

## Pylera™ 3-in-1 Capsule

### *Taking the Complexity out of Treating H. pylori Infection*

The 1982 discovery by Drs. Barry Marshall and Robin Warren of the bacterium *Helicobacter pylori* (*H. pylori*) led not only to a Nobel Prize in medicine, it ultimately revolutionized the treatment of many upper gastrointestinal disorders. Their discovery showed that this bacterial infection was responsible for causing ulcers in the stomach and intestine, eventually transforming peptic ulcer disease (PUD) from a chronic, frequently debilitating condition to one that can be cured with a short course of medication. *H. pylori* is believed to be the underlying pathogen causing a wide spectrum of diseases in addition to ulcers, including gastritis, dyspepsia, gastric cancer, and gastric MALT lymphoma. It is estimated that approximately 30 percent of the US adult population is infected with *H. pylori*.<sup>1</sup>

#### Axcan Pharma Inc. (MontSaint-Hilaire, Quebec),

recently announced the FDA approval of Pