

HYDR ZID[®]

INSTRUCTIONS
FOR USE



Read all instructions for use.

For prescription use only.

Caution: Federal law restricts this device to sale by or on the order of physician.

Manufacturer:

BIBAWO Medical A/S

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Hydrozid® is a registered trademark of BIBAWO Medical A/S

3 years shelf life from manufacturing date.

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1. Cryosurgery

The mechanism of action for Hydrozid® is based on the principle of cryosurgery (also referred to as cryotherapy). Cryosurgery is performed using a cryogen and freezing the target tissue temperature to below the level that correlates with cell destruction also known as necrosis. When the cryogen evaporates, it absorbs heat from its surroundings causing cell destruction.

Cryosurgery includes 3 phases: (1) heat transfer, (2) cell death, and (3) inflammation.

- *Heat transfer:* The mechanism by which cryosurgery destroys the targeted cells is the quick transfer of heat from the damaged tissue to a cryogen. When the cryogen evaporates, it takes heat from its surroundings causing a freezing effect.

When using Hydrozid®, its cryogen is applied directly on the skin lesion, and evaporation occurs in which a significant amount of thermal energy (the heat in the damage skin cells is quickly transferred to the cryogen.) This process results in the cryogen evaporating almost immediately, and simultaneously greatly lowering the temperature of the skin.

- *Cell death:* Cell death or necrosis occurs during the thaw, right after the cell is frozen. When the cells are frozen, their liquid content (cytoplasm) freezes and expands. Subsequently, their membrane also freezes and loses its elasticity. Hence, the expansion of the cytoplasm can rupture the cell membrane releasing its content and causing the cell organelles to stop functioning which results in cell death or necrosis. Because of the hyperosmotic intracellular conditions, ice crystals do not form until -5°C (23°F) to -10°C (14°F). The transformation of water to ice concentrates the extracellular solutes and results in an osmotic gradient across the cell membrane, causing further damage. Slow freezing produces extracellular ice formation whereas rapid freezing produces intracellular ice formation and thus maximizing cell damage due to rupture of cells during thawing. Rapid freezing with repeated freeze-thaw cycles is more effective than a single long freezing period because in each freeze-thaw cycle more cell damage is achieved. In addition, the patient experience is improved with repeated freeze-thaw cycles as the treatment is gentler, less painful, and less prone to causing hypopigmentation or scarring. The action of cryosurgery is based on the principle that different types of skin cells vary in their sensitivity to being frozen. The target temperature for the destruction of benign cells is between -20°C (-4°F) to -30°C (-22°F) and for pre-malignant cells, temperatures of -40°C (-40°F) to -50°C (-58°F) are necessary for destruction (Andrews, 2004) (Nasr, 2020).

Hydrozid® delivers temperatures of at least -54°C (-65.2°F) to the treated area ensuring that both extracellular and intracellular ice formation occurs, with fast freezing in the center of the lesion and slow freezing on the outside border. This is an optimal freezing temperature as it ensures the destruction of cells and avoids the complications as such as scarring or hypopigmentation associated with the lower freeze temperatures.

- *Inflammation:* The last response to cryosurgery is inflammation, which is usually observed as redness of the skin or mucous membranes (erythema) and swelling (edema) (vascular stasis). Inflammation is the response to cell death and helps in local cell destruction. Full recovery takes about 10 to 14 days, with new tissue growing inwards from the surrounding epidermis and more deeply situated adnexa.

A single treatment with Hydrozid® keeps the skin temperature low enough to effectively treat the lesion up to 395 seconds. Besides freezing of the damage skin cells, the prolonged cooling effect promotes the loss of blood supply to the treated area and reduces the likelihood of survival of the damage skin cells.

2. About Hydrozid®

Hydrozid® is a portable cryosurgery device intended for the treatment of skin lesions.

3. Component Identification

The Hydrozid® kit consists of:

- 200 ml Hydrozid® canister of cryogen
- Single-use application templates
- Instructions for Use

4. Instructions for Use

a. Indications for use

Hydrozid® contains 1,1,1,2-tetrafluoroethane (also known as R134A, HFC-134a, HFA-134a and/or fluorocarbon 134a) and is to be used for the treatment of verruca (warts) including plantar warts, seborrheic keratosis, actinic keratosis, achrochordon (skin tags), molluscum contagiosum, age spots, dermatofibroma, small keloids, granuloma annulare, porokeratosis plantaris, angiomas, keratoacanthoma, chondrodermatitis, epithelial nevus, leukoplakia, granuloma pyogenicum, and pyogenic granuloma.

b. Contraindications

Hydrozid® is to be used only on benign lesions or pre-malignant lesions (actinic keratosis).

Do not treat lesion if the diagnosis is uncertain or cancer is suspected. If there is doubt that is a lesion is benign or pre-malignant, a biopsy is recommended.

Do not use on healthy skin. Improper use may lead to unwanted damage to the skin and underlying tissues, including nerves.

Do not use in irritated, eczematous, or infected skin.

Do not use on open, bleeding or bleached skin.

Do not use on mucus membrane areas.

Cryosurgery is not recommended for use in treatment of children under the age of 5 years old.

Cryosurgery is reported to be safe in pregnancy (Pennycook KB, McCreedy TA, 2020). As no clear guidelines are available (Sugai S all, 2020) caution and physician's discretion are advised for the patient and treatment selection.

c. Warnings

Read all instructions prior to use Hydrozid®.

Hydrozid® is non-flammable, non-toxic and non-oxidizer. Neither protective equipment or well-ventilated areas are required.

The application templates must be used only with Hydrozid®. Their use is optional. Due to the risk of infection, the application templates are for single use. Do not attempt to clean Hydrozid®. All application templates are disposable. Application templates may be use multiple times on the same patient with similar lesions in the same anatomical location but should be disposed between patients or treatment of different lesions to avoid spreading potential bacteria, diseases, or viruses.

Do not attempt treatment without the application templates until you have substantial experience and are familiar with the device and recommended treatment times. Failure to use an application template and attempt an open spray could result in damage of the surrounding healthy tissue.

Do not treat lesions that cannot be diagnosed with certainty. If there is doubt that is a lesion is benign or pre-malignant, a biopsy is recommended to determine classification and if cryosurgery with Hydrozid® is an option.

Do not attempt facial treatments until you have substantial experience and are familiar with the device, applications templates, and recommended treatment times.

When treating sensitive areas of the body such as around the eyes and ears, be sure to shield or protect the areas so that the cryogen does not come into contact with healthy tissue. Avoid contact with eyes.

Never freeze scrotum tissue with testicle directly beneath. Always gently separate scrotum tissue that is being treated away from the testicle, then perform the procedure.

Caution is advised in the treatment of patients who have sensitive skin, heavily pigmented skin, sensory loss, poor blood supply, children and/or the elderly. It is not recommended for use with children under the age of 5 years. Those with collagen vascular disease, cryoglobulinemia, Raynaud's disease, cold urticaria, blood dyscrasias, diabetes, stasis problems, pyoderma gangrenosum and ulcerative bowel disorders may present special complications including slower healing time. Physician's discretion should be used for patient and treatment selection.

d. Cautions

Pressurized container; may burst if heated. Protect from sunlight. Do not expose to temperatures exceeding 50 °C/122°F. Keep away from the heat, hot surfaces, sparks, open flames, and other ignition sources. No smoking. Do not pierce or burn, even after use.

Hydrozid® can be disposed in normal household. Do not attempt to refill an empty canister. Federal law prohibits transportation if refilled and a penalty of up to \$500,000 fine and 5 years imprisonment (49 USC 5124).

If the canister is dropped, inspect for damage or leakage. Damage may not be visible, and practitioner may not know if the canister was dropped since it was last used. DO NOT USE. Contact the BIBAWO Medical A/S for further support or replacement.

Always use gentle pressure when activating the trigger nozzle. This will reduce the cryogen waste and prevent splatter. Reducing waste means more treatment per canister.

Always placed the disk in lock position after use (see directions for use) to avoid inadvertent spraying in the next use.

Do not attempt to remove the tip mounted into the distal end of the tube. The narrow aperture of the tip makes it easier to target the damaged tissue mitigating the risk of damaging the surrounding healthy skin. The tip also compromises a conical inner shape that prevents condensation and dripping during the treatment.

For thin skin or sensitive areas, it is recommended to under-treat the patient.

