

PRODUCT MONOGRAPH

NYDA

Dimeticone 100 cSt
Solution, 50% w/w

Pediculicide

G. Pohl-Boskamp GmbH & Co. KG
Kieler Strasse 11, 25551 Hohenlockstedt, Germany

Date of Preparation:
September 11, 2012

Distributed by:
Pediapharm Licensing Inc.
Dundas, Ontario L9H 7P3

Submission Control No: 156818

Table of Contents

PART I: HEALTH PROFESSIONAL INFORMATION.....	3
SUMMARY PRODUCT INFORMATION	3
INDICATIONS AND CLINICAL USE.....	3
CONTRAINDICATIONS	3
WARNINGS AND PRECAUTIONS.....	3
ADVERSE REACTIONS.....	4
DRUG INTERACTIONS	4
DOSAGE AND ADMINISTRATION.....	5
OVERDOSAGE	6
ACTION AND CLINICAL PHARMACOLOGY	6
STORAGE AND STABILITY.....	7
SPECIAL HANDLING INSTRUCTIONS	7
DOSAGE FORMS, COMPOSITION AND PACKAGING	7
PART II: SCIENTIFIC INFORMATION	8
PHARMACEUTICAL INFORMATION.....	8
CLINICAL TRIALS.....	8
DETAILED PHARMACOLOGY	9
TOXICOLOGY	10
REFERENCES	11
PART III: CONSUMER INFORMATION.....	12

NYDA

Dimeticone 100 cSt
Solution, 50% w/w

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Non-medicinal Ingredients
Topical	Solution, 50 % w/w	For a complete listing, see the Dosage Forms, Composition and Packaging section.

INDICATIONS AND CLINICAL USE

NYDA is a topical treatment of scalp hair in case of infestation with head lice (pediculosis capitis). If used as instructed, NYDA is also effective against nymphs and eggs (nits).

CONTRAINDICATIONS

NYDA must not be used in people with known allergies (hypersensitivity) to any of its ingredients. For a complete ingredient listing, see the Dosage Forms, Composition and Packaging section of the product monograph.

NYDA should not be used in pregnant or breast-feeding women or in children under the age of two because of lack of experience in these patient groups.

WARNINGS AND PRECAUTIONS

General

For external use only.

Patients should be warned to not use NYDA near the eyes or mucosa membranes (nose or mouth). If product gets into their eyes, patients should immediately rinse for 10-15 minutes with water.

Patients should be warned to avoid inhaling or ingesting NYDA.

Patients should be told that NYDA could react with certain hair care and hair tinting products.

Patients should be told to keep away from any open flame or intense heat source which uses an open flame and to keep away of any sources of ignition and not to smoke while using this product as the mixture is volatile.

If NYDA is spilled accidentally, there is a danger of slipping. Spillages should therefore be cleaned up immediately.

Special Populations

Pregnant Women: No clinical studies have been performed in pregnant women; therefore NYDA should be used with caution.

Nursing Women: No clinical studies have been performed in nursing women; therefore NYDA should be used with caution.

Pediatrics: Clinical studies have been performed in children; therefore NYDA can be used with children from ages 2 and up.

Geriatrics: No clinical studies have been performed in elderly patients; however the use of NYDA should not be of concern.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

In a clinical study, 145 subjects were treated with either NYDA or with a permethrin-based product. The number of subjects experiencing any adverse events was similar in both groups.

In the NYDA group, 29 adverse events were reported in 25 participants; all but two of them were classified as being unrelated to the treatment (e.g., superficial wound after a fall, otitis externa following swimming in a pool). Two subjects in the NYDA group experienced ocular irritation after treatment when the product entered the eyes. The irritation resolved spontaneously in both cases after washing the eyes with clean water.

In a large Postmarketing Surveillance Study in Germany, (833 patients) a total of six adverse events were reported; these included four occurrences of a bothersome hair odour and one occurrence each of a headache and a burning sensation in the eyes.

