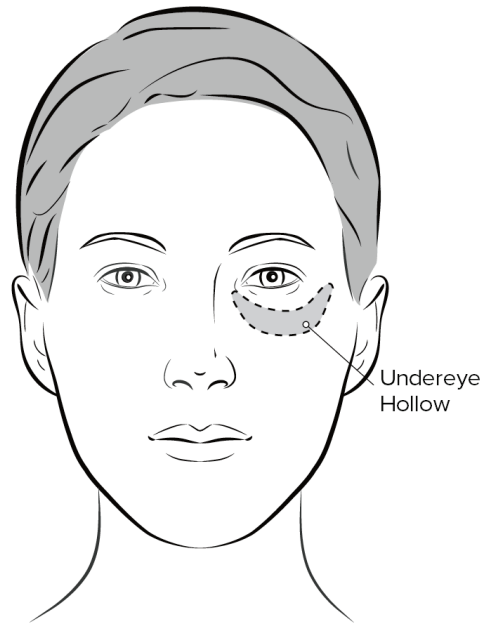
Caution: Federal (USA) law restricts this device to sale by or on the order of a physician or other licensed healthcare practitioner.

### What is Belotero Balance® (+)?

Belotero Balance® (+) is a clear, hyaluronic acid gel and a small quantity of an anaesthetic (lidocaine) to reduce the sensation of pain, and the chemical BDDE to make it last longer. Hyaluronic acid is a naturally occurring substance in the body. One of the natural functions of hyaluronic acid in the skin is to provide firmness and hold water in the deep portions of the skin (dermis). Belotero Balance® (+) is manufactured using the cohesive polydensified matrix (CPM®) technology, in which the HA is cross-linked to BDDE in two consecutively executed reactions. The result is a soft and cohesive gel filler. Lidocaine reduces the sensation of pain, helping to improve the comfort of the injection.

### What is Belotero Balance® (+) used for?

Belotero Balance® (+) is used to improve the appearance of undereye hollows in adults over the age of 21 (see Figure 1). The lidocaine in the gel reduces discomfort from the injection.



**Figure 1 Treatment area for BELOTERO BALANCE® (+)**

### **How Is Belotero Balance® (+) Administered?**

Your doctor will inject a small amount of Belotero Balance® (+) into the skin with a small needle or cannula. A ‘touch-up’ injection is often given four weeks after the first injection to get the optimal improvement or to make the effect last longer. You and your doctor will decide whether a second ‘touch-up’ injection is needed later on. Over half the subjects in the clinical study received a touch-up injection. See Section 6. Clinical Study.

### **3. CONTRAINDICATIONS**

#### **Who should not use Belotero Balance® (+)?**

Your doctor will ask about your medical history to determine if Belotero Balance® (+) is right for you. You should not use Belotero Balance® (+) if you have a history of:

- You have severe allergies, marked by history severe allergic reactions or a history or presence of multiple severe reactions. Use may result in an allergic reaction, anaphylactic shock, or death.
- You are allergic to local anaesthetics, such as lidocaine. Use may result in an allergic reaction.
- You have previous experience with allergic reactions to HA fillers. Use may result in an allergic reaction.

If you are unsure about this, talk about the details of your medical history with your doctor and the risks versus the benefits of using Belotero Balance® (+).

## 4. 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 Belotero Balance<sup>®</sup> (+) 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.
- Do not use Belotero Balance<sup>®</sup> (+) if you have a history of developing big scars or keloids on your skin, as you will most likely get a scar where Belotero Balance<sup>®</sup> (+) is injected.

## 5. Precautions

### What are some of the precautions my doctor should advise me about?

The following are important treatment considerations for you to discuss with your doctor and understand to help avoid unsatisfactory results and/or complications:

- In the clinical studies, Belotero Balance<sup>®</sup> (+) was evaluated in subjects with moderate or severe undereye hollows.
- Do not use Belotero Balance<sup>®</sup> (+) if you have a skin infection or inflammation such as a pimple, cyst, cold sore, or rash at the injection site. Skin infections or inflammations increase the risk of infection from an injection. Wait until the infection is cleared up before using Belotero Balance<sup>®</sup> (+).
- 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.
- Belotero Balance<sup>®</sup> (+) 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.
- Belotero Balance<sup>®</sup> (+) has not been evaluated in pregnant women, lactating women who are breast feeding, or in subjects less than 22 years of age. Tell your doctor if you are or suspect you are pregnant.
- Tell your doctor if you are using any medication that prolong bleeding, such as aspirin or other blood thinners. As with any injection, this may increase risk of bruising or bleeding at the injection site.
- Radiation therapy or drugs that decrease your immunity or resistance to infections, such as chemotherapy and immune suppressing drugs, may increase your risk of infection from an injection of Belotero Balance<sup>®</sup> (+).
- Tell your doctor if you are planning laser treatments, chemical peels, or other procedures performed on your skin after treatment with Belotero Balance<sup>®</sup> (+), as there may be an increased risk that you will have a reaction at the injection site.

- Discuss with your doctor all questions you may have about the risks from using Belotero Balance® (+) in relation to any of the above precautions and/or warnings concerning the use of Belotero Balance® (+).

## 6. CLINICAL STUDY

### How was the product studied?

To establish the safety and effectiveness of Belotero Balance® (+) for the treatment of under-eye hollows, 144 patients received treatment with Belotero Balance® (+) using either a needle or cannula. An optional touch-up was performed at 4 weeks to achieve optimal aesthetic correction.

To evaluate the safety of Belotero Balance® (+), subjects noted common side effects in daily diaries. Side effects were also reported by doctors based on office visits with each subject. These office visits included discussing any symptoms or complaints with the subjects and assessing the appearance of their undereye hollow area. To evaluate the effectiveness of the product for the treatment of undereye hollowing, a 5-point scale (Merz Infraorbital Hollow Assessment Scale, MIHAS) (Figure 1) was used. In addition, subjects reported how satisfied they were with their eyes and appearance after treatment.

Figure 1 Merz Infraorbital Hollow Assessment Scale, MIHAS



# Merz Infraorbital Hollow Assessment Scale

## Grade 0 None to Minimal

Nominal to no hollowing; smooth lid to cheek transition along the infraorbital rim

## Grade 1 Mild

Defined hollowing is medial and may extend short of the lateral limbus; no lateral depression

## Grade 2 Moderate

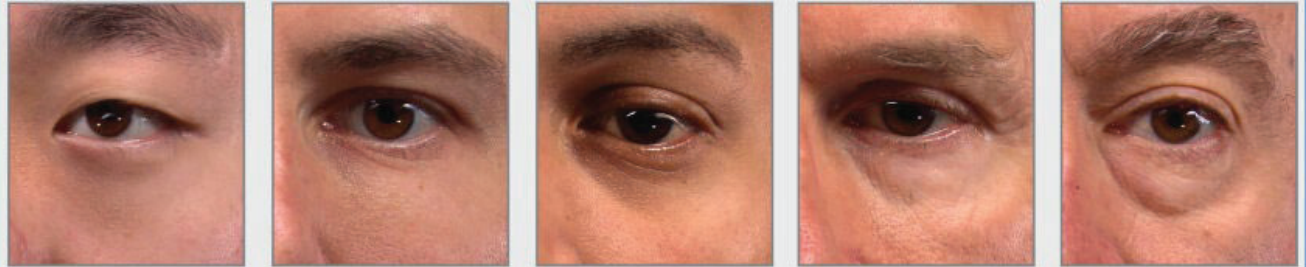
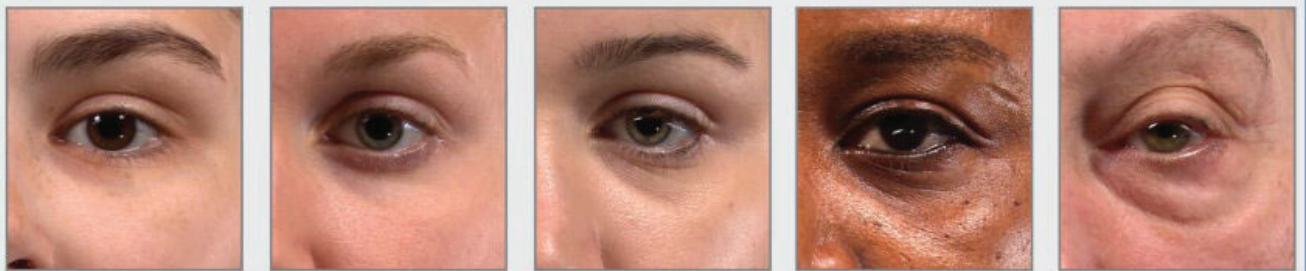
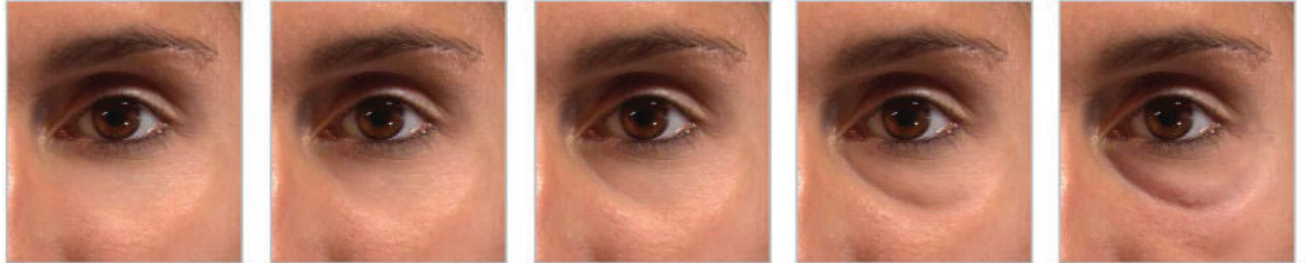
Defined hollowing is to or beyond the lateral limbus but not to the lateral orbital rim; possible mild lateral depression

