BELOTERO® BALANCE
(Injectable hyaluronic acid)
Belotero® Balance implant package is provided sterile.

Caution: Federal (USA) law restricts this device to sale by or on the order of a physician or other licensed healthcare practitioner.
Information for the use of **BELOTERO BALANCE** is provided in this Labeling for Physicians and the Instructions for Use, as well as in Labeling for Patients.
BEFORE USING **BELOTERO BALANCE**, PLEASE READ THE FOLLOWING INFORMATION THOROUGHLY. Please direct any questions to Merz Pharmaceuticals, LLC, Greensboro, NC, 27410; (866) 862-1211.

DESCRIPTION
BELOTERO BALANCE is a sterile, bioresorbable, non-pyrogenic, viscoelastic, clear, colorless, homogeneous gel device. **BELOTERO BALANCE** is a bacterially fermented, injectable, hyaluronic-acid-based dermal filler. After extraction and purification, hyaluronic acid manufactured from streptococcal cultures is cross-linked with a binding agent 1,4-butanediol diglycidyl ether (BDDE) in two consecutively executed reactions and reconstituted in a physiologic buffer at pH 7 and concentration of 22.5 mg/mL.

INTENDED USE/INDICATIONS
BELOTERO BALANCE is indicated for injection into the mid-to-deep dermis for correction of moderate-to-severe facial wrinkles and folds, such as nasolabial folds.

CONTRAINDICATIONS
- **BELOTERO BALANCE** is contraindicated in patients with severe allergies manifested by a history of anaphylaxis, or history or presence of multiple severe allergies.
- **BELOTERO BALANCE** contains trace amounts of gram-positive bacterial proteins, and is contraindicated for patients with a history of allergies to such material.
- **BELOTERO BALANCE** must not be implanted into blood vessels, Implantation of BELOTERO BALANCE into dermal vessels may cause vascular occlusion, infarction, or embolic phenomena.

WARNINGS
- Use of **BELOTERO BALANCE** at specific sites in which an active inflammatory process (skin eruptions such as cold sores, cysts, pimples, rashes, or hives) or infection is present should be deferred until the underlying process has been controlled.
- **BELOTERO BALANCE** must not be injected into blood vessels of any size. Introduction of **BELOTERO BALANCE** into the vasculature may occlude the vessels and can cause infarction of overlying tissue or embolization with resultant necrosis of potentially large areas of distant tissue such as the lip or the nose.
- Injection site responses to **BELOTERO BALANCE** have been observed, consisting mainly of short-term inflammatory symptoms starting early after treatment and with 7 days duration or less. Refer to the ADVERSE EVENTS section for details.

PRECAUTIONS
- **BELOTERO BALANCE** is packaged and designed for single use only. Do not resterilize. Discard any unused product.
- Do not use if the package is opened or damaged or beyond the expiration date cited on the package.
- The safety or effectiveness of **BELOTERO BALANCE** for the treatment of dermal contour defects other than nasolabial folds has not been established in controlled clinical studies. The safety and effectiveness of **BELOTERO BALANCE** use in the lips has also not been evaluated.
- The long term safety and effectiveness of **BELOTERO BALANCE** beyond 96 weeks has not been investigated.
- Based on clinical studies, patients should be limited to 6.0 ml of **BELOTERO BALANCE** per year. The safety of injecting greater amounts has not been established.
- As with all transcutaneous procedures, **BELOTERO BALANCE** injection carries a risk of infection. Standard precautions associated with injectable materials should be followed.
- The safety of **BELOTERO BALANCE** for use during pregnancy, in breastfeeding females, or in patients under 18 years has not been established.
- The safety of **BELOTERO BALANCE** in patients with known susceptibility to recurrent sore throat, or Osler Rendu endocarditis has not been studied.
- **BELOTERO BALANCE** should be used with caution in patients on immunosuppressive therapy.
- Patients who are using substances that reduce coagulation, such as aspirin, non-steroidal anti-inflammatory drugs, and warfarin may, as with any injection, experience increased bruising or bleeding at injection sites.
- As with all invasive procedures, **BELOTERO BALANCE** sessions should be conducted with aseptic technique. Observe universal precautions to minimize risks of potential contact with patient body fluids such as blood at the injection site.
- After use, treatment syringes and needles may be potential biohazards. Handle and dispose of these items in accordance with accepted medical practice and applicable local, state, and federal requirements.
- **BELOTERO BALANCE** is a clear colorless gel without particulates. In the event that the content of a syringe shows signs of separation and/or appears cloudy, do not use the syringe and notify Merz Pharmaceuticals, LLC at (XXX) XXX-XXXX.
- Laser treatment, chemical peeling, or any other procedure based on active dermal response performed after treatment with **BELOTERO BALANCE** may increase the risk of an inflammatory reaction at the injection site. Similarly, the administration of **BELOTERO BALANCE** before the skin has healed completely after such a procedure may also increase the risk of inflammatory reactions.
- **BELOTERO BALANCE** is supplied in a syringe ready for use. **BELOTERO BALANCE** should not be directly mixed with any other products prior to injection of the device. No studies of interactions of **BELOTERO BALANCE** with drugs or other substances or implants have been made.
- The patient should be informed that he or she should minimize exposure of the treated area to excessive sun, UV lamp exposure, and extreme cold weather until any initial swelling and redness have resolved and puncture sites have healed.

