

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use NITROLINGUAL® PUMPSpray safely and effectively. See full prescribing information for NITROLINGUAL® PUMPSpray.

**NITROLINGUAL® PUMPSpray (nitroglycerin) lingual spray**

Initial U.S. Approval: 1997

**INDICATIONS AND USAGE**

Nitrolingual Pumpspray is a nitrate vasodilator indicated for acute relief of an attack or prophylaxis of angina pectoris due to coronary artery disease (1).

**DOSAGE AND ADMINISTRATION**

- At the onset of an attack, administer onto or under the tongue. Repeat every 5 minutes as needed (2.1).
- Do up to three metered sprays within a 15-minute period. If chest pain persists, advise prompt medical attention (2.1).
- May be used prophylactically 5 to 10 minutes prior to engaging in activities that might precipitate an acute attack (2.1).

**DOSAGE FORMS AND STRENGTHS**

Lingual spray, 400 mcg per spray, available in 60 or 200 metered sprays per container (3).

**CONTRAINDICATIONS**

- Use of phosphodiesterase type 5 (PDE-5) Inhibitors,

such as avanafil, sildenafil, tadalafil, or vardenafil, or soluble guanylate cyclase (sGC) stimulator (riociguat). (4.1, 7.1)

- Severe anemia. (4.2)
- Increased intracranial pressure. (4.3)
- Hypersensitivity to Nitrolingual Pumpspray or to other nitrates or nitrites or any excipient. (4.4)

**WARNINGS AND PRECAUTIONS**

Tolerance: Excessive use may lead to tolerance. (5.1)

Hypotension: Severe hypotension may occur. (5.2)

**ADVERSE REACTIONS**

Most common adverse reactions occurring at a frequency greater than 2% are headache, dizziness and paresthesia (6).

To report SUSPECTED ADVERSE REACTIONS, contact Allegis Pharmaceuticals, LLC at 1-866-633-9033 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

**DRUG INTERACTIONS**

- Antihypertensives: possible additive hypotensive effects. (7.2)
- Ergotamine: increased bioavailability of ergotamine. Avoid concomitant use (7.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

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**FULL PRESCRIBING INFORMATION****1 INDICATIONS AND USAGE**

Nitrolingual Pumpspray is indicated for acute relief of an attack or prophylaxis of angina pectoris due to coronary artery disease.

**2 DOSAGE AND ADMINISTRATION****2.1 Recommended Dosage**

Instruct the patient to administer one or two metered sprays (400 mcg of nitroglycerin per spray) at the onset of an attack onto or under the tongue. A spray may be repeated approximately every five minutes as needed. No more than three metered sprays are recommended within a 15-minute period. If the chest pain persists after a total of three sprays, advise prompt medical attention. Nitrolingual Pumpspray may be used prophylactically 5 to 10 minutes prior to engaging in activities that might precipitate an acute attack.

**2.2 Priming**

The pump must be primed prior to the first use. Each metered spray of Nitrolingual Pumpspray delivers 48 mg of solution containing 400 mcg of nitroglycerin after an initial priming of five sprays. It will remain adequately primed for 6 weeks. If the product is not used within 6 weeks it can be adequately re-primed with one spray. If the product is not used within 3 months it can be adequately re-primed with up to five sprays. There are 60 or 200 metered sprays per bottle. The total number of available doses is dependent, however, on the number of sprays per use (1 or 2 sprays), and the frequency of priming.

**2.3 Administration**

Instruct patients that during administration, the patient should rest, ideally in the sitting position. Hold the container vertically with the valve head uppermost and the spray orifice as close to the mouth as possible.

Spray the dose preferably onto or under the tongue by pressing the grooved-button firmly and the mouth closed immediately after each dose.

THE SPRAY SHOULD NOT BE INHALED. The medication should not be expectorated or the mouth rinsed for 5 to 10 minutes following administration. Instruct patients to familiarize themselves with the position of the spray orifice, which can be identified by the finger rest on top of the valve, in order to facilitate orientation for administration at night [see Patient Information (17)].

The amount of liquid remaining in the container should be checked periodically. The transparent container can be used for continuous monitoring of the consumption. With the container upright and level, check to be sure the end of the center tube extends below the level of the liquid. Once fluid falls below the level of the center tube, remaining sprays will not deliver intended dose.

**3 DOSAGE FORMS AND STRENGTHS**

Lingual spray, 400 mcg per spray available in either 60 or 200 metered sprays per container.

**4 CONTRAINDICATIONS****4.1 PDE-5-Inhibitors and sGC-Stimulators**

Do not use Nitrolingual Pumpspray in patients who are taking PDE-5-Inhibitors, such as avanafil, sildenafil, tadalafil, or vardenafil. Concomitant use can cause severe hypotension, syncope, or myocardial ischemia [see Drug Interactions (7.1)].

Do not use Nitrolingual Pumpspray in patients who are taking soluble guanylate cyclase (sGC) stimulators, such as riociguat. Concomitant use can cause hypotension.