DRUG INTERACTIONS

No drug interaction studies have been conducted for NYDA.

DOSAGE AND ADMINISTRATION

Appropriate dosage for adult and/or children (2 years or older).

NYDA is sprayed carefully over the whole hair. The solution should be massaged in well until the hair is completely wetted with the solution. Dosage varies dependent upon thickness and length of hair.

Administration

Before NYDA is used for the first time, the enclosed dispensing pump must be screwed onto the glass bottle. Always hold the spray bottle upright or the pump will not be able to work properly. Please note that the pump will need to be primed, by pumping, when used for the first time and when it has been unused for a long period.

Before treatment with NYDA

Inspect all scalp hair of each family member or care giver with the NYDA lice comb. Treat everyone with lice on the same day to avoid re-infestation. A normal comb or brush can be used before treatment to remove any tangles. This comb should be cleaned thoroughly after use. Cover the shoulders with a towel to protect the clothing.

Administration of NYDA

NYDA should be applied to dry hair.

1. The infested hair should be completely covered with NYDA and left for 30 minutes.

NYDA is sprayed carefully over the whole hair. The solution should be massaged in well until the hair is completely wetted with the solution. This can be done using the lice comb, for example. This ensures that all lice, nymphs and nits come into contact with this solution and that the product can work with optimum efficacy.

The amount of NYDA needed depends on the thickness and length of the hair. The hair near the scalp and behind the ears should be well covered with NYDA, as this is where most lice and nits are found. NYDA should be left on for at least 30 minutes.

Usual dose:

Appropriate dosage for adult and/or children (2 years or older).

Hair Length	Average vol. per appl. (mL)
Short	10
Shoulder length (medium)	18
Long	22
Very Long	34

2. After 30 minutes, the hair may be carefully combed using a lice comb.

After NYDA has been left on for at least 30 minutes, the hair may be combed carefully with the lice comb to remove the suffocated lice and nymphs. NYDA makes combing easier because it contains special ingredients which make even long hair very easy to comb.

3. The hair should be left to dry for at least 8 hours (e.g. overnight).

4. The hair can then be washed with normal commercial shampoo.

5. After 8 to 10 days, the treatment must be repeated.

For complete control of head lice and nits, the treatment must be repeated as described above after 8 to 10 days.

OVERDOSAGE

For management of patients who ingest NYDA, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

The efficacy of NYDA is exclusively based on a physical mode of action. This is important given the resistance present for current pesticide therapies approved in Canada.⁸ The “point of attack” of the physical mode of action of NYDA is the insect’s respiratory system. NYDA works by suffocating the lice, nymphs and the embryos in the eggs. The unique physical properties including the viscosity and creeping/spreading properties of this solution allow it to readily flow into the breathing system of all developmental stages of the insect, thus leading irreversibly to suffocation and death.^{1,3} It creeps through the stigmata (spiracles) deep into the tracheae of the head lice as well as through the aeropyles of the operculum of the eggs inside the eggs. When it reaches there, the solution displaces the air (oxygen). The low viscosity, volatile dimeticone enables the NYDA solution to penetrate into the breathing system. Its evaporation causes the thickening of the NYDA solution. The remaining high viscosity dimeticone finally seals the respiratory system and thus leading to suffocation of all stages of head lice (adult lice, larvae and eggs). This mode of action prevents development of resistance.

Studies done with house crickets and lice demonstrate a close correlation between death of the lice and the influx of the solution into the head tracheae. This strongly suggests that the complete filling of the head tracheae effectively and immediately blocks the oxygen supply of the central nervous system. Death, following various phases of disability after the entrance of dimeticones into the abdominal tracheal system, reflects the sequence of oxygen deprivation. This is further supported by the fact that NYDA had no effect on the insect when applied solely to the outside of the head or mouth. If the solution had a chemical neurotoxic effect, similar to permethrin or

other chemical insecticides, one would expect mortality to occur upon contact, regardless of where the solution is applied on the body of the insect.