ADVERSE EVENTS
The safety of **BELOTERO BALANCE** has been evaluated in three studies and 211 patients. These studies are described below.

Pivotal Clinical Study
Controlled Phase (0-24 Weeks):
In a randomized, controlled clinical trial, 118 subjects at 6 centers, were injected with **BELOTERO BALANCE** in one NLF and bovine collagen control dermal filler (Control) in the contralateral NLF to evaluate the safety and effectiveness of BELOTERO BALANCE in comparison with the Control. Pre-printed diary forms were used by subjects to record specific signs and symptoms experienced during each of the first 14 days after initial and touch-up treatments. Subjects were instructed to rate each common treatment response listed on the diary as "Mild", "Moderate", "Severe", or "None." The combined rates of injection site

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responses reported by >5% of subjects in the pivotal clinical study and the Fitzpatrick Skin Type IV, V, and VI study are summarized by maximum intensity in Table 1 and by duration in Table 2. Adverse events recorded by investigators at study visits are presented in Table 3

Open Label Extension (OLEX) Phase (24-96 Weeks):
95 of 118 subjects who completed the 24 week controlled-phase of the pivotal study received additional treatments with **BELOTERO BALANCE** from Weeks 24 to 96 after the initial treatment. Follow-up visits occurred at 24, 32, 48, 72, and 96 weeks after the initial treatment. At the Week 24 study visit all enrolled subjects received **BELOTEERO BALANCE** in both NLFs to achieve optimal correction. At the Week 32 visit, subjects were allowed a touch-up treatment on one side to balance any observed differences. Subjects could receive additional treatments to both NLFs at weeks 48, 72, or 96 if their wrinkle severity score met the injection criteria (SRS of 2 or 3). No single AE was reported with more than a 5% rate of incidence during the OLEX phase and the safety profile observed during the OLEX phase was similar to that described above during the controlled-phase.

Fitzpatrick Skin Type IV, V and VI Study:
The safety and effectiveness of BELOTERO BALANCE was evaluated in 93 subjects with Fitzpatrick skin phototype scores of IV, V, and VI at 3 U.S. Centers Safety and during a 24 week open label study. Subjects received an initial treatment of BELOTERO BALANCE and were eligible to receive an additional touch-up treatment 2 weeks after the initial treatment if necessary. Subject follow-up visits occurred at weeks 2, 4, 8, 12, 16, and 24 weeks. The safety profile observed during this study was similar to that observed in the pivotal controlled clinical study.

Table 1 - Maximum Intensity of Symptoms Occurring in >5 % of Subjects, Patient Diary

	Belotero Balance Maximum AE Severity [N = 211]				Collagen Control Maximum AE Severity [N = 118]			
Injection Site Response	**Total n(%)**	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**	**Total n(%)**	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Swelling	145 (68.7)	60 (28.4)	65 (30.8)	20 (9.5)	86 (72.9)	36 (30.5)	38 (32.2)	12 (10.2)
Nodule	92 (43.6)	46 (21.8)	37 (17.5)	9 (4.3)	79 (66.9)	32 (27.1)	35 (29.7)	12 (10.2)
Bruising	115 (54.5)	46 (21.8)	51 (24.2)	18 (8.5)	53 (44.9)	26 (22.0)	21 (17.8)	6 (5.1)
Induration	107 (50.7)	52 (24.6)	45 (21.3)	10 (4.7)	62 (52.5)	28 (23.7)	25 (21.2)	9 (7.6)
Erythema	109 (51.7)	55 (26.1)	48 (22.7)	6 (2.8)	79 (66.9)	37 (31.4)	32 (27.1)	10 (8.5)
Pain	103 (48.8)	68 (32.2)	26 (12.3)	9 (4.3)	63 (53.4)	32 (27.1)	26 (22.0)	5 (4.2)
Discoloration	61 (28.9)	32 (15.2)	25 (11.8)	4 (1.9)	35 (29.7)	22 (18.6)	11 (9.3)	2 (1.7)
Pruritus	46 (21.8)	37 (17.5)	9 (4.3)	0	32 (27.1%)	25 (21.2)	7 (5.9)	0

