BELOTERO BALANCE®

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

PATIENT INFORMATION SHEET

BEFORE USING **BELOTERO BALANCE**, PLEASE READ THE FOLLOWING INFORMATION THOROUGHLY. Please direct any questions to Merz North America, Inc, Franksville, WI 53126; (866) 862-1211.

DESCRIPTION OF DEVICE

BELOTERO BALANCE is a hyaluronic acid gel. It has no color.

INDICATIONS/INTENDED USE

BELOTERO BALANCE is used to smooth out and fill in the fold or wrinkle that goes from the side of the nose to the corner of the mouth (nasolabial fold) as shown in figure 1 below.

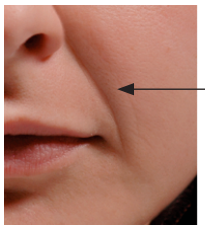


Figure 1. Facial Nasolabial Fold

HOW IS BELOTERO BALANCE ADMINISTERED?

Your doctor will inject a small amount of BELOTERO BALANCE into the skin using a small needle. The doctor may first inject a local anesthetic such as lidocaine to numb the area.

A "touch up" injection is often given 2 weeks after the first injection to get the optimal smoothing and rounding of skin or to make the effect last longer. You and your doctor will decide whether a second "touch up" injection is needed later on. In one study, 67 out of 93 subjects had a second injection of BELOTERO BALANCE. In another study, 103 out of 118 subjects were given a second injection.

CONTRAINDICATIONS

You should not use BELOTERO BALANCE if you have severe allergies or a history of allergic reactions to hyaluronic acid, local anesthetics such as lidocaine, or to small amounts of protein from bacteria. Injections in such patients could result in allergic reactions, anaphylactic shock, or death.

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.

WARNINGS

- BELOTERO BALANCE should not be injected into blood vessels. Injection into blood vessels will block and destroy the vessel.
- If you easily develop big scars or keloids on your skin do not use BELOTERO BALANCE because you will most likely get a scar where BELOTERO BALANCE is injected.

PRECAUTIONS

- Injection site reactions to BELOTERO BALANCE injection include the following: swelling, bruising, redness, pain, rash, development of small bumps, inflammation, itching, and discomfort. One out of two subjects had at least one of these reactions after injection of BELOTERO BALANCE. In 9 out of 10 people these reactions are not serious and go away within 1 to 2 weeks. There is a small chance that they will last longer than 2 weeks in some people.
- Do not use BELOTERO BALANCE 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.
- Until any initial swelling and redness have gone away and puncture sites have healed you should minimize exposure of the treated area to excessive sun, UV lamp exposure, and extreme cold weather.
- BELOTERO BALANCE should only be used by a physician trained in the correct procedure to inject dermal fillers and who completely understands the entire package insert and physician label.
- BELOTERO BALANCE has not been evaluated in pregnant women, lactating women who are breast feeding, or in subjects less than 21 years of age.
- Patients who bleed easily or are taking aspirin or other drugs which prevent blood clotting (blood thinners) may have a greater risk for bleeding and/or bruising at the site where BELOTERO BALANCE is injected.
- Radiation therapy or drugs which decrease your immunity or resistance to infections, such as anti-cancer drugs, may increase your risk of infection from an injection of BELOTERO BALANCE.
- Laser treatments, chemical peels, or other procedures performed on your skin after treatment with BELOTERO BALANCE, may increase the 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.

RISKS OF USING BELOTERO BALANCE

Injection Site Reactions

Injection site reactions to BELOTERO BALANCE are common. In three US clinical studies, more than half of all subjects injected with BELOTERO BALANCE had one or more injection site reactions. All subjects were asked to keep a daily diary to record any injection site reaction, how severe the reaction was, how long it lasted and how fast it improved. Table 1 below lists the reactions that were reported by patients during the studies, the number of patients who had them, and the maximal severity of the reactions.

