For Patients Scheduled to Undergo Regenerative Treatment for Tympanic Membrane (Eardrum) Perforation Using Retympa® 250 μg Set for Otology

Supervising Editor

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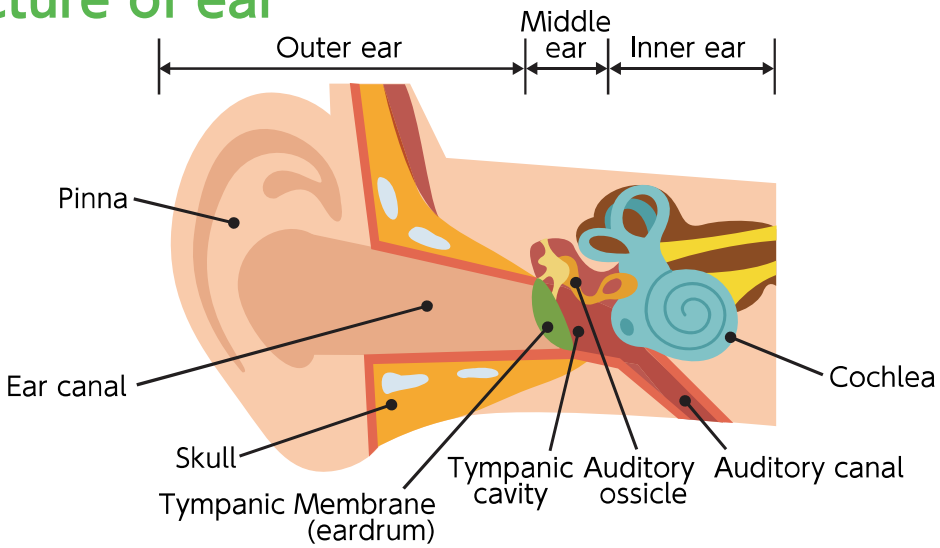
Mechanism of hearing voices and sounds

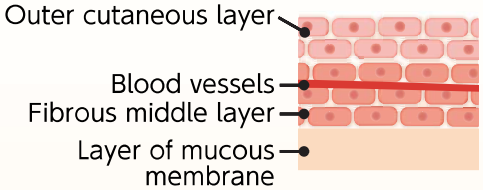
Structure of ear



- Voices or sounds from the external environment are transmitted to the ear as air vibrations.
- Voices or sounds from the external environment are collected by the pinna (earlobe), are funnelled into the ear canals. These voices or sounds make the tympanic membrane vibrate.
- The tympanic membrane vibrations move a chain of three tiny bones called auditory ossicles in the middle ear, transferring the sound vibrations into the inner ear.
- The tympanic cavity in the middle ear is connected to the nose and mouth by the Eustachian tube of the inner ear.
- The cochlea in the inner ear transforms the sound vibrations into electrical signals, conveying auditory information to the brain.
- When the brain receives electrical signals from the inner ear, it turns it into a voice or sound that we recognize and understand.

Structure of tympanic membrane

- The tympanic membrane is comprised of three layers of tissue: the outer cutaneous layer, the fibrous middle layer, and a layer of mucous membrane.



- The outer cutaneous layer is formed by keratinocytes (cells protecting the living body from external stimulation); the fibrous middle layer consists of blood vessels, fibroblasts and endothelial cells needed to repair cells; and the layer of mucous membrane is composed of a single layer of squamous epithelium.

Tympanic membrane perforation

Tympanic membrane perforation and its effects

- A tympanic membrane perforation is a small hole or tear in your eardrum. The perforated tympanic membrane cannot vibrate as well as it should, resulting in the weakened vibrations to the cochlea. At the same time, sound waves entered directly from the ruptured tympanic membrane interfere with the original ones, leading to the attenuated signals. This can cause a hearing loss.
- It can cause infection in the middle ear or ear discharge (otorrhea).
- It has been reported that hearing loss can cause the onset of dementia or accelerate the disease.

Treatment for tympanic membrane perforation

A small perforated tympanic membrane may close (heal) spontaneously. If the tear or hole in your tympanic membrane does not heal by itself, procedures (surgeries) to close the tear or hole will be performed taking into consideration the duration or status of the perforation. A variety of procedures are performed according to the cause and size of the perforation. Typical procedures include:

◆Tympanic membrane perforation closure

Surgical closure of tympanic membrane perforation is often chosen for a tympanic membrane perforation due to traumatic injury caused by an ear pick or air pressure changes in the ear canal in case of an ear slap. With this procedure, the tympanic membrane perforation is closed and covered with an artificial material (membrane created artificially similar to the human one).

◆Tympanoplasty

Tympanoplasty is performed when the middle ear has no lesion and if the perforation is temporarily closed with paper or cotton, it can improve hearing substantially. This procedure uses tissue collected from the back of your ear as a material to cover the perforated tympanic membrane.

