Dear Doctor,

Aptalis Pharma US, Inc. has announced the availability of **RECTIV** (nitroglycerin) Ointment 0.4%, a nitroglycerin formulation approved by the FDA for the treatment of moderate to severe pain associated with chronic anal fissure (CAF). RECTIV does not need to be compounded and is available at most pharmacies, including chain pharmacies.

The dosing for patients with moderate to severe pain from CAF is 1 inch of RECTIV ointment applied intra-anally every 12 hours for up to 3 weeks.*

In a 21-day, randomized, double-blind, placebo-controlled clinical trial of 247 patients, RECTIV significantly reduced moderate to severe pain from CAF vs placebo. Adjusted mean change in average pain visual analog scale (VAS) score from baseline to between days 14 and 18 was 44 mm for RECTIV and 37 mm for placebo ($P=0.038$; 95% CI: -13.6 mm, -0.4 mm).†

†When used BID based on absolute change in 24-hour average pain intensity from baseline to days 14 and 18, as measured by VAS. Mean VAS score at baseline was 72.7 mm for RECTIV and 73.0 mm for placebo; mean VAS score on days 14-18 was 30.7 mm for RECTIV and 37.8 mm for placebo. Based on a hybrid analysis of baseline observation carried forward/last observation carried forward.‡

The most common adverse events (≥2%) for RECTIV were headache (64%) and dizziness (5%). The incidences of headache and dizziness for placebo were 41% and 0%, respectively.† However, headache was not treatment limiting in most patients—nearly 93% of RECTIV patients and nearly 97% of placebo patients completed the trial. All patients were instructed to take a standard dose (650 mg) of acetaminophen before each application of RECTIV or placebo.‡

RECTIV produces dose-related headaches, which may be severe. Tolerance to headaches occurs. Headaches may recur after each dose of RECTIV; they are typically short in duration, can be treated with an OTC analgesic, and are reversible upon discontinuation of treatment.†

*375 mg of ointment is equivalent to 1.5 mg of nitroglycerin.

CI, confidence interval.

**Important Safety Information**

- RECTIV is contraindicated in patients:
  - Taking phosphodiesterase type 5 (PDE5) inhibitors (eg, sildenafil, vardenafil, and tadalafil), which can potentiate the hypotensive effect of organic nitrates
  - With severe anemia
  - With increased intracranial pressure
  - With known hypersensitivity to nitroglycerin, other nitrates and nitrites, or any components of the ointment

- Patients with cardiovascular disorders should be closely monitored while using RECTIV
Venous and arterial dilation as a consequence of nitroglycerin treatment can result in hypotension.

Exercise caution when treating patients with any of the following conditions: blood volume depletion, existing hypotension, cardiomyopathies, congestive heart failure, acute myocardial infarction, or poor cardiac function for other reasons.

The adverse reactions of RECTIV are likely to be more pronounced in the elderly.

Nitroglycerin produces dose-related headaches, which may be severe.

The following drug interactions may occur in patients taking RECTIV:

- PDE5 inhibitors: potentiation of hypotensive effects of organic nitrates; concomitant use is contraindicated.
- Antihypertensives: possible additive hypotensive effects.
- Aspirin: increased nitroglycerin levels.
- Tissue-type plasminogen activator (t-PA): decreased thrombolytic effect.
- Heparin: anticoagulant effect of heparin may be reduced. Monitor activated partial thromboplastin time (APTT).
- Ergotamine: increased bioavailability of ergotamine.
- Alcohol: additive vasodilatory effects to nitroglycerin. Consumption of alcohol should be avoided.

The most common adverse reaction (≥2%) are headache and dizziness.

RECTIV ointment is for intra-anal use, and not for oral, ophthalmic, or intravaginal use.


For more information on RECTIV and Aptalis’ Patient Assistance Program, please visit www.RECTIV.com/.

Steven Merahn, MD
Chief Medical Officer
Physicians’ Desk Reference®

References:


RECTIV (nitroglycerin) Ointment 0.4%, for intra-anal use
Rx Only
Initial U.S. Approval: 1995
Brief summary of Prescribing Information. Please consult package insert for full Prescribing Information.
INDICATIONS AND USAGE: RECTIV™ (nitroglycerin) Ointment 0.4% is indicated for the treatment of moderate to severe pain associated with chronic anal fissure.
CONTRAINDICATIONS: PDE5 inhibitor use - Administration of RECTIV is contraindicated in patients who are using a selective inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE5), such as sildenafil, vardenafil, and tadalafil, as these are shown to potentiate the hypotensive effects of organic nitrates [see DRUG INTERACTIONS]. Severe anemia - RECTIV is contraindicated in patients with severe anemia. Increased intracranial pressure - RECTIV is contraindicated in patients with increased intracranial pressure. Hypersensitivity - RECTIV is contraindicated in patients who have shown hypersensitivity to it or to other nitrates or nitrites. Skin reactions consistent with hypersensitivity have been observed with organic nitrates.
WARNINGS AND PRECAUTIONS: Cardiovascular disorders - Venous and arterial dilatation as a consequence of nitroglycerin treatment including RECTIV, can decrease venous blood returning to the heart and reduce arterial vascular resistance and systolic pressure. Exercise caution when treating patients with any of the following conditions: blood volume depletion, existing hypotension, cardiomyopathies, congestive heart failure, acute myocardial infarction, or poor cardiac function for other reasons. If patients with any of these conditions are treated with RECTIV, monitor cardiovascular status and clinical condition. The adverse reactions of RECTIV are likely to be more pronounced in the elderly. Headache - RECTIV produces dose-related headaches, which may be severe. Tolerance to headaches occurs.
ADVERSE REACTIONS: 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 practice. The most common adverse reaction of RECTIV (nitroglycerin) Ointment 0.4% applied to the anal canal is headache. Headache may be recurrent following each dose. Headaches are typically of short duration and can be treated with an analgesic, e.g., acetaminophen, and are reversible upon discontinuation of treatment. In Study REC-C-001, a double-blind, placebo-controlled trial in patients with a painful chronic anal fissure, the most frequent (2%) adverse reactions reported as adverse events were as follows (Table 1):