1 General Information

1.1 Name or Trade Name

Belotero® Revive

1.2 Device Description

Belotero® Revive is a sterile, non-pyrogenic, viscoelastic, colourless, transparent cross-linked sodium hyaluronate gel of non-animal origin in a physiological phosphate buffer containing glycerol.

Belotero® Revive is an injectable resorbable implant intended to treat early-signs of photodamaged skin via rehydration of dry and very dry skin and smoothening of superficial fine lines.

Belotero® Revive is indicated for treatment of early signs of photodamaged facial skin, as characterized by dehydration and presence of superficial fine lines.

The expected lifetime of Belotero® Revive after injection depends on several procedural (e.g. injection technique, injectable implant characteristics, etc.), treatment-related (e.g. injection site, injection volume, touch up treatments etc.) and patient related (desired filling effect, patient metabolism rate, etc.) factors and can last up to 9 months after injection.

1.3 List of Ingredients

Belotero® Revive is composed of high molecular weight sodium hyaluronate (20.0 mg/ml), cross-linked using 1,4-Butanediol Diglycidyl Ether (BDDE), in a physiological phosphate buffer containing glycerol (17.5 mg/mL).

Cross-linked sodium hyaluronate:	20.0 mg/ml
Glycerol:	17.5 mg/ml
Phosphate buffer pH 7 q.s.:	1 ml

Belotero® Revive is latex and pyrogen free, it does not contain any animal or blood derivate substance. Belotero® Revive does not contain carcinogenic, mutagenic or toxic to reproduction substances (‘CMR’), nor substances having endocrine-disrupting properties.

Belotero® Revive contains 1,4-butanediol diglycidyl ether (BDDE) which is considered to be the safest of the commonly used cross-linkers for dermal fillers. The BDDE solution used during manufacturing of Belotero® Revive is considered as safe regarding impurities since none is considered as hazardous molecules.

Validated quality controls ensure that the residual BDDE content in Belotero® Revive does not exceed predefined limits which do not point to any potential safety concern and allow to warrant that Belotero® Revive has an excellent safety profile. If you have any concern or questions with regard to BDDE (e.g. in case of known allergies), please consult your healthcare professional.

2 Contraindications

Belotero® Revive is contra-indicated:

  - In case of known hypersensitivity to one of the product's components, especially to sodium hyaluronate or to glycerol or BDDE,
  - In pregnant and breast-feeding women,
  - In young patients under 18 years old,
  - In patients presenting a general infection.
  - In patients presenting an active auto-immune disease.
- Do not inject Belotero® Revive into blood vessels.
- Do not inject Belotero® Revive into areas presenting cutaneous inflammation or infection due to e.g. immunological, allergic, bacterial, fungal or viral causes.
- Do not inject Belotero® Revive into an area previously treated with a permanent dermal filler.
- Do not inject Belotero® Revive in the glabellar or nose region.

3 Warnings

- Sodium hyaluronate precipitates in the presence of quaternary ammonium salts (such as benzalkonium chloride). It is therefore recommended that Belotero® Revive does not come into contact with such substances.
- Rare but serious adverse events associated with the intravascular injection of soft tissue fillers in the face have been reported and include temporary or permanent vascular complication, vision impairment, blindness, cerebral ischemia or cerebral hemorrhage, leading to stroke, skin necrosis, and damage to underlying facial structures. Practitioners should immediately stop the injection if a patient exhibits any of the following symptoms, including changes in vision, signs of a stroke, blanching of the skin or unusual pain during or shortly after the procedure. Patients should receive prompt medical attention and possibly evaluation by an appropriate health care practitioner specialist should an intravascular injection occur.

4 Precautions

- Health care practitioners are encouraged to discuss all potential risks of soft tissue injection with their patients prior to treatment and ensure that patients are aware of signs and symptoms of potential complications.
- In the absence of available clinical data on tolerance and efficacy of the injection of Belotero® Revive in patients with antecedents or with an active autoimmune disease or in patients presenting a history of severe multiple allergies or anaphylactic shock, the practitioner must decide whether to inject Belotero® Revive on a case-by-case basis depending on the nature of the disease as well as the associated treatment. It is recommended to propose a prior double test to these patients and to not inject if the disease is evolving. It is also recommended to carefully monitor these patients after injection.
- It is recommended not to inject Belotero® Revive in patients with a history of streptococcal diseases or in patients pre-disposed to hypertrophic scars or keloids.