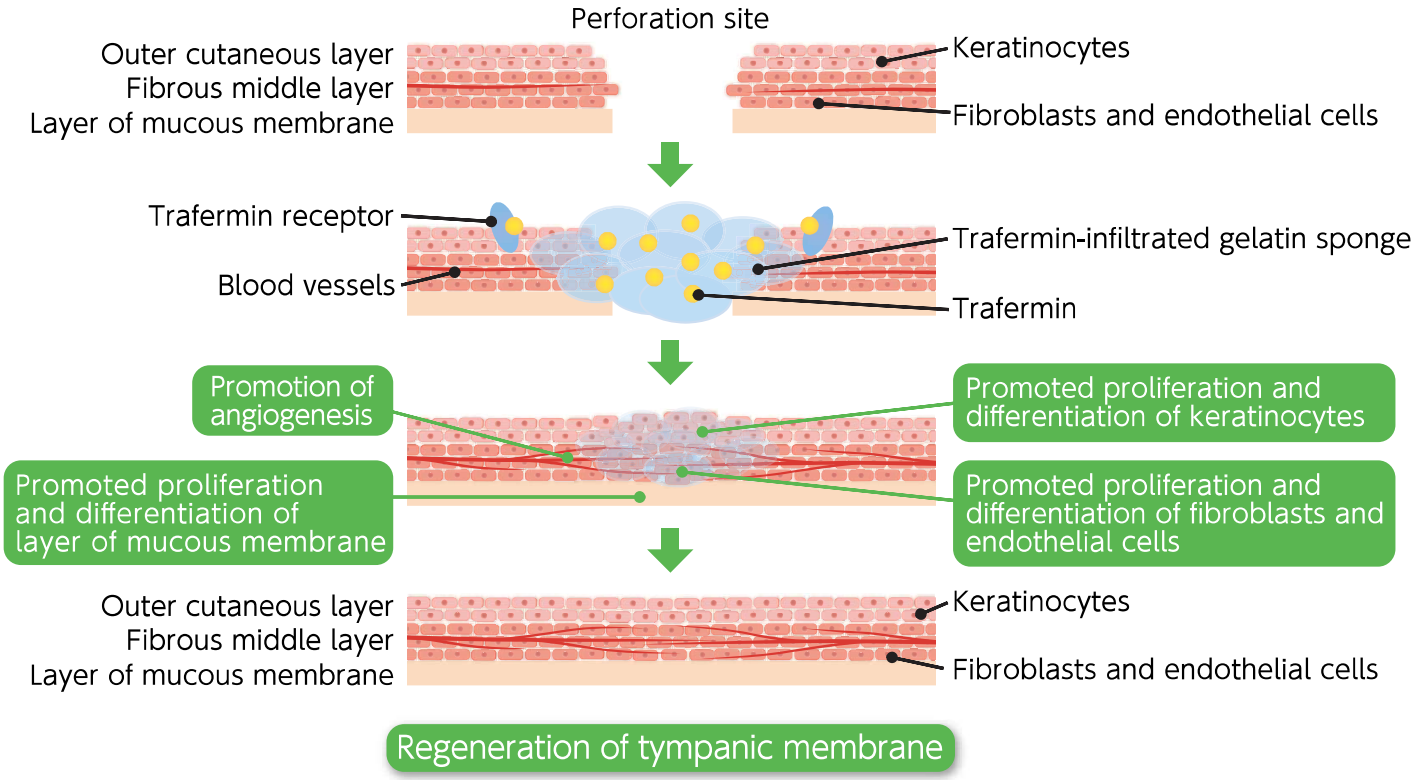
◆Treatment using Retympa® (treatment of tympanic membrane perforation)

This is a new treatment for regenerating and closing tympanic membrane perforated.
It can also be indicated for complicated shape of or large perforation.

Treatment using Retympa®

Treatment using Retympa® is done using a drug called trafermin(genetic recombination), solution to dissolve the drug and gelatin sponge infiltrated with the drug to close the hole of the tympanic membrane.

Mechanism of action of Retympa®

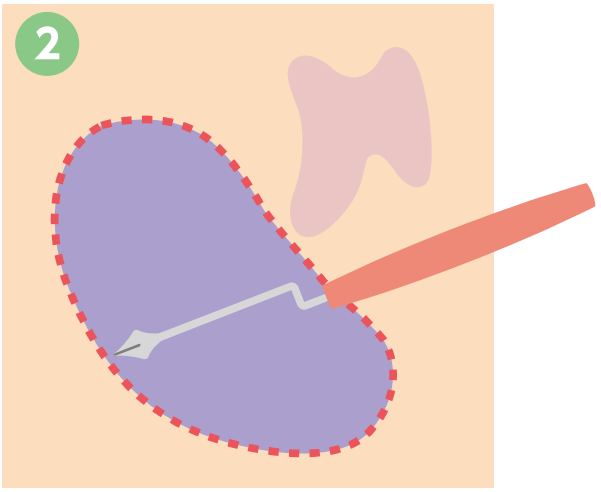


- Trafermin* receptors (the site where drugs acts) are distributed in the tympanic membrane, especially in the outer cutaneous layer.
- Retympa® acts on trafermin* receptors residing in the outer cutaneous layer and stimulates proliferation and differentiation (its functions and natures change to different ones) of endothelial cells, fibroblasts and keratinocytes, resulting in the regeneration of tympanic membrane.
- Retympa® also forms a new blood vessel (angiogenesis). It is presumed to facilitate the regeneration of three layers (outer cutaneous layer, fibrous middle layer and layer of mucous membrane) by increasing blood flow to the tympanic membrane.