Note 1: Total number of subjects injected with BELOTERO BALANCE includes 118 subjects from the Pivotal study and 93 subjects from the Fitzpatrick IV, V, and VI study.
Note 2: Each subject is counted only once by maximum severity of injection site response.

Table 2 - Duration of Injection Site Responses Occurring in >5% of Treated Subjects, Patient Diary

	Belotero Balance Maximum Duration of Event [N = 211]				Collagen Control Maximum Duration of Event [N = 118]			
Injection Site Response	**≤ 3 Days n(%)**	**4-7 Days n(%)**	**8-14 Days n(%)**	**>14 Days n(%)**	**≤ 3 Days n(%)**	**4-7 Days n(%)**	**8-14 Days n(%)**	**>14 Days n(%)**
Swelling	66 (31.3)	51 (24.2)	17 (8.1)	11 (5.2)	52 (44.1)	24 (20.3)	6 (5.1)	4 (3.4)
Nodule	27 (12.8)	31 (14.7)	17 (8.1)	17 (8.1)	11 (9.3)	10 (8.5)	19 (16.1)	39 (33.1)
Bruising	29 (13.7)	46 (21.8)	34 (16.1)	6 (2.8)	18 (15.3)	27 (22.9)	6 (5.1)	2 (1.7)
Induration	46 (21.8)	29 (13.7)	20 (9.5)	12 (5.7)	27 (22.9)	13 (11.0)	8 (6.8)	14 (11.9)
Erythema	66 (31.3)	27 (12.8)	10 (4.7)	6 (2.8)	45 (38.1)	13 (11.0)	7 (5.9)	14 (11.9)
Pain	72 (34.1)	22 (10.4)	4 (1.9)	5 (2.4)	36 (30.5)	18 (15.3)	7 (5.9)	2 (1.7)
Discoloration	24 (11.4)	14 (6.6)	17 (8.1)	6 (2.8)	19 (16.1)	6 (5.1)	3 (2.5)	7 (5.9)
Pruritus	32 (15.2)	8 (3.8)	3 (1.4)	3 (1.4)	23 (19.5)	2 (1.7)	4 (3.4)	3 (2.5)

Note 1: Total number of subjects on BELOTERO BALANCE includes 118 subjects from the Pivotal study and 93 subjects from the Fitzpatrick IV, V, and VI study.

Note 2: A subject is counted only once by maximum duration of injection site response.

Table 3 – Adverse Events Occuring in >2% of Subjects, Physician Reported

Description of Adverse Event	Belotero Balance Maximum AE Severity [N = 211] Total n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Collagen Control Maximum AE Severity [N = 118] Total n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
Any Adverse Event	189 (89.6)				108 (91.5)			
Injection Site Swelling	135 (64.0)	55 (26.1)	60 (28.4)	20 (9.5)	77 (65.3)	31 (26.3)	35 (29.7)	11 (9.3)
Injection Site Induration	104 (49.3)	50 (23.7)	44 (20.9)	10 (4.7)	57 (48.3)	24 (20.3)	25 (21.2)	8 (6.8)
Injection Site Bruising	104 (49.3)	40 (19.0)	49 (23.2)	15 (7.1)	48 (40.7)	23 (19.5)	21 (17.8)	4 (3.4)
Injection Site Erythema	102 (48.3)	53 (25.1)	44 (20.9)	5 (2.4)	69 (58.5)	32 (27.1)	27 (22.9)	10 (8.5)
Injection Site Pain	95 (45.0)	63 (29.9)	24 (11.4)	8 (3.8)	57 (48.3)	26 (22.0)	25 (21.2)	6 (5.1)
Injection Site Nodule	91 (43.1)	46 (21.8)	36 (17.1)	9 (4.3)	77 (65.3)	30 (25.4)	35 (29.7)	12 (10.2)
Injection Site Discoloration	61 (28.9)	33 (15.6)	24 (11.4)	4 (1.9)	32 (27.1)	19 (16.1)	11 (9.3)	2 (1.7)
Injection Site Pruritus	44 (20.9)	35 (16.6)	9 (4.3)	0	28 (23.7)	21 (17.8)	7 (5.9)	0
Application Site Exfoliation	6 (2.8)	4 (1.9)	1 (0.5)	1 (0.5)	0	0	0	0
Injection Site Rash	5 (2.4)	3 (1.4)	2 (0.9)	0	0	0	0	0

Note 1: Total number of subjects on BELOTERO BALANCE includes 118 subjects from the Pivotal study and 93 subjects from the Fitzpatrick IV, V, and VI study.
Note 2: A subject is counted only once by maximum severity of the adverse event.
Note 3: Adverse events are sorted in decreasing order of incidence for Total Subjects injected with BELOTERO BALANCE.

Non-local Adverse Events (All Causality)
Non-local Adverse Events occurred in 7/211 (3.3%) of the study subjects in the combined pivotal and Fitzpatrick IV, V, VI studies. From the pivotal clinical study, 3/118 (2.5%) subjects had at least one non-local adverse event. The non-local AEs included moderate urticaria, mild herpes simplex, and mild headache. Since each patient received **BELOTERO BALANCE** and Collagen Control, the causality of these events could not be identified. In the Fitzpatrick IV, V, VI study 4/93 (4.3%) subjects experienced 5 non-local Adverse Events. These were moderate headache, moderate swelling on the right side of the nose, moderate cold sore, moderate lip numbness, and milde lip dryness..

Serious Adverse Events
During clinical studies with **BELOTERO BALANCE**, one subject underwent hip arthroplasty, which was classified as a serious adverse event (SAE). There were no SAEs experienced that were related to treatment with **BELOTERO BALANCE**.

Post Marketing Surveillance
The following adverse events were received from post-marketing surveillance for Belotero Balance outside of the United States, that were not observed in the clinical trials with Belotero Balance:

Suspicion of allergic reaction including Quincke's edema, tissues necrosis in the glabellar area after injection, inflammation reaction, injection site granuloma, injection site indurations, hematoma after injection, Tyndall effect, Cordon like effect, bump and pustule at injection site, scarring after injection in the chest.

Time to onset ranged from a few hours to 24 months post-injection and outcome ranged from 'improved' to 'on-going' at last contact.

No serious adverse events has been reported more than 5 times during post-marketing surveillance.

CLINICAL STUDIES
PIVOTAL CLINICAL STUDY

STUDY DESIGN
Controlled Phase (0-24 Weeks):
A blinded, active-controlled, randomized, multicenter trial investigated the effectiveness and safety of **BELOTERO BALANCE** in the treatment of nasolabial fold (NLF) wrinkles. Treatment was determined by a random allocation schedule that assigned one NLF of each subject to **BELOTERO BALANCE** and the opposite NLF to a bovine collagen control dermal filler.

The initial treatment was first evaluated after 2 weeks, at which time an optional touch-up treatment was administered in order to achieve optimal correction. The follow-up phase of the main trial consisted of visits at 2, 4, 8, 12, 16, and 24 weeks after the last treatment.

OLEX Phase (24-96 Weeks):
Upon completion of the controlled phase, subjects were invited to participate in an open-label extension (OLEX) of the trial in which they received treatment with **BELOTERO BALANCE** on both NLFs. The OLEX phase included follow-up visits at 32, 48, 72, and 96 weeks after the initial visit. At each subsequent visit in the OLEX phase, subjects were eligible for retreatment to one or both NLFs if they met the injection criteria of having an SRS of 2 or 3. The OLEX study was designed to obtain data on repeated treatments with respect to both safety and duration of effectiveness.

