MEDCO FORUM®
PRESENTING INNOVATIVE PRODUCTS AND SERVICES TO HEALTHCARE PROFESSIONALS
VOLUME 18 NUMBER 6
MAY 2011
REPRINT

PHYSICIAN RECOMMENDATIONS INFLUENCE PATIENT ACCEPTANCE OF ULCERATIVE PROCTITIS THERAPY

Ulcerative proctitis (UP) is a type of inflammatory bowel disease in which mucosal inflammation is limited to the rectum. UP is chronic and the symptoms, including bleeding, diarrhea, tenesmus and rectal pain, can be debilitating. In the past, appropriate treatment has been limited, and there have been misconceptions between patient needs and physician understanding of UP. Improvements in diagnostic procedures and the development of topical medications have improved the outlook for proctitis patients.

The key to treatment success in UP is delivering therapeutic levels of medication, such as 5-aminosalicylic acid (5-ASA) or mesalamine to the site of inflammation.[1] Topical 5-ASA therapies (i.e., suppositories and enemas) are first-line medications for treating the symptoms of UP according to guidelines developed by the American College of Gastroenterology (2010) and Crohn's and Colitis Foundation of America (2006).[1,2] Although both oral and topical formulations of mesalamine are effective treatments for UP, topical formulations generally result in quicker relief of symptoms, require less frequent dosing, and have less systemic absorption than oral formulations.[1,3] The choice of topical medication is guided by extent of disease as well as patient preference.[1] Mesalamine suppositories target the rectal vault (disease limited to 20 cm), whereas >90% of the liquid in 5-ASA enemas tends to bypass the rectum, making the latter more appropriate for distal or left-sided disease.[4,5,6] Suppositories may also be a more practical alternative for patients with UP, because they are easier to administer and retain than enemas.[7]

Despite the morbidity associated with UP, and the availability of efficacious and well-tolerated topical treatments, only about half of patients with newly diagnosed UP or UP flares are treated with mesalamine suppositories.[8,9] The reluctance of physicians to prescribe suppositories may be due to the perception that patients will resist rectal therapy.[9]

Helping patients to understand the disease process, how the medications work, and the time course for relief of symptoms can overcome initial patient reluctance to use topical therapies. According to Neil Stollman, MD, a gastroenterologist and Chairman of the Department of Medicine at Alta Bates Summit Medical Center in Oakland, CA, "I find a simple anatomy lesson works to start. 'The problem is down there and your mouth is up here. It doesn't make much sense to deliver medicine that needs to travel through 30 feet of intestine to treat the bottom three inches which is diseased.' That logic speaks to people. It's hard to argue with that... it gets patients to try it." Dr. Stollman goes on to explain that there are differences in the practicality of the various rectal treatment regimens, "People tend to throw enemas and suppositories together, but they are largely different. There is minimal impact on a patient's daily activities with suppository treatment. They can take it in the bathroom before bed. It is completely invisible to the world."

Steven J. Sanderson, MD, a Minneapolis, MN-based gastroenterologist, recently co-authored a study assessing patient perceptions and preferences for topical treatment in the management of UP.[10] This survey-based study of 250 patients diagnosed with UP, was presented at the Advances in Inflammatory Bowel Diseases meeting in Hollywood, FL in December, 2010. The investigators found that of patients prescribed topical 5-ASA (see Figure 1 below), 62% would use a suppository without hesitation versus 38% who would use an enema without hesitation. Among patients who perceived that their disease was worsening, acceptance of suppositories was even higher. "This study is like a tale of two cities," notes Dr. Sanderson, "what patients are telling us about their preferences vs. physicians' own beliefs and tendencies. According to the study, among patients who perceive their ulcerative proctitis is worsening, 93 percent are willing to take suppositories, vs. 53 percent for enemas. There was a clear patient preference for suppositories in this survey."

James F. Marion, MD, an Associate Clinical Professor at The Mount Sinai School of Medicine in New York City, feels that empathy and patient education are important in ensuring acceptance of treatment with mesalamine suppositories:

"Most patients have never had to use suppositories. It's an unusual delivery system for an adult. We need to be extremely sensitive to this, especially with newly diagnosed patients. You have to be incredibly empathetic. Communicate that they can take it at night if they have trouble with it during the day. Help teach them how to take it more comfortably – be explicit about it. When you do this, patients acclimate quite nicely. I don't remember a patient who said they would never take a suppository again. Laying the groundwork in the beginning is also important to adherence."

