The most common adverse reactions occurring in >10% of patients include runny nose, nasal congestion, swelling of the membranes, lips and nail beds. In severe cases, symptoms may include central cyanosis, headache, dyspnea, and circulatory collapse. Methemoglobinemia: Tetracaine may cause methemoglobinemia, particularly in conjunction with methemoglobin-inducing agents. Based on the literature, patients with glucose-6-phosphate dehydrogenase deficiency or congenital or idiopathic methemoglobinemia are more susceptible to drug-induced methemoglobinemia. Use of KOVANAZE in patients with a history of congenital or idiopathic methemoglobinemia is not advised. Patients taking concomitant drugs associated with drug-induced methemoglobinemia, such as sulfonamides, acetaminophen, acetanilide, aniline dyes, benzocaine, chloroquine, dapsone, naphthalene, nitrites and nitrates, nitrofurantoin, nitroglycerin, nitroprusside, pamaquine, p-aminosalicylic acid, phenacetin, phenobarbital, phenytoin, primaquine, and quinine, may be at greater risk for developing methemoglobinemia. Initial signs and symptoms of methemoglobinemia (which may be delayed for up to several hours following exposure) are characterized by a slate grey cyanosis seen in, e.g., buccal mucous membranes, lips and nail beds. In severe cases, symptoms may include central cyanosis, headache, lethargy, dizziness, fatigue, syncope, dyspnea, CNS depression, seizures, dysrhythmia and shock. Methemoglobinemia should be considered if central cyanosis unresponsive to oxygen therapy occurs, especially if methemoglobinemia-inducing agents have been used. Calculated oxygen saturation and pulse oximetry are inaccurate in the identification of methemoglobinemia. Confirm diagnosis by measuring methemoglobin level with CO-oximetry. Normally, methemoglobinemia levels are <1%, and cyanosis may not be evident until a level of at least 10% is present. Treat clinically significant symptoms of methemoglobinemia with a standard regimen such as a slow intravenous infusion of methylene blue at a dosage of 1-2 mg/kg given over a 5 minute period. Anaphylactic Reactions: Allergic or anaphylactic reactions have been associated with tetracaine, and may occur with other components of KOVANAZE. They are characterized by urticaria, angioedema, bronchoconstriction, and anaphylactic shock. In severe cases, anaphylactic shock may be fatal. Use of KOVANAZE with other products containing these components should be avoided. Epistaxis: In clinical trials, epistaxis occurred more frequently with KOVANAZE than placebo. Either do not use KOVANAZE in patients with a history of frequent nose bleeds (>5 per month) or monitor patients with frequent nose bleeds more carefully if KOVANAZE is used. Dysphagia: In clinical trials, dysphagia occurred more frequently with KOVANAZE than placebo. Carefully monitor patients for this adverse reaction. Pseudocholinesterase Deficiency: Because of an inability to metabolize local anesthetics, those patients with pseudocholinesterase deficiency may be at a greater risk of developing toxic plasma concentrations of tetracaine. Monitor patients with hepatic disease for signs of local anesthetic toxicity. OVERDOSAGE No addictive properties have been reported in the literature for either tetracaine or oxymetazoline, but there have been numerous case reports of unintended overdose for both compounds. Side effects in adults and children associated with oxymetazoline overdose include dizziness, chest pain, headache, myocardial infarction, stroke, visual disturbances, arrhythmia, hypertension, or hypotension. Side effects of tetracaine overdose include rapid circulatory collapse, cardiac arrest, and cerebral events. Possible rebound nasal congestion, irritation of nasal mucosa, and adverse systemic effects (particularly in children), including serious cardiac events, have been associated with overdosage and/or prolonged or too frequent intranasal use of oxymetazoline containing agents. Accidental ingestion of midazolam derivatives (i.e., oxymetazoline, tetracaine, naproxenol, tetracyrozinol) in children has resulted in serious adverse events requiring hospitalization (e.g., coma, bradycardia, decreased respiration, sedation, and somnolence). Patients should be instructed to avoid using oxymetazoline-containing products (such as Afrin®) and other α-adrenergic agonists in 24 hours prior to their scheduled dental procedure. Management of an overdose includes close monitoring, supportive care, and symptomatic treatment.

HOW SUPPLIED
KOVANAZE Nasal Spray is a pre-filled, single-use, intranasal spray containing a 0.2 ml aqueous solution at pH 6.0 ± 1.0 comprising 30 mg/mL of tetracaine hydrochloride and 0.5 mg/mL of oxymetazoline hydrochloride (equivalent to 26.4 mg/mL tetracaine and 0.44 mg/mL oxymetazoline). Each nasal spray unit delivers 0.2 ml spray. Each 0.2 ml spray contains 6 mg tetracaine hydrochloride (equivalent to 5.27 mg tetracaine) and 0.1 mg oxymetazoline hydrochloride (equivalent to 0.088 mg oxymetazoline). NDC: 69803-100-10

STORAGE AND HANDLING
Store between 2° and 8°C (36° and 46°F); excursions permitted between 0° and 15°C (32° and 59°F) [see Store between 36° and 46°F]. Discard any unused solution. DO NOT use if drug is left out at room temperature for more than 5 days.

PATIENT COUNSELING INFORMATION
Inform patients of the likelihood of expected side effects (including runny nose, nasal congestion, mild nose bleeds, dizziness, and/or a sensation of difficulty in swallowing) that should resolve within the same day. Instruct patients to contact their dental or health care professional if these symptoms persist.

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