Study Population
The study enrolled subjects with bilateral nasolabial folds (NLFs) with a 2 or 3 SRS score. Patients were excluded if they had (or were): history of allergic/anaphylactic reactions including hypersensitivity to local anesthetics (e.g., lidocaine), hyaluronic acid preparations and/or gram-positive bacterial proteins; known history of keloids or bleeding disorders; active inflammatory process in the NLF area (skin eruptions such as cysts, pimples, rashes, cancerous/pre-cancerous lesions, psoriasis, neurodermatitis or any other active skin disease) or severe scarring that might interfere with the study assessments; pregnant, planning to become pregnant during the study or breast feeding; planning to undergo major facial surgery during the course of the study; clinically important disease within 3 months of the study (e.g., significant laboratory test abnormalities, MI, stroke, cancer, connective tissue diseases, systemic infection, uncontrolled diabetes, and medical conditions that might require use of immunosuppressive medications during the trial); severe physical, neurological or mental disease; excessive facial hair that might interfere with wrinkle evaluation; any systemic or dermatologic disorder which would interfere with the study results or increase the risk of an adverse event; used exclusionary medications or treatments; or participated in a clinical investigation within 30 days prior to the first planned injection. Entry criteria also required females were post-menopausal for at least 1 year, had a hysterectomy or tubal ligation or agreed to use an approved method of birth control.

STUDY ENDPOINTS
Wrinkle evaluations (Severity Rating Scale [SRS]) were made by a Blinded Evaluator at each study site with the aid of a validated photo-numeric scale. The primary effectiveness comparison between study treatments was made on the difference in SRS rating (assessed by the Blinded Evaluator) at the 12-Week follow-up time point during the controlled phase. Effectiveness of **BELOTERO BALANCE** treatment was determined by demonstrating non-inferiority of **BELOTERO BALANCE** to the bovine collagen dermal filler control with respect to the primary efficacy endpoint.

NLF correction during the OLEX phase was assessed by the treating investigator at each of the study visits by rating the wrinkle SRS scores. Duration of effectiveness was determined in comparison with the subject's baseline investigator SRS rating from the controlled-phase.

SUBJECT DEMOGRAPHICS
Controlled Phase (0-24 weeks):
A total of 118 subjects at 6 investigational sites in the United States (US) were enrolled in the study and received at least one injection in each NLF. Entrance to the study required an SRS score of 2 (moderate) or 3 (severe) on each NLF. Of the 118 subjects treated, 106 (89.8%) subjects completed all assessments through Week 24. Subject demographics are summarized in Table 4.

Table 4 – Controlled Phase Subject Demographics

	Number of Subjects (%)
Sex	
Female	109 (92.4)
Male	9 (7.6)
Race	
White	114 (96.6)
Black/African-American	2 (1.7)
Asian	1 (0.8)
Other	1 (0.8)
	Mean (SD)
Age	52.4 (9.5)

OLEX Phase (24-96 Weeks)
95 of the 106 (89.6%) subjects who completed the controlled phase study elected to receive retreatment with **BELOTERO BALANCE** on both sides in the OLEX portion of the study. Subject demographics in the OLEX phase were similar to the controlled phase described above.

STUDY TREATMENT
Controlled Phase (0-24 Weeks):
Subjects received an average of 1.16 mL of **BELOTERO BALANCE** and 1.37 ml of Control implant at the initial injection. 94 of 118 (79.7%) subjects received retreatment 2 weeks later for optimal correction and received an average of 0.81 mL of **BELOTERO BALANCE** and 0.94 ml of Control implant at retreatment (touch-up)

OLEX Phase (24-96 Weeks):
During the OLEX phase, 85 of 95 (89.5%) subjects were evaluated through Week 96. The mean cumulative volume of **BELOTERO BALANCE** received from Week 24 through Week 96 was 1.75 mL in the NLF initially treated with **BELOTERO BALANCE** and 2.45 mL in the NLF initially treated with Control. The mean number of injections received during the OLEX phase was 2.6 in the NLF initially treated with **BELOTERO BALANCE** and 2.9 in the NLF initially treated with Control with a mean time between injections of 37 weeks and 31 weeks respectively. The average time between injections following the Week 24 injection (start of OLEX phase) is presented in Table 5.

Table 5 – Average Time between Injections During the OLEX Phase

Study Visit	Side Previously Injected with Belotero	Side Previously Injected with Collagen Control
Number of Injections	85	87
Mean Number of Weeks between injections (SD)	37.04 (15.62)	30.87 (13.59)
Min, Max (Weeks)	15.4, 73.1	9.7, 71.9

EFFECTIVENESS

Controlled Phase

The results from the controlled phase demonstrate that **BELOTERO BALANCE** is non-inferior to the Control in the correction of NLFs. The primary effectiveness results from the pivotal clinical study for **BELOTERO BALANCE** were based on the Blinded Evaluator's assessment of NLF severity (SRS) at Week 12 and are presented in Table 6.