Do not touch the lesion until the ice formation disappear. Allow the lesions to thaw naturally. Early thawing will reduce the effectiveness of the freeze and lesion destruction. If lesion persist, post treatment lesions should be re-inspected and confirmed the diagnosis.

e. Potential Complications and Side effects of cryosurgery

The most common complications and side effect related with cryosurgery are described bellow (Sharma & Khandpur S. 2009):

Acute complications:

- Local pain
- Edema especially facial use and when used in infants and elderly
- Cryoblisters formation

- Syncope in anxious patients
- Headache after treatment of head and neck
- Hemorrhagic necrosis
- Wound infection and delayed wound healing
- Temporary scar hypertrophy
- Subcutaneous emphysema

Long-term complications:

- Hypopigmentation
- Local hypoaesthesia due to nerve damage
- Milia formation
- Cicatricia
- Alopecia

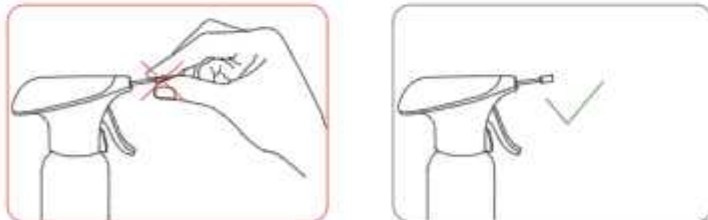
Common side effects:

- Skin may turn white temporarily
- Overexposure may cause damage to the top layers of the skin resulting in scars and/or nerve damage
- Exposure of healthy skin may cause local tissue death
- Formation of large blisters which may cause pain
- Hypopigmentation and scars
- Post-inflammatory hyperpigmentation

f. Directions for Use

Hydrozid® is applied to a lesion directly from the canister.

Do not attempt to remove the tip mounted into the distal end of the tube.

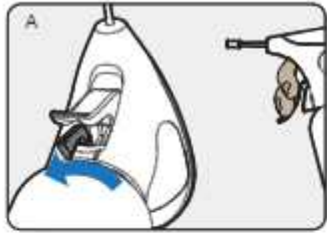


The narrow aperture of the tip makes it easier to target the damaged tissue mitigating the risk of damaging the surrounding healthy skin. The tip also comprises a conical inner shape that prevents condensation and dripping during the treatment.

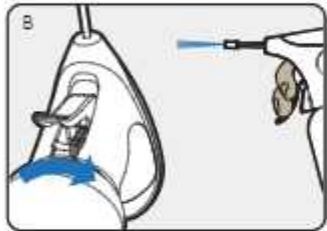
Hydrozid® should be applied from approximately 1 inch (2 to 3 cm).

Hydrozid® should be used according to illustration A, B, and C.

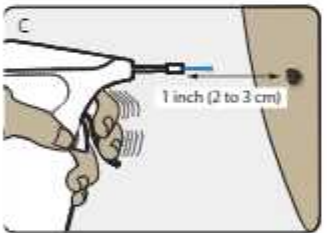
In illustration A the spray head is locked.



In illustration B, the spray head is open.



In illustration C, hydrozid is ready to use. Always use gentle pressure when activating pushing the trigger nozzle. This will reduce the cryogen waste and prevent splatter. Reducing waste means more treatment per canister.



Several repeated freeze-thaw cycles are recommended as part of a single treatment. The total freeze time and freeze-thaw cycles vary according to the type of skin lesion being treated, the size of the skin lesion as well as the anatomical location but can range from 3-6 seconds per freeze. As hypopigmentation and scarring is more frequently associated with single, long spray times, care should be taken when determining how long to freeze. In between freezes, the frozen skin lesion should be allowed to thaw naturally. The thaw is complete when the ice ball on the skin disappears, which may take up to 30 seconds. Premature warming of the cells will minimize the effectiveness of the freeze, and the procedure may need to be repeated.

Type of skin lesion. Hydrozid® may be used for the treatment of verruca (warts) including plantar warts, seborrheic keratosis, actinic keratosis, achrochordon (skin tags), molluscum contagiosum, age spots, dermatofibroma, small keloids, granuloma annulare, porokeratosis plantaris, angiomas, keratoacanthoma, chondrodermatitis, epithelial nevus, leukoplakia, granuloma pyogenicum, and pyogenic granuloma.

Size of the skin lesion. Larger skin lesions will require longer spraying time to treat the full, damaged area.

Location of the skin lesion: The skin thickness varies according to the anatomical location. The thinner the skin, the higher the likelihood of side effects and increased pain. Thus, the freezing time should be shorter when treating lesions on thin skin and somewhat longer in treating lesions on thicker skin.

If ever in doubt when treating a skin lesion, always under-treat rather than over-treat, as refreezing is possible.

The table below provides recommended freeze times for the commonly treated skin lesion. The freeze times are per lesion per treatment session.

Type of Lesion	Approximate Total Freezing Time
Verruca plantaris	24-36 seconds
Verruca vulgaris	24-36 seconds
Verruca plana	18 seconds
Keratosis seborrheic	12-18 seconds
Lentigo (facial) (age spots)	6 seconds
Lentigo (non-facial)(age spots)	6 seconds
Acrochordon (skin tags)	6-12 seconds
Keratosis actinica (facial)	8-10 seconds
Keratosis actinica (non-facial)	8-10 seconds
Condyloma	12-36 seconds
Molluscum contagiosum	6-12 seconds

The freeze times provide in the table above are only approximations. When using cryosurgery, achieving optimal results will improve over time with practice and familiarity with the freeze-thaw procedure and results.










To avoid damaging the surrounding tissue, use one of the optional, application templates provided, carefully selecting the hole matching the size of the individual lesion. The spray jet intensity should also be adjusted to the selected hole in the application template. Some conditions may need repeated treatment to successfully remove a skin lesion. When repeat treatment is needed intervals of 1 to 2 weeks between treatments are recommended. Cryosurgery may produce a stinging or burning sensation on the skin. Necrosis of epidermal cells may result in the development of a blister. Full recovery takes about 10 to 14 days. Overexposure may lead to hypopigmentation, scarring or post-inflammatory hyperpigmentation.

5. Common CPT Codes for Cryosurgery

Due to a wide range of reimbursement schedules, it is recommended that the following American Medical Association (AMA) CPT Codes are used. The CPT codes and procedures may vary from time to time, carrier to carrier and are ultimately left up to the physician to interpret

Code	Description
17000	Benign Lesions: Destruction of 1 Benign Lesion
17003	Benign Lesions: Destruction of 2-15 benign lesions
17004	Benign Lesions: Destruction of 15 or more benign lesions
17110	Warts & Molluscum: Destruction of 1-14 flat warts, molluscum, or miha
17111	Warts & Molluscum: Destruction of 15 or more flat warts, mollusc um, or milia.
11200	Skin Tags: Destruction of 1-15 skin tags
11201	Skin Tags: Destruction of each additional 10 skin tags
46916	Anal Lesions: Simple destruct ion of anal lesion, SIMPLE
46924	Anal Lesions: Extensive destruction of anal lesion,) EXTENSIVE
54056	Penile Lesions: Simple destruction of penile lesion, SIMPLE
54065	Penile Lesions: Extensive destruction of penile lesion, EXTENSIVE
56501	Vulva Lesions: Destruction of Vulva Lesions- SIMPLE
56515	Vulva Lesions: Destruction of Vulva Lesions- EXTENSIVE
57061	Vaginal Lesions: destruction of lesion, SIMPLE
57065	Vaginal Lesions: destruction of lesion, EXTENSIVE

6. Explanation of Symbols

Symbol	Used for
	Consult instructions for use
	Keep away from sunlight
	Caution
	Do not expose to temperatures exceeding 50 °C
	Manufacturer
	Application template
	Use-by
	Batch code
	See bottom of the canister

7. References

- Andrews, M. D. (2004). Cryosurgery for Common Skin Conditions. *Am Fam Physician.*, May 15;69(10):2365-2372.
- Nasr, I. (2020). Review of cutaneous cryosurgery *Dermatological Nursing*, 19(2):36-46.
- Pennycook KB, McCready TA. (2020) Condyloma Acuminata. In: *StatPearls*. Treasure Island (FL): Stat Pearls Publishing; 2020 Jan.
- Sharma VK, Khandpur S. (2009) Guidelines for cryotherapy. *IJDVL Indian Journal of Dermatology, Venereology and Leprology* 2009; 75: 90-100.
- Sugai S, Nishijima K, Enomoto T. (2020). Management of Condyloma Acuminata in Pregnancy: A Review. *Sex Transm Dis*. 2020 Oct 21.