Canasa® (mesalamine, USP) 1000 mg rectal suppositories are the only FDA-approved, once-daily suppositories indicated for the treatment of active ulcerative proctitis. The usual dosage of Canasa® is one rectal suppository once daily at bedtime. Canasa® is contraindicated in patients who have demonstrated hypersensitivity to mesalamine or to the suppository vehicle, or to salicylates (including aspirin).[4] As with other mesalamine-containing products, less common but possible serious side effects such as acute intolerance syndrome, pericarditis, and pancolitis may occur. Canasa® is generally well-tolerated; the most common adverse events observed in clinical trials were dizziness (3%), rectal pain (1.8%), fever, rash, acne, and colitis (1.2%).[4]

Canasa® and Axcan Pharma™ are trademarks of Axcan Pharma US, Inc. or its subsidiaries.

For full U.S. Prescribing Information, go to www.canasa.com.

For more information about **Canasa®** or other Axcan Pharma™ products, please call (800)950-8085, or visit the company's website at www.axcan.com.

Trademarks are owned by their respective companies.

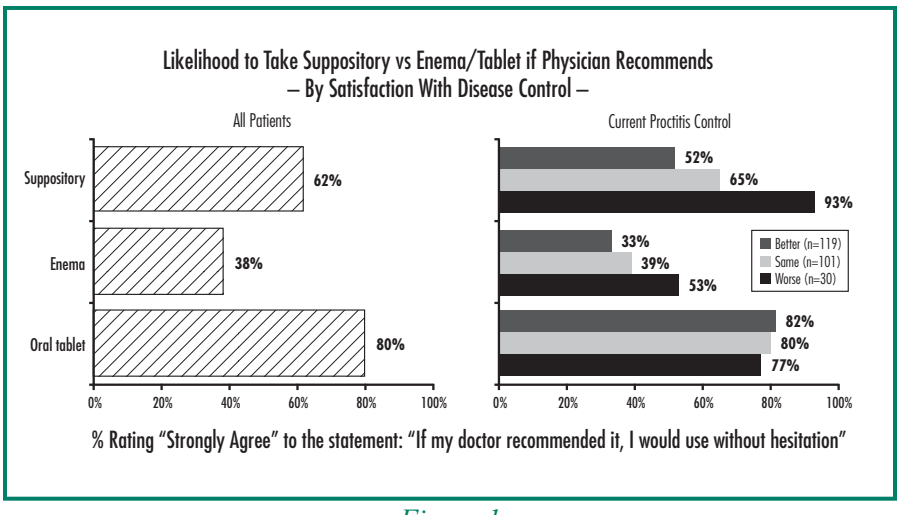

Figure 1

References

1. Kornbluth A, Sachar DB. *Am J Gastroenterol*. 2010;105(3):501-523.
2. Regueiro M, Loftus EV Jr, et al. *Inflamm Bowel Dis*. 2006;12(10):972-978.
3. Cohen, RD, Woseth, DM, et al. *Am J Gastroenterol*. 2000;95(5):1263-1276.
4. CANASA® [package insert]. Birmingham, AL: Axcan Pharma US, Inc; 2008.
5. Van Bodegraven AA, Boer RO, et al. *Aliment Pharmacol Ther*. 1996;10:327-332.
6. Travis, SPL. *Gut*. 2002;51:548-549.
7. Campieri, M, Gionchetti, P, et al. *J Clin Gastroenterol*. 1988;10(4):406-409.
8. Richter JG, Kushkuley, S, et al. Poster. American College of Gastroenterology, October 19, 2010. San Antonio, TX.
9. Data on file. Axcan Pharma US, Inc.
10. Sanderson SJ , Barrett, JA, et al. Poster. Advances in Inflammatory Bowel Diseases, December 9-12, 2010. Hollywood, FL.; Data on file. Axcan Pharma US, Inc.

CANASA®
(Mesalamine, USP)
Rectal Suppository 1000 mg
NDC 58914-501-56
NDC 58914-501-42
Rx Only

Brief summary of Prescribing Information. Please consult package insert for full Prescribing Information.

INDICATIONS AND USAGE
CANASA® 1000 mg suppositories are indicated for the treatment of active ulcerative proctitis.

CONTRAINDICATIONS
CANASA® 1000 mg suppositories are contraindicated in patients who have demonstrated hypersensitivity to mesalamine (5-aminosalicylic acid) or to the suppository vehicle [saturated vegetable fatty acid esters (Hard Fat, NF)], or to salicylates (including aspirin).