## Grade 3 Severe

Defined hollowing is to or beyond the lateral limbus with extension of hollowing or a significant depression to the lateral orbital rim

## Grade 4 Extreme

Severe hollowing extends across the entire infraorbital rim



## 7. BENEFITS OF BELOTERO BALANCE® (+)

### What will it accomplish?

Belotero Balance® (+) will add volume to your under-eye area to improve the appearance of under-eye hollowing.

### What did the clinical study show?

Belotero Balance® (+) was found to effectively reduce the appearance of under-eye hollows. The clinical study showed improvement in appearance lasts through 48 weeks for most subjects. 85% of subjects had at least a 1-point improvement in their under-eye hollows 8 weeks after treatment; among these, 81% of subjects had retention of greater than 1-point improvement in the appearance of under-eye hollows 48 weeks after treatment

The study doctors reported:

- 99% of subjects had overall improvement in appearance 8 weeks after treatment
- 95% had overall improvement in appearance 48 weeks after treatment

Subjects reported:

- 98% had overall improvement in appearance 8 weeks after treatment; they were satisfied with the appearance of their eyes 8 weeks after treatment
- On average, looking younger by 2.5 years at 8 weeks after treatment
- 89% would be likely to receive future treatment with Belotero Balance® (+)

### How long does Belotero Balance® (+) last?

While individual results may vary, in the clinical study, the results lasted for over 48 weeks in the majority of subjects. Repeat injections are usually needed to maintain your desired result.

## 8. RISKS

### Have there been side effects (adverse events) reported in clinical studies?

Previously reported injection site responses to Belotero Balance® consisted mainly of short-term inflammatory symptoms including: swelling, induration (firmness of the skin), bruising, redness, erythema (redness), pain, nodule formation, discoloration, itching, and rash. These observations began soon after treatment and typically resolved within 14 days or less.

During the pivotal study, subjects reported side effects in 28-day daily diaries. Adverse events could also be reported by doctors at any time throughout the study.

Based on the clinical study, the likelihood of experiencing an injection site reaction after treatment with Belotero Balance® (+) is shown in Table 1. These injection site reactions were usually mild



(easily tolerated) or moderate (cause discomfort and interfere with daily activities but are tolerable), although a few subjects experienced severe injection site reactions (incapacitating, interrupt daily activities), which included bruising, swelling, redness, itching, and visible lumps and bumps you can feel but not see. At initial injection 132 of the 143 subjects reported at least one injection site reaction. Most of these side effects (90.2%) went away on their own within 4 weeks. Subjects also experienced similar side effects after repeat injection.

**Table 1 Injection Site Reactions<sup>1</sup>**

Injection Site Reactions	Likelihood of Experiencing Under-Eye Injection Site Reaction Belotero Balance® (+)
<b>Swelling</b>	109 out of 143 patients treated (76%)
<b>Bruising</b>	102 out of 143 patients treated (71%)
<b>Visible lumps</b>	93 out of 143 patients treated (65%)
<b>Redness</b>	75 out of 143 patients treated (52%)
<b>Bumps you can feel but not see</b>	69 out of 143 patients treated (48%)
<b>Pain/discomfort (including burning/stinging)</b>	52 out of 143 patients treated (36%)
<b>Itching</b>	27 out of 143 patients treated (19%)
<sup>1</sup> Based on the 143 subjects treated with Belotero Balance® (+) who provided information about side effects after their initial treatment.	

**Have there been unwanted side effects reported from the use of this product from regular use, outside of clinical trials?**

The following unwanted side effects were reported after the product was approved for use. Because it is not known how many people have been treated with this product since it was approved, it is not possible to estimate reliably what percent of patients have had each of these side effects.