- Belotero® Revive can be used in combination with other Belotero® products during the same session but in different facial areas. Instructions for use of each product should be followed.
- No clinical data is available on the injection of Belotero® Revive into patient with a Fitzpatrick skin type V/VI.
- No clinical data are available on the injection of Belotero® Revive into the hands.
- Belotero® Revive can be used in combination treatments such as with botulinum toxin and/or calcium hydroxylapatite (Radiesse®) only if injected in different facial areas. Practitioners should be experienced and patients appropriately selected as benefits but also adverse events can be cumulative and causality of adverse events could become difficult to determine. Instructions for use, depth of injection and appropriate recommendation of each product should be followed. No clinical data are available on the injection of Belotero® Revive into an area already treated with other aesthetic products or procedures.
- Belotero® Revive must not be used in association with other aesthetic medicine techniques such as peeling, dermabrasion, or any type of laser treatment before complete healing of the last treatment. In any case, even if the healing occurs earlier, Belotero® Revive must not be used earlier than 2 weeks after the last treatment. No clinical data is available on the combined use of Belotero® Revive with the above-mentioned treatments.
- Patients using anti-coagulation, anti-platelet, or thrombolytic medications (e.g. warfarin), anti-inflammatory drugs (oral/injectable corticosteroids or non-steroidal anti-inflammatory drugs (NSAIDs; e.g. aspirin, ibuprofen)), or other substances known to increase coagulation time (vitamins or herbal supplements, e.g. Vitamin E, garlic, Gingko biloba and St. John's Wort), from 10 days pre- to 3 days post-injection may have increased reactions of hematomas, nodules or bleeding at the injection site.
- Injection of Belotero® Revive into patients with a history of previous herpetic eruption may be associated with reactivation of the herpes (HHV related diseases, e.g. pityriasis rosea).
- In cases of patients suffering from epilepsy, impaired cardiac conditions, severely impaired hepatic function or severe renal dysfunction or porphyria, the practitioner must decide whether to inject Belotero® Revive on a case-by-case basis depending of the nature of the disease as well as the associated treatment.
- There is no known interaction with other local or loco-regional anesthetics.

5 Undesirable Side-effects

Patients must be informed by the practitioner about possible side effects before treatment.

- Side effects:

Injection site reactions may occur following injection into the skin but disappear spontaneously within a few days. This includes swelling, nodule or lump/bump, bruising, hematoma, ecchymosis, induration, erythema/redness, tenderness, pain, discoloration and pruritus/ itching, tingling, paraesthesia, numbness, hypoesthesia, scabbing, needle mark and discomfort or irritation. These injection site reactions are generally of mild or moderate intensity. A transient bleeding may also occur at the injection site and usually stops spontaneously as soon as the injection is finished.

- Adverse events:

In occasional cases, one or more of the following may occur in conjunction with the use of products of the Belotero portfolio either immediately or as a delayed reaction: acne cystic, milia, skin dryness (rough facial skin, exfoliation), injection site erosion, inflammation, shivering, fatigue, lymphatic system disorder, rash, burning sensation, injection site sore/warmth/fever, pruritus/ itching, urticaria, hematoma, telangiectasia, ecchymosis, edema (including lymph edema), headache/cephalgia, tumefaction, tension, swelling (including persistent swelling), hyper- or hypopigmentation, angioedema, induration, blister vesicle, papule, lump/ bump (visible and/or palpable material) or nodule (including inflammatory nodules), mass, granuloma (including inflammatory signs and foreign body reactions), necrosis, ischemia, vascular occlusion, embolization, infarction, Tyndall effect (including translucent chords), hypersensitivity, allergic reactions (including asthma attack, Quincke's edema, anaphylactic shock or throat tightening) to one of the product's components (e.g. hyaluronic acid, BDDE), oral and dental disorders, nervous system impairment, impairment of the otorhinolaryngological system (e.g. nasal congestion, oropharyngeal pain, dysgeusia, rhinorrhea, epistaxis, sinusitis, transient hearing loss), mastication pain, parotid gland enlargement, muscle twitching, muscle injury/disorder, nausea, vomiting, circulatory collapse, presyncope, peripheral venous disease, hot flush, anxiety caused by trypanophobia, patient dissatisfaction and disappointment (due to lack of or reduced performance, decreased firmness/response, undesirable aesthetic effect), injection site discharge, device migration, product distribution issue (e.g. product accumulation), injection site indentation, superficial vein prominence, overcorrection or cranial nerve disorder (e.g. cranial nerve paralysis, facial paralysis, trigeminal neuralgia).

Rare cases of the following adverse events with hyaluronic acid products such as infection (e.g. erysipelas, phlegmon, cellulitis, including open or draining wounds and (dental) abscess, impetigo, pustules), chronic infection (including biofilm formation), scarring, persistent skin discoloration, sensory dysfunction, non-thrombotic lung embolism as well as sarcoid granuloma formation in subjects with hepatitis C and interferon treatment, cerebral injuries (e.g. intracranial penetration, subarachnoid hemorrhage), strabismus, ophthalmoplegia, iris adhesions, cataract, conjunctival hemorrhage, eyelid ptosis and lacrimation.