PRECAUTIONS
Mesalamine has been implicated in the production of an acute intolerance syndrome characterized by cramping, acute abdominal pain and bloody diarrhea, sometimes fever, headache and a rash; in such cases prompt withdrawal is required. The patient's history of sulfasalazine intolerance, if any, should be re-evaluated. If a rechallenge is performed later in order to validate the hypersensitivity, it should be carried out under close supervision and only if clearly needed, giving consideration to reduced dosage. In the literature, one patient previously sensitive to sulfasalazine was rechallenged with 400 mg oral mesalamine; within eight hours she experienced headache, fever, intensive abdominal colic, profuse diarrhea and was readmitted as an emergency. She responded poorly to steroid therapy and two weeks later a pancolectomy was required. The possibility of increased absorption of mesalamine and concomitant renal tubular damage as noted in the preclinical studies must be kept in mind. Patients on CANASA® 1000 mg, especially those on concurrent oral products which contain or release mesalamine and those with pre-existing renal disease, should be carefully monitored with urinalysis, BUN and creatinine testing.

In a clinical trial most patients who were hypersensitive to sulfasalazine were able to take mesalamine enemas without evidence of any allergic reaction. Nevertheless, caution should be exercised when mesalamine is initially used in patients known to be allergic to sulfasalazine. These patients should be instructed to discontinue therapy if signs of rash or fever become apparent.

A small proportion of patients have developed pancolitis while using mesalamine. However, extension of upper disease boundary and/or flare-ups occurred less often in the mesalamine-treated group than in the placebo-treated group.

Rare instances of pericarditis have been reported with mesalamine containing products including sulfasalazine. Cases of pericarditis have also been reported as manifestations of inflammatory bowel disease. In the cases reported there have been positive rechallenges with mesalamine or mesalamine containing products. In one of these cases, however, a second rechallenge with sulfasalazine was negative throughout a 2 month follow-up. Chest pain or dyspnea in patients treated with mesalamine should be investigated with this information in mind. Discontinuation of CANASA® suppositories may be warranted in some cases, but rechallenge with mesalamine can be performed under careful clinical observation should the continued therapeutic need for mesalamine be present.

There have been two reports in the literature of additional serious adverse events: one patient who developed leukopenia and thrombocytopenia after seven months of treatment with one 500 mg suppository nightly, and one patient with rash and fever which was a similar reaction to sulfasalazine.

ADVERSE REACTIONS
Clinical Adverse Experience
The most frequent adverse reactions observed in the double-blind, placebo-controlled trials are summarized in the Table below.

ADVERSE REACTIONS OCCURRING IN MORE THAN 1% OF MESALAMINE SUPPOSITORY TREATED PATIENTS (COMPARISON TO PLACEBO)

Symptom	Mesalamine (n=177)		Placebo (n=84)	
	N	%	N	%
Dizziness	5	3.0	2	2.4
Rectal Pain	3	1.8	0	0.0
Fever	2	1.2	0	0.0
Rash	2	1.2	0	0.0
Acne	2	1.2	0	0.0
Colitis	2	1.2	0	0.0

In the multicenter, open-label, randomized, parallel group study comparing the CANASA® 1000 mg suppository (HS) to that of the CANASA® 500 mg suppository (BID), there were no differences between the two treatment groups in the adverse event profile. The most frequent AEs were headache (14.4%), flatulence (5.2%), abdominal pain (5.2%), diarrhea (3.1%), and nausea (3.1%). Three (3) patients had to discontinue medication because of a treatment emergent AE; one of these AEs (headache) was deemed possibly related to study medication.

In addition to the events observed in the clinical trials, the following adverse events have been associated with mesalamine containing products: nephrotoxicity, pancreatitis, fibrosing alveolitis and elevated liver enzymes. Cases of pancreatitis and fibrosing alveolitis have been reported as manifestations of inflammatory bowel disease as well.

Hair Loss
Mild hair loss characterized by "more hair in the comb" but no withdrawal from clinical trials has been observed in seven of 815 mesalamine patients but none of the placebotreated patients. In the literature there are at least six additional patients with mild hair loss who received either mesalamine or sulfasalazine. Retreatment is not always associated with repeated hair loss.

Drug-Drug Interactions: The potential for interactions between mesalamine, administered as 1000 mg rectal suppositories, and other drugs has not been studied.

Special Populations (Patients with Renal or Hepatic Impairment): The effect of renal or hepatic impairment on elimination of mesalamine in ulcerative proctitis patients treated with mesalamine 1000 mg suppositories has not been studied.

Nursing Mothers
It is not known whether mesalamine or its metabolite(s) are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when CANASA® 1000 mg suppositories are administered to a nursing woman.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

Geriatric Use
Clinical studies of CANASA® did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Mesalamine is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function.

OVERDOSAGE
There have been no documented reports of serious toxicity in man resulting from massive overdosing with mesalamine. Under ordinary circumstances, mesalamine absorption from the colon is limited.

Rx only

Date of Revision: October 2008
AXCAN PHARMA™
Distributed by:
AXCAN PHARMA US, INC.
22 Inverness Center Parkway
Birmingham, Alabama 35242 USA

www.axcan.com