Table 6 – Mean Blinded Evaluator SRS Scores

Timepoint	N	Belotero	Collagen Control
Initial Treatment	118	2.5	2.5
Week 12	118	1.25	1.51

Immunogenicity

A pre-existing antibody response against **BELOTERO BALANCE** was not observed in any subjects and 5/116 (4.3%) subjects developed an antibody response after BELOTERO BALANCE injection. None of the subjects with elevated anti-**BELOTERO BALANCE** titers post-treatment experienced adverse events that were consistent with the clinical symptoms identified in MedDRA as possibly reflecting a local or systemic hypersensitivity reaction. No patient displayed a positive IgE response against the device.

FITZPATRICK SKIN TYPE IV, V, VI STUDY:

STUDY DESIGN

The safety and effectiveness of **BELOTERO BALANCE** in the treatment of NLFs in subjects with Fitzpatrick Skin Phototype scores of IV, V and VI was investigated in an open label, multi-center trial. Treatment consisted of injection of **BELOTERO BALANCE** into both nasolabial folds of subjects who were an IV, V or VI on the Fitzpatrick Skin Type Scale and whose nasolabial folds were a 2 or 3 on the Wrinkle Severity Scale (SRS). The initial treatment was evaluated after 2 weeks and if necessary, an optional touch-up treatment was administered in order to achieve optimal correction. The follow-up phase consisted of visits at Weeks 2, 4, 8, 12, 16, and 24 after the last treatment. Wrinkle evaluations (SRS) were made by an Evaluator Investigator at each study site with the aid of a validated, photonumeric scale.

STUDY ENDPOINTS

The primary objective of this study was to evaluate the safety of **BELOTERO BALANCE** in the treatment of NLFs in individuals with Fitzpatrick Skin Type scores IV and greater. The safety profile of **BELOTERO BALANCE** in this study population was similar to that observed in the pivotal study (see Adverse Events). Effectiveness of NLF correction (as evaluated by the Evaluator Investigator) was evaluated as a secondary objective. The main effectiveness comparison between baseline rating and after treatment rating was made on the difference in SRS rating (assessed by Evaluator Investigator) at the 12 week follow-up time point. Secondary effectiveness evaluations included investigator/global assessments, investigator visual analogue scale assessments, and Treating Investigator SRS grades.

STUDY DEMOGRAPHICS

A total of 93 subjects with Fitzpatrick skin type IV, V or VI were enrolled at 3 investigational sites in the US. Of 93 subjects treated, 88 subjects completed the study. Subject demographics are summarized in Table 7.

Table 7: Demographic Summary by Fitzpatrick Skin Type for All Subjects with Skin Types IV, V and VI

	Number of Subjects (%)
Sex	
Female	80 (86.0)
Male	13 (14.0)
Race	
White	1 (1.1)
Black/African-American	90 (96.8)
Asian	1 (1.1)
Other	0
Fitzpatrick Skin type	
IV	4 (3.7)
V	37 (34.4)
VI	52 (48.4)
	Mean (SD)
Age	51.5 (10.1)

STUDY TREATMENT

The mean volumes of **BELOTERO BALANCE** initially injected into the left and right NLFs were 1.46 and 1.47 mLs, respectively. 66 of 93 subjects (70.1%) received touch-up injections. All but 1 subject received touch-up injections in both NLFs. The mean volumes of **BELOTERO BALANCE** injected for the touch-up procedure were 0.93 mL in the left NLF and 0.90 mL in the right NLF.

HOW SUPPLIED

BELOTERO BALANCE is supplied in a sterile 1-mL prefilled glass syringe with an ergonomically shaped injection plunger and finger grip. Individual treatment syringes are provided with 30-gauge needles for single patient use and ready for injection. Do not resterilize the needle. Do not use if package is opened

or damaged. In the event that the package is opened or damaged, do not use the syringe and return to Merz Pharmaceuticals, LLC at 4215 Tudor Lane, Greensboro, NC, 27410-8105.

STORAGE
BELOTERO BALANCE should be stored at room temperature (up to 30°C/86°F), away from heat. DO NOT REFRIGERATE

BELOTERO BALANCE has a clear colorless (transparent) appearance. In the event that the syringe contains material that is not clear, do not use the syringe and notify Merz Aesthetics, Inc immediately at (866) 862-1211 or email complaints@merzaesthetics.com.

To place an order, contact Merz Aesthetics, Inc. at (866) 862-1211.

Patient Treatment

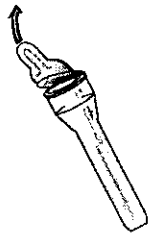
1. Patient Counseling.

o **BELOTERO BALANCE** is a monophasic gel with variable density zones that can be injected using a 30-gauge needle. Prior to treatment with **BELOTERO BALANCE**, the patient's medical history should be obtained, and the patient should be fully apprised of the indications, contraindications, warnings, precautions, treatment responses, adverse reactions, and method of administration.

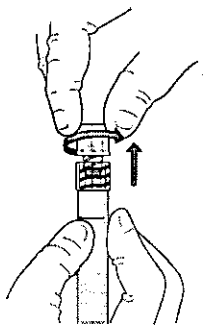
2. Injection Needle.

To attach needle to syringe (to assure proper needle attachment, use needles provided)

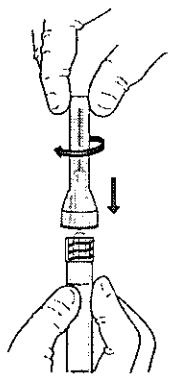
a. Peel sealed cover off needle guard.



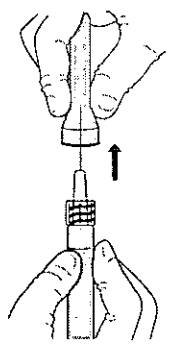
b. Remove Luer Lok™ end closure (tip cap) from syringe.



c. Attach needle to syringe and twist to secure. Fully seat hub of needle in syringe. Do not over-tighten as this may break the needle and/or dislodge the syringe.



d. Pull off the needle guard to expose needle.



STERILE NEEDLES

- Follow national, local, or institutional guidelines for use and disposal of medical sharp devices. Obtain prompt medical attention if injury occurs.
- To help avoid needle breakage, do not attempt to straighten a bent needle. Discard it and complete the procedure with a replacement needle.
- Do not reshield used needles. Recapping by hand is a hazardous practice and should be avoided.
- Discard unshielded needles in approved sharps collectors.

3. Depth of Injection and Injection Technique.

- The injection technique of **BELOTERO BALANCE** with regard to the angle and orientation of the bevel, the depth of injection, and the quantity administered may vary. A linear-threading technique, tunneling technique, serial puncture injections, or a combination of these have been used to achieve optimal results. Care must be used to avoid intravascular injection regardless of technique used.
- For the linear threading technique and/or tunneling technique, the needle is inserted at an approximate angle of 30° parallel to the length of the wrinkle or fold. **BELOTERO BALANCE** should be injected into the mid-to-deep dermis. The injection can be performed with a constant low-to-moderate pressure on the plunger while slowly and gradually withdrawing the needle. Slight elevation of the skin should be observed without significant blanching of the skin. To avoid visible lumps and/or discoloration, avoid injection of **BELOTERO BALANCE** into the superficial dermis when removing the needle.
- Signs of blanching are indicative of injection in the mid-to-superficial dermis or intravascular injection, which should be avoided. If blanching occurs, the injection should be stopped immediately and the area massaged until it returns to normal color. If normal color does not return, consider institution of vasodilatory measures.

4. Volume per Injection.

In clinical trials, the average volume of **BELOTERO BALANCE** needed to achieve optimal correction was 1.5 mL per nasolabial fold. Correct only to 100% of the volume desired. It is important to avoid overcorrection.

5. Massage During Injection Site.

When the injection is complete, the site may be gently massaged, if necessary.

6. Post Treatment Care.

The physician should instruct the patient to promptly report to her/him any evidence of problems possibly associated with the use of **BELOTERO BALANCE**, such as vascular compromise, or redness and/or visible swelling that lasts for more than a few days or any other symptoms that may cause the patient concern. Patients should also be advised that additional injections may be required to achieve and maintain maximum correction, and that individual results may vary.

PATIENT INSTRUCTIONS

It is recommended that the following information be shared with patients:

- Within the first 24 hours, patients should avoid strenuous exercise, extensive sun or heat exposure, aspirin or non-steroidal anti-inflammatory drugs, and alcoholic beverages. Exposure to any of the above may cause temporary redness, swelling, and/or itching at the injection sites.
- To report an adverse reaction, contact Merz Aesthetics, Inc at (866) 862-1211.

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