The risk of granuloma, ischemia, necrosis and vascular occlusion is higher with deep injections and high volumes.

Isolated cases of visual impairment or blindness following unintentional intra-arterial injection have been reported in literature.

Patients should be instructed to report any side effects which last for more than one week and any adverse event as soon as it occurs to his/ her practitioner, especially if patient has changes in his/ her vision, signs of a stroke (including sudden difficulty speaking, numbness or weakness in his/ her 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. The practitioner may then refer the patient to the appropriate treatment.

Patients with lighter skin types are more likely to develop injection-related adverse events. However, patients with skin of color are more likely to develop post-inflammatory hyperpigmentation and / or hypertrophic scar/keloid formation following injection procedures. Patients with specific ethnic characteristics, e.g. Asian population, should be informed of a higher risk of tissue reactions, e.g. itching, swelling, erythema, inflammation.

6 Residual Risks

The overall residual design risks, and manufacturing risks, and the benefit/risk ratio of the devices when used on patients according to the manufacturer's instructions for use are fully acceptable.

Please refer to above safety information for details on residual risks of the product. Please ensure you follow the post-procedural care advice below and directions from your healthcare professional to minimize procedural risk.

7 Reporting Information

Contact your healthcare professional if you are experiencing any side effects or are concerned about any aspect of your treatment. Please seek immediate medical attention if you experience changes in vision, signs of a stroke, blanching of the skin, or unusual pain during or shortly after the procedure.

Patients should be instructed to report any side effects which last for more than one week and any adverse event as soon as it occurs to his/ her practitioner, especially if patient has changes in his/ her vision, signs of a stroke (including sudden difficulty speaking, numbness or weakness in his/ her 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. The practitioner may then refer the patient to the appropriate treatment.

Adverse events are unintended and sometimes harmful occurrences, associated with the use of a therapeutic good, and include incidents involving medical devices. These can be reported to Merz Australia on our website at https://merzaustralia.com.au/adverse-event-reporting/ or to the TGA at https://www.tga.gov.au.

8 Additional Information

Belotero® Revive must not be used in association with other aesthetic medicine techniques such as peeling, dermabrasion or any type of laser treatment before complete healing of the last treatment. In any case, even if the healing occurs earlier, Belotero® Revive must not be used earlier than 2 weeks after the last treatment. No clinical data is available on the combined use of Belotero® Revive with the above-mentioned treatments.

The patient must avoid applying makeup (including skin care products) for at least 12 hours after treatment as well as avoid saunas, peeling, Turkish baths and prolonged exposure to the sun, UV rays, extreme heat and cold for 2 weeks after the treatment. Patients should also avoid putting pressure on and/or handling the treated area and should avoid strenuous physical activity following treatment.

The patient must avoid drinking alcohol for 24 hours before and after treatment. Alcohol may cause the blood vessels to dilate and cause more bruising.

Patient counseling information

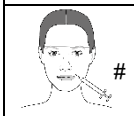
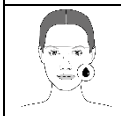
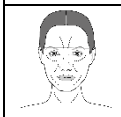
The patient should be instructed in appropriate post-procedural care, which may include the following, to promote normal healing and avoid complications.

- The patient should be instructed in appropriate post-procedural care, which may include the following, to promote normal healing and avoid complications.
- Apply cool compresses to areas of injection for approximately 24 hours.
- Promote facial rest for one week by encouraging patients to limit talking, smiling and laughing.

9 Implant Card Information

After injection, your physician will provide you with an implant card. This card contains all information related to your injection including product traceability information.

It is recommended to keep the implant card with you and present it to your physician in case of other appointments. Information about previous treatment must be presented to your physician before treatment.

Symbol	Title of symbol
	Patient name or ID
	Date of implantation
	Name and address of healthcare provider
	Number of injections
	Total volume injected
	Injection site(s)
	Catalogue number
	Information website for patients
	Name and address of the manufacturer
	Lot number
	Use-by-date

10 Legal Manufacturer

Manufacturer

Anteis SA

18 Chemin des Aulx

1228 Plan-les-Ouates

Switzerland

11 Australian Sponsor

Australian Sponsor Name and Address:

Merz Australia Pty Ltd

Suite 8.01A, 189 O'Riordan Street

Mascot, NSW, 2020

Australia

12 Date of Issue and Version

Version: 01

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