STORAGE AND STABILITY

Store between 15-30°C.

SPECIAL HANDLING INSTRUCTIONS

Keep away from heat, and open flames.

Do not smoke while using product as the mixture is volatile.

If NYDA is spilled accidentally, there is a danger of slipping. Spillages should therefore be cleaned up immediately.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Medicinal Ingredients:

Dimeticone 100 cSt

Non-medicinal Ingredients:

Alpha-terpineol, *Corymbia citriodora* (boabo oil), Jojoba wax, low viscosity dimeticone and triglycerides.

NYDA is supplied in a 50 mL amber glass bottle with a white screw cap.

NYDA's package includes the 50 mL amber glass bottle containing dimeticone 100 cSt 50% w/w solution, a lice comb and a spray nozzle.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

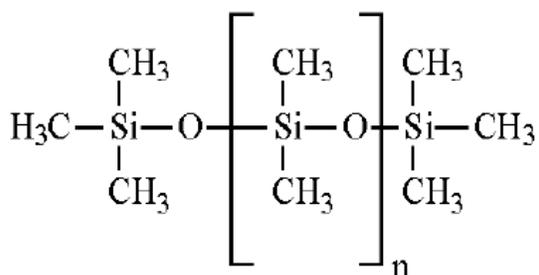
Drug Substance

Proper name: Dimeticone (dimethicone) 100 cSt

Chemical name: poly(dimethylsiloxane)

Molecular formula and molecular mass: $\text{CH}_3[\text{Si}(\text{CH}_3)_2\text{O}]_n\text{Si}(\text{CH}_3)_3$

Structural formula:



Physicochemical properties: Dimeticone 100 cSt is a clear, colorless, hydrophobic liquid. Dimeticone 100 cSt is miscible with many organic solvents such as ethyl acetate or methyl ethyl ketone. It is sparingly soluble in ethanol (ratio of 1:9) and insoluble in water. The refractive index at 25°C for dimeticone 100 cSt is 1.4032. Dimeticone 100 cSt has a low surface tension and can therefore coat most surfaces.

CLINICAL TRIALS

A randomized, controlled, observer-blinded study was performed in 145 infested children (ages 5-15 years) in Brazil.² The study was registered in the database of the Brazilian Ministry of Health for studies involving human subjects. Lice infestation and its relative intensity for each subject were verified by visual inspection prior to treatment by a trained observer without combing. Combing was not used because this may have affected the number of lice present on the subject's hair prior to treatment and thus may confound the results. Participants with head lice were randomized to receive either topical treatment with a solution exactly equivalent in composition to NYDA or to topical permethrin 1% aqueous solution.

Table 1 Overall cure rates one day after first and second treatment

	NYDA		Permethrin		P value
	Cured/total	%	Cured/total	%	
Day 2	69/73	94.5%	48/72	66.7%	P<0.0001
Day 9	70/72	97.2%	48/71	67.6%	P<0.0001

The number of subjects experiencing any adverse events was similar in both groups.

In the dimeticone group, 29 adverse events were reported in 25 participants; all but two of them were classified as being unrelated to the device or the treatment (e.g., superficial wound after a fall, otitis externa following swimming in a pool). Two subjects in the NYDA group experienced ocular irritation after treatment when the product entered the eyes. The irritation resolved spontaneously in both cases after washing the eyes with clean water. In the permethrin group, 32 adverse events were reported in 26 subjects. None of the adverse events were deemed to be related to the product.

A large post marketing surveillance study (PMSS) was conducted in Germany with NYDA. In this investigation 833 patients (191 male, 642 female) from a total of 296 pediatric and general practitioner practices took part. The average age was 8.84 years (median 8 years), with the youngest participant being 1 year and the oldest being 58 years of age. Of the 781 patients in the ITT group, 97.4% were free of head lice after one or two treatments (95% confidence interval 96.8 - 99.1%).