These side effects are listed here because they are serious or because they might have been caused by Belotero Balance®:

- Allergic reactions including localized swelling of the skin and soft tissues, possibly including the airway opening (Quincke’s edema);
- A severe allergic reaction which needs medical treatment right away (Anaphylactic shock)
- Uneven sides of the face
- Bruising
- Bumps/Lumps
- Discoloration
- Swelling (Edema)
- Redness (Erythema)
- Firm, inflamed bump under the skin (Granuloma)
- Collection of blood under the skin (Hematoma)
- Hives
- Firmness of the skin from swelling or inflammation (Indurations)
- Infection

- Inflammation
- Movement of the filler to another area in the skin where it was not injected
- Numbness
- Blockage of a blood vessel (Vascular Occlusion)
- Death of an area of skin (Necrosis)
- Solid or cyst like bumps under the skin (Nodules)
- Pain
- Small skin lesion with pus (Pustule)

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.

Rarely, the doctor may accidentally inject the product into a blood vessel, which can cause injury to the blood supply. 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 death of tissue (skin necrosis) with temporary scabs, permanent scarring of the skin or vision changes (including blindness), and stroke. Please contact your doctor immediately if you experience these symptoms.

Based on information reported to Merz about the use of Belotero Balance (+)<sup>®</sup>, your physician may recommend additional treatments after Belotero Balance (+)<sup>®</sup>: antibiotics, corticosteroids, antihistamines, pain medications, hyaluronidase, massage, warm compress, surgical removal, and drainage.

This information is not medical advice and is not intended to be read as medical advice. You should discuss with your doctor what treatments are right for you, if any.

## ABOUT THE PROCEDURE

### Do the injections hurt?

Injections may cause some discomfort during and after the procedure. Belotero Balance® (+) contains the anaesthetic lidocaine, which can reduce the sensation of pain. You and your doctor may also decide to numb the treatment area with a topical or injected anaesthetic to further reduce your discomfort.

### What can I expect to happen at a treatment session?

Note that each doctor may have a different process for assessing and treating patients. The following is an example of what you would experience with a typical procedure:

#### **Before Treatment:**

- Your doctor will answer all your questions and prepare you for the treatment. You can use the space at the end of this Guide to write down your questions before you see your doctor.
- Your doctor will ask you questions about your medical history. You should inform your doctor about any medicines and nutritional supplements that you are taking.
- Your doctor will clean the area where the injections will be given.
- You and your doctor will determine if a topical or local anaesthetic is needed.

#### **During Treatment:**

- Your doctor will inject small amounts of Belotero Balance® (+) into the skin using a thin needle until you have received the amount of visible change.
- Your doctor may gently massage the treatment area to ensure the product is evenly distributed.

#### **After Treatment:**

- Your health care provider will give you specific after treatment care instructions.
- 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), white appearance of the skin, or unusual pain during or shortly after treatment, you should notify your health care practitioner immediately.
- Within the first 12-24 hours, patients should avoid touching/pressing treated parts of the face, applying make-up to treated parts of the face, strenuous exercise, and consuming alcoholic beverages. Patients should also avoid taking anti-coagulation, anti-platelet, or thrombolytic medications, aspirin or non-steroidal anti-inflammatory drugs or other substances known to increase coagulation time for three days after treatment.
- Your doctor may periodically apply an ice pack to the treatment area to help reduce swelling.

## **How many treatments are required to get the look I want?**

The number of treatments required to get the look you want depends on your face and your personal treatment plan. Your doctor and you will decide the number of treatment sessions you will need and the amount of Belotero Balance® (+) you will need at each treatment session. A touch-up treatment may be required to get the desired outcome.

## **How do I decide about using Belotero Balance® (+)?**

Ask your doctor if you will benefit from treatment with Belotero Balance® (+). If you and your doctor decide that Belotero Balance® (+) is for you, you will then talk about your complete medical history with your doctor. It is important to tell your doctor everything in your medical history, including but not limited to, all medicines and supplements that you are taking, any past and present allergies and their seriousness, and all current or past medical conditions. Your doctor will discuss the possibility of developing any of the side effects from the injection of Belotero Balance® (+) and how serious these may be.

## **WHEN TO CALL YOUR DOCTOR**

### **When should I call my doctor?**

Call your doctor immediately if you have:

- 1) Changes in your vision
- 2) 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)
- 3) White appearance of the skin
- 4) Unusual pain during or shortly after treatment

Be sure to call your doctor if you have:

- 1) Significant pain away from the injection site
- 2) Any redness and/or visible swelling that lasts for more than a few days
- 3) Any side effect that occurs weeks or months after treatment
- 4) Any other symptoms that cause you concern

## **WHERE DO I GO FOR MORE INFORMATION?**

If you believe that you have experienced a serious problem related to Belotero Balance® (+) injectable gel, you should call your doctor. You may also contact Merz North America, Inc immediately at 1-844-469-6379 or email [AxUS-adverse.events@merz.com](mailto:AxUS-adverse.events@merz.com).

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

## QUESTIONS FOR MY DOCTOR

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