Table 1. Number of Subjects with Injection Site Reactions to BELOTERO BALANCE and Maximal Severity of Reactions*

	Number of Subjects who had Reactions and the Maximum Severity of the Reactions (out of 211 subjects total)			
Injection Site Response	TOTAL	MILD	MODERATE	SEVERE
Swelling	145 (68.7%)	60 (28.4%)	65 (30.8%)	20 (9.5%)
Nodule (Solid Raised Area)	92 (43.6%)	46 (21.8%)	37 (17.5%)	9 (4.3%)
Bruising	115 (54.5%)	46 (21.8%)	51 (24.2%)	18 (8.5%)
Induration (Hardening of the Tissue)	107 (50.7%)	52 (24.6%)	45 (21.3%)	10 (4.7%)
Erythema (Redness)	109 (51.7%)	55 (26.1%)	48 (22.7%)	6 (2.8%)
Pain	103 (48.8%)	68 (32.2%)	26 (12.3%)	9 (4.3%)
Discoloration	61 (28.9%)	32 (15.2%)	25 (11.8%)	4 (1.9%)
Pruritus (Itching)	46 (21.8%)	37 (17.5%)	9 (4.3%)	0 (0%)
*Reported by patients				

Swelling (145 out of 211 subjects), bruising (115 out of 211 subjects), redness (109 out of 211 subjects), and induration or hardening of the tissue (107 out of 211 subjects) were the four most commonly reported skin reactions to BELOTERO BALANCE. These occurred in more than half of all subjects.

Table 2 shows how long each skin reaction lasted after injection of BELOTERO BALANCE and for how many patients, as reported in the patient diaries.

Table 2. Duration of Injection Site Skin Reactions

	Number of Subjects who had Skin Reactions and # of Days Each Skin Reaction Lasted (out of 211 subjects total)			
Injection Site Reaction	≤3 DAYS	4-7 DAYS	8-14 DAYS	>14 DAYS
Swelling	66 (31.3%)	51 (24.2%)	17 (8.1%)	11 (5.2%)
Nodule (Solid Raised Area)	27 (12.8%)	31 (14.7%)	17 (8.1%)	17 (8.1%)
Bruising	29 (13.7%)	46 (21.8%)	34 (16.1%)	6 (2.8%)
Induration (Hardening of the Tissue)	46 (21.8%)	29 (13.7%)	20 (9.5%)	12 (5.7%)
Erythema (Redness)	66 (31.3%)	27 (12.8%)	10 (4.7%)	6 (2.8%)
Pain	72 (34.1%)	22 (10.4%)	4 (1.9%)	5 (2.4%)
Discoloration	24 (11.4%)	14 (6.6%)	17 (8.1%)	6 (2.8%)
Pruritus (Itching)	32 (15.2%)	8 (3.8%)	3 (1.4%)	3 (1.4%)

The results showed that:

- The majority of skin reactions are gone within one week
- Injection site reactions in 9 out of 10 subjects lasted less than 2 weeks.
- Swelling, pain, and redness lasted less than 3 days in 1 out of 3 subjects
- Skin discoloration, "dent" in the skin, bruising, swelling, and nodules may last longer than 2 weeks in approximately 1 out of 10 people.

During the clinical studies for BELOTERO BALANCE, the physicians recorded reactions to BELOTERO BALANCE that were seen at each visit during the study. Table 3 presents the reactions that were recorded by the physician during the study.

Table 3. Reactions Recorded by the Physician

Description of Reaction	BELOTERO BALANCE Maximum Reaction Severity (out of 211 subjects total)			
	TOTAL	MILD	MODERATE	SEVERE
Any Reaction	189 (89.6%)			
Injection Site Swelling	135 (64.0%)	55 (26.1%)	60 (28.4%)	20 (9.5%)
Injection Site Induration (Hardening)	104 (49.3%)	50 (23.7%)	44 (20.9%)	10 (4.7%)
Injection Site Bruising	104 (49.3%)	40 (19.0%)	49 (23.2%)	15 (7.1%)
Injection Site Erythema (Redness)	102 (48.3%)	53 (25.1%)	44 (20.9%)	5 (2.4%)
Injection Site Pain	95 (45.0%)	63 (29.9%)	24 (11.4%)	8 (3.8%)
Injection Site Nodule (Raised, Hard Area)	91 (43.1%)	46 (21.8%)	36 (17.1%)	9 (4.3%)
Injection Site Discoloration	61 (28.9%)	33 (15.6%)	24 (11.4%)	4 (1.9%)
Injection Site Pruritus (Itching)	44 (20.9%)	35 (16.6%)	9 (4.3%)	0 (0%)
Application Site Exfoliation (Skin Peeling)	6 (2.8%)	4 (1.9%)	1 (0.5%)	1 (0.5%)
Injection Site Rash	5 (2.4%)	3 (1.4%)	2 (0.9%)	0 (0%)

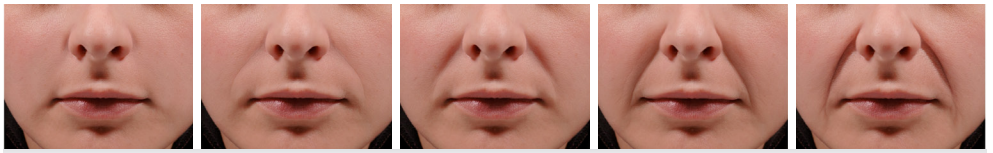
In the main clinical study, 3/118 (2.5%) subjects had at least one non-injection site adverse event. The non-injection site AEs included moderate hives-like reaction, mild herpes simplex, and mild headache. Since each patient received BELOTERO BALANCE and Collagen Control, the cause of these events could not be determined. In the Fitzpatrick IV, V, VI (individuals with darker skin) study 4/93 (4.3%) subjects experienced 5 non-injection site AEs. These were moderate headache, moderate swelling on the side of the nose, moderate cold sore, moderate lip numbness, and mild lip dryness. BELOTERO BALANCE is a prescription medical device and should only be administered by a trained physician. BELOTERO BALANCE has not been evaluated in pregnant women, lactating women who are breastfeeding, or in subjects less than 21 years of age.

BENEFITS OF BELOTERO BALANCE?

Hyaluronic acid is a naturally occurring substance in the body. One of the natural functions of hyaluronic acid is to help provide structural form and shape to the external features of the body. This property of hyaluronic acid is the basis for BELOTERO BALANCE's effectiveness as a dermal filler.

BELOTERO BALANCE smoothes, adds volume, and fills out folds in the skin such as the nasolabial fold. The photos below in Figure 2 show variations in the appearance of the facial nasolabial folds from extremely deep (#4) on the far right to absent (#0) on the far left. You and your doctor will decide how much smoothing is right for you to get the desired effect.

Figure 2. Gradation of Facial Nasolabial Fold Appearance from Absent, #0 (Far Left) to Extreme, #4 on the Far Right



0 - Absent
no visible fold; continuous skin line

1 - Mild
shallow but visible fold with a slight indentation; minor facial feature

2 - Moderate
moderate deep folds; clear feature visible at normal appearance but not when stretched

3 - Severe
very long and deep folds; prominent facial feature; less than 2 mm visible fold when stretched

4 - Extreme
extremely deep and long folds, detrimental to facial appearance; 2 to 4 mm V-shaped fold when stretched

HOW LONG DOES BELOTERO BALANCE LAST?

The filling effect of BELOTERO BALANCE lasts about 6 months and then slowly goes away. The photographs in Figure 2 show the rating scale used during the studies to rate the appearance of nasolabial folds. In clinical trials, 170 out of 211 subjects still demonstrated an effect of at least 2 points on the rating scale 6 months after an initial BELOTERO BALANCE treatment and one touch-up treatment. For example, a subject that started the study with a wrinkle rating of 3 (severe) would be rated either 0 (absent) or 1 (mild). The appearance of the folds over time as the filling and smoothing effect of BELOTERO BALANCE wears off is illustrated in Figure 2 generally moving from left to right on the scale.

CLINICAL TRIALS WITH BELOTERO BALANCE

Three clinical trials were conducted in the United States which evaluated the safety and effectiveness of BELOTERO BALANCE for a period of 24 weeks, in a total of 211 adult subjects, 18 to 75 years of age. The subjects consisted of both light and dark skin types and approximately 9 out of 10 subjects were female. In these studies an optional "touch-up" injection of a lesser volume of BELOTERO BALANCE was given to almost all subjects about 2 weeks after the first treatment.

The results indicated that BELOTERO BALANCE when injected into the skin, was clinically effective for filling and smoothing the nasolabial folds on the face. The smoothing and filling effects of BELOTERO BALANCE on the nasolabial fold were similar in light skin and dark skin type subjects.

The only adverse events or side effects that were related to injection of BELOTERO BALANCE were skin reactions at the injection site. These occurred in one-third to one-half of all subjects. None was serious and most were gone in 1 to 2 weeks (see RISKS above).

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, about all medicines that you are taking, any past and present allergies and their seriousness, and all current or past medical conditions you have had. Your doctor will discuss what your chances are for getting any of the side effects from injection of BELOTERO BALANCE and how serious they may be.

WHERE DO I GET MORE INFORMATION?

For further information please call Merz North America at (866) 862-1211.

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