For the whole study population (833 patients) a total of six adverse events were reported; these included four occurrences of a bothersome hair odour and one occurrence each of a headache and a burning sensation in the eyes.

DETAILED PHARMACOLOGY

The studies outlined in the Table below have been completed with NYDA.

Title	Purpose
<i>In vitro</i> studies to demonstrate physical mode of action	Demonstrate that NYDA works by a physical mode of action; show that the fragrance components have no impact on the pediculicidal effect.
<i>In vitro</i> Study on the Efficacy of the Dimeticone-Based Pediculicide NYDA and of Three Reference Medical Products Against Human Head Lice (<i>Pediculus humanus capitis</i>)	Examination of the pediculicidal efficacy of NYDA in comparison to three reference products.
Comparative <i>in-vitro</i> Study on the Efficacy of Five Head Lice Products Against Human Head Lice	Examination of the pediculicidal efficacy of NYDA in comparison to four reference products.
Ovicidal Efficacy of NYDA, Infectopedicul [®] , Mosquito [®] Laushampoo, Goldgeist [®] forte and Etopril [®] against Young and Mature Eggs of Human Head Lice	Examination of the ovicidal efficacy of NYDA on young and mature eggs of head lice in comparison to several other lice treatments.
Ovicidal response of NYDA formulations on the human head louse (Anoplura: Pediculidae) using a hair tuft bioassay	Demonstrate 100% ovicidal effect after 8-h exposure of the eggs of the permethrin-resistant human head lice.

TOXICOLOGY

The following studies have been conducted with NYDA.

Test	Result	Test article	Conclusion
Cytotoxicity	None of the extract concentrations showed any cytotoxic reactions.	NYDA <u>without</u> fragrances	NYDA without fragrances is not cytotoxic.
Irritation (Intracutaneous Reactivity)	No irritant effects on intact skin after a contact time of 4 hours.	NYDA	No irritant/corrosive effects and NYDA is classified into the lowest response category (negligible).
Sensitization	The test item caused no reactions identified as sensitization.	NYDA	No sensitizing properties.
Acute Eye Irritation	Slight irritation (Redness of conjunctivae (grade 1)) in 2 out of 3 test animals at 24 hours post instillation, changes were fully reversible within 48 hours.	NYDA	Not an-eye irritant.

REFERENCES

1. Richling I. and Böckeler W. (2008): Lethal effects of treatment with a special dimeticone formula on insects (Orthoptera, Ensifera: *Acheta domestica* and Anoplura, Phthiraptera: *Pediculus humanus*) – Insights into physical mechanisms. *Arzneimittelforschung (Drug Research)* 58 (5), 248-254.
2. Heukelbach J. *et al.* (2008): A highly efficacious pediculicide based on dimeticone: randomized observer blinded comparative trial. *BMC Infect. Dis.* 8 (115); doi:10.1186/1471-2334-8-115.
3. Richling I. and Böckeler W. (2007): Physical effects on the tracheal system of lice (Anoplura, Phthiraptera: *Pediculus humanus*) after treatment with the special dimeticone formula NYDA[®]. Presented on the 41st Annual Meeting of the Austrian Society of Tropical Medicine and Parasitology, Vienna, Austria.
4. Oliveira F.A.S., Speare R., Heukelbach J. (2007): High *in vitro* efficacy of Nyda[®] L, a pediculicide containing dimeticone. *J. Dermatol. Venereol.*, 21 (10), 1325-1329.
5. Oliveira F.A.S. *et al.* (2008): *In vitro* efficacy of five current head lice products. *Monatsschr. Kinderheilkd.*, Band 156, suppl. 1, S. 82. Poster presentation.
6. Sonnberg S. *et al.* (2008): Ovicidal efficacy of head lice products. *Monatsschr. Kinderheilkd.*, Band 156, suppl. 1, S. 82-83. Poster presentation.
7. J Heukelbach. *et al.* (2009): A new two-phase dimeticone pediculicide shows high efficacy in a comparative bioassay. *BMC Dermatol.* 2009: 9:12; doi:10.1186/1471-5945-9-12.
8. Marcoux *et al.* (2010): Pyrethroid Pediculicide Resistance of Head Lice in Canada Evaluated by Serial Invasive Signal Amplification Reaction. *Journal of Cutaneous Medicine and Surgery*, Vol 14, No 3 (May/June), pp 115–118.
9. Strycharz JP *et al.* (2012): Ovicidal response of NYDA formulations on the human head louse (Anoplura: Pediculidae) using a hair tuft bioassay. *Journal of Medical Entomology*, Vol 49, No 2 (March), pp 336-342.

PART III: CONSUMER INFORMATION

**NYDA
Dimeticone 100 cSt Solution, 50% w/w**

This leaflet is part III of a three-part "Product Monograph" published when NYDA was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about NYDA. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

NYDA is used for the physical treatment of scalp hair in case of infestation with head lice (pediculosis capitis). If used as instructed, NYDA is also effective against nymphs and eggs (nits).

What it does:

NYDA solution creeps deeply into the breathing system of the lice, nymphs and eggs resulting in suffocation.

When it should not be used:

NYDA must not be used in people with known hypersensitivity (e.g. allergic reaction) to any of its ingredients (see **What the non-medicinal ingredients are**).

If any allergic reactions should occur, stop treatment with NYDA.

NYDA should not be used in pregnant or breastfeeding mothers or children under the age of 2.

What the medicinal ingredient is:

Dimeticone 100 cSt

What the non-medicinal ingredients are:

Alpha-terpineol , *Corymbia citriodora* (boabo oil), Jojoba wax, low viscosity dimeticone and triglycerides.

What dosage forms it comes in:

NYDA is available as a Lice Treatment Solution. NYDA is supplied in a 50 mL bottle with a plastic screw cap. It is packaged with a threaded pump with spray nozzle. The spray nozzle must be attached and primed before use.

WARNINGS AND PRECAUTIONS

CAUTION: FLAMMABLE:

- Keep away from any open flame or heat source which uses an open flame.
- Keep away from sources of ignition and do not smoke while using this product.

BEFORE you use NYDA talk to your doctor if:

- You are allergic to dimeticones
- You are pregnant or breast feeding

- You are allergic to any ingredients in NYDA

When using this product

For external use only.

- You should make sure that NYDA does not come into contact with the eyes or mucous membranes (nose or mouth). If product accidentally gets into the eyes, rinse immediately for 10-15 minutes with water.
- Avoid inhaling or swallowing NYDA.
- NYDA could react with certain hair care and hair tinting products.
- Keep out of reach of children.
- If the infestation recurs or persists after the second application, consult your doctor.
- Keep away from any open flame or heat source which uses an open flame.
- Keep away from sources of ignition and do not smoke while using this product.
- Close eyes tightly while applying NYDA.
- If skin irritation occurs, discontinue use and contact your doctor.

Care should be taken when applying this product since it will make hard surfaces such as floors and baths slippery.

INTERACTIONS WITH THIS MEDICATION

There are no drugs that are known to interact with NYDA. Some hair products or hair tinting products may interact with NYDA.

No drug interaction studies have been conducted for NYDA.

PROPER USE OF THIS MEDICATION

Usual dose:

Appropriate dosage for adult and/or children (2 years or older).

Hair Length	Average vol per appl. (part)
Short	1/5 of a bottle
Shoulder length (medium)	1/3 of a bottle
Long	1/2 of a bottle
Very Long	3/4 of a bottle

Directions

Before NYDA is used for the first time, the enclosed dispensing pump must be screwed onto the glass bottle. Always hold the spray bottle upright or the pump will not be able to work properly. Please note that the pump will need to be primed, by pumping, when used for the first time and when it has been unused for a long period.