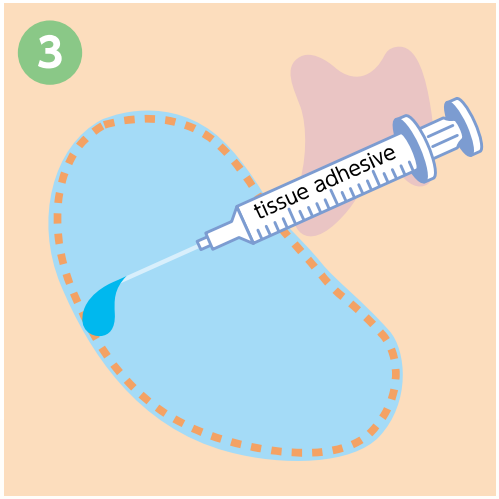
* Basic fibroblast growth factor

Surgical flow

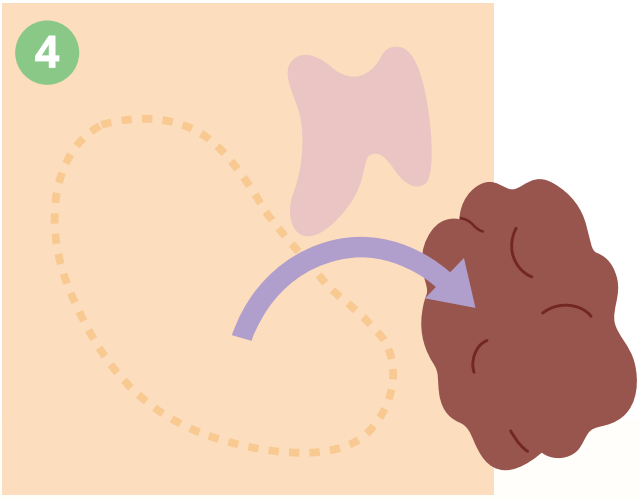
Administer local anesthesia to the tympanic membrane around the perforation site with absorbent cotton infiltrated with anesthetic solution.



Make an incision around the perforation site with a surgical knife. Remove a part of tissues around the perforation site circumferentially (as dotted line shown above) to facilitate tissue regeneration. This process is called fresh wound creation.



Close the perforation site with gelatin sponge infiltrated with trafermin and fixate with a tissue adhesive.



Check whether the tympanic membrane is closed at 3 to 4 weeks after the procedure. If it is closed, remove unnecessary gelatin sponge adhered to the tympanic membrane. This treatment is now completed. If it is not closed, reoperation may be performed up to 4 times.

Precautions after surgery

When the gelatin sponge comes off or the drug leaks, it may be unable to regenerate the tympanic membrane. Please be noted that you should observe the following precautions for 4 weeks or so after the surgery:

Do not fight off a sneeze or cough. Leave it to nature. Do not cover your mouth with your hands.

Do not do anything like putting pressure on your ear. For example, blowing hard and sniffing.

Do not avoid vehicles as much as possible such as airplane, high-rise elevator which causes air pressure change greatly. Do not touch your ear more than needed.

Pay attention so that you will not get water in your ears when washing your hair or taking a bath.

FAQ

Q1 Who cannot receive treatment using Retympa®?

A1 Patients with malignant tumor in the ear or those with prior malignant tumor are not allowed to undergo the treatment with Retympa®. It is because the drug promotes cell proliferation.

Q2 Are there adverse effects?

A2 Otorrhea may occur. Systemic reddening, difficulty of breathing or facial pallor, cold sweat and lightheadedness caused by lowering of blood pressure and so on may develop. If any of these happens, go to see the doctor and follow his/her instructions.

Q3 How many times can I receive this treatment at most?

A3 The closure of your tympanic membrane will be checked at 4 weeks after the procedure. If the tympanic membrane is not regenerated, you can undergo the treatment with Retympa® up to 4 times.

Q4 Is the gelatin sponge left in my ear?

A4 The gelatin sponge on the side of the ear canal will be removed at the end of the treatment. If it is left on the side of tympanic cavity, it will be degraded within two months or so and absorbed naturally.

If you have any questions or concerns, feel free to contact with your doctor or nurse.

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