**4.2 Severe Anemia**

Nitrolingual Pumpspray is contraindicated in patients with severe anemia (large doses of nitroglycerin may cause oxidation of hemoglobin to methemoglobin and could exacerbate anemia).

**4.3 Increased Intracranial Pressure**

Nitrolingual Pumpspray may precipitate or aggravate increased intracranial pressure and thus should not be used in patients with possible increased intracranial pressure (e.g. cerebral hemorrhage or traumatic brain injury).

**4.4 Hypersensitivity**

Nitrolingual Pumpspray is contraindicated in patients who are allergic to nitroglycerin, other nitrates or nitrites or any excipient.

**4.5 Circulatory Failure and Shock**

Nitrolingual Pumpspray is contraindicated in patients with acute circulatory failure or shock.

**5 WARNINGS AND PRECAUTIONS****5.1 Tolerance**

Excessive use may lead to the development of tolerance. Only the smallest number of doses required for effective relief of the acute angina attack should be used [see Dosage and Administration (2.1)].

**5.2 Hypotension**

Severe hypotension, particularly with upright posture, may occur even with small doses of nitroglycerin particularly in patients with constrictive pericarditis, aortic or mitral stenosis, patients who may be volume-depleted, or are already hypotensive. Hypotension induced by nitroglycerin may be accompanied by paradoxical bradycardia and increased angina pectoris. Symptoms of severe hypotension (nausea, vomiting, weakness, pallor, perspiration and collapse/syncope) may occur even with therapeutic doses.

**5.3 Hypertrophic Obstructive Cardiomyopathy**

Nitrate therapy may aggravate the angina caused by hypertrophic obstructive cardiomyopathy.

**5.4 Headache**

Nitroglycerin produces dose-related headaches, especially at the start of nitroglycerin therapy, which may be severe and persistent but usually subside with continued use.

**6 ADVERSE REACTIONS****6.1 Clinical Trials Experience**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Adverse reactions occurring at a frequency greater than 2% and greater than placebo included: headache, dizziness, and paresthesia.

**6.2 Postmarketing Experience**

The following adverse reactions have been identified during post-approval use of Nitrolingual Pumpspray and other nitroglycerin drugs. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably or establish a causal relationship to drug exposure.

Neurologic: weakness, drowsiness

Dermatologic: cutaneous vasodilation, flushing, drug rash, exfoliative dermatitis

Gastrointestinal: nausea, vomiting

Respiratory: transient hypoxemia

Cardiovascular: tachycardia

**7 DRUG INTERACTIONS****7.1 PDE-5-Inhibitors and sGC-Stimulators**

Nitrolingual Pumpspray is contraindicated in patients who are using a selective inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE-5). PDE-5-Inhibitors such as avanafil, sildenafil, vardenafil, and tadalafil have been shown to potentiate the hypotensive effects of organic nitrates.

Nitrolingual Pumpspray is contraindicated in patients who are taking soluble guanylate cyclase (sGC) stimulators. Concomitant use can cause hypotension.

The time course and dose dependence of these interactions have not been studied, and use within a few days of one another is not recommended.

Appropriate supportive care for the severe hypotension has not been studied, but it seems reasonable to treat this as a nitrate overdose, with elevation of the extremities and with central volume expansion.

**Nitrolingual® Pumpspray****INFORMATION FOR THE PATIENT****Instructions for Use****Nitrolingual® Pumpspray (ni-trō-ling gwāl)****(nitroglycerin)****lingual spray**

Read this Instructions for Use before you start using Nitrolingual Pumpspray and each time you get your prescription refilled. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

**Important information:****Nitrolingual Pumpspray is for use onto or under the tongue.**

Do not inhale Nitrolingual Pumpspray.

A dose of Nitrolingual Pumpspray may be either 1 or 2 sprays. Follow your healthcare provider's instructions about how many sprays you should use for each dose. Doses should be separated by approximately 5 minutes.

You should not use more than 3 sprays of Nitrolingual Pumpspray within 15 minutes.

Get emergency medical help right away if you still have chest pain after using a total of 3 sprays of Nitrolingual Pumpspray.

**Nitrolingual Pumpspray parts:****Figure A**

Grooved button (to position your finger on the bottle for correct orientation, even at night)

Black nozzle

Actuator

Red-coated see-thru bottle

Cap

**Priming Nitrolingual Pumpspray:**

Before you use Nitrolingual Pumpspray for the first time, you must prime it. To prime your Nitrolingual Pumpspray, follow the steps below:

**Step 1.**

Remove the plastic cap from the container. (See Figure B)

**Step 2.**

Hold the container upright and facing away from yourself and others. Press down on the top of the grooved button 5 times. (See Figure C)

Your Nitrolingual Pumpspray is now primed. You are ready to give your first dose.

If you do not use your Nitrolingual Pumpspray within 6 weeks, you will need to prime it again by pressing down on the top of the grooved button 1 time.

If you do not use your Nitrolingual Pumpspray within 3 months, you will need to re-prime it by pressing down on the top of the grooved button up to 5 times.

Figure B



Figure C