Before treatment with NYDA

Inspect all scalp hair of each family member or close contacts, with a comb. Treat everyone with lice on the same day to avoid re-infestation. A normal comb can be used before treatment to remove any tangles. This comb should be cleaned thoroughly after use.

According to various Canadian guidelines, additional measures recommended are as follows.

Most household articles in contact with the infested individual, which could harbor the lice and nits, should be examined and appropriately treated. Clothes worn 48 hours prior to treatment, hats, towels and bed linens should be washed in hot water, or dry cleaned, and put in a dry hot setting for 20 minutes or sealed in a plastic bag for 2 weeks, then washed normally.

Items that cannot be washed or dry cleaned, such as mattresses, upholstery, or car seats should be thoroughly vacuumed.

Combs, brushes and other hair care articles can be disinfected by soaking in hot water (above 54°C or 130°F) for 5 to 10 minutes. It is advisable that all members of a family be treated at the same time.

All family members should avoid borrowing personal items (e.g. combs, brushes, hairstyling tools, hats, towels, clothing, etc.) from each other or from friends.

Do not use other topical scalp medications or hair care products while using NYDA.

Treatment with NYDA

NYDA should be applied to dry hair.

1. Wet hair completely with NYDA and leave for 30 minutes.

Apply NYDA to the dry hair close to the scalp. To make sure that an adequate coverage is achieved divide the hair in sections. Pick up hair by sections and carefully spray the roots and scalp of each section. When all sections of the scalp and hair roots have been well coated with NYDA, massage the solution well into the rest of the hair until all the hair including the tips is completely covered.

The amount of NYDA needed depends on the thickness and length of the hair. Make sure that the hair near the scalp and behind the ears is particularly well covered with NYDA, as this is where most lice and nits are found. Leave NYDA on for at least 30 minutes.

2. After 30 minutes, comb hair carefully using a lice comb.

After NYDA has been left on for at least 30 minutes, you may comb the hair carefully with the lice comb to remove the suffocated lice. NYDA makes combing easier because it

contains special ingredients which make even long hair very easy to comb.

What is the correct way to use a lice comb for detection and removing of head lice?

Part the hair on the head into several sections and divide each section into fine strands. Comb each strand individually, starting as close to the scalp as possible; i.e. combing from the roots to the tips of the hair. In this way, you can stop the lice from creeping back. Pin back each strand of hair which has been treated with the comb and clean the comb with a paper tissue before continuing.

3. Do not washout! Leave the hair to dry for at least 8 hours (e.g. overnight).

Lice eggs (nits) are very resilient and particularly difficult to remove. Lice stick nits to the hair like strings of tiny white beads. The glue is very resistant and similar in structure to the hair. Even careful combing is not enough to remove all nits from the hair.

You should leave NYDA on the hair for at least 8 hours (e.g. overnight) so that even the most tenacious nits will suffocate.

4. Wash out with normal commercial shampoo.

After a total of at least 8 hours, NYDA can be washed out with your usual shampoo. Any residue of the solution still present after the first wash can be removed easily with a second hair wash.

5. After 8 to 10 days, the treatment must be repeated.

For complete control of head lice and nits, the treatment must be repeated as described above after 8 to 10 days.

Overdose:

In case of oral ingestion, contact a healthcare practitioner (e.g. doctor), hospital emergency department or regional Poison Control Centre, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Adverse reactions are not common with NYDA. If irritation occurs, stop treatment with NYDA.

Irritation of the eyes can occur with NYDA if they come into contact. Flush with water for 10 to 15 minutes if this occurs.

HOW TO STORE IT

Store between 15-30°C.

Keep out of reach of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701D
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.nyda.ca>

or by contacting the marketer, Pediapharm Inc. at:
1-877-630-5674.

This leaflet was prepared by G. Pohl Boskamp GmbH & Co. KG,
Kieler Strasse 11, 25551 Hohenlockstedt, Germany.

Distributed by: Pediapharm Licensing Inc., Dundas, Ontario, L9H
7P3

Last revised: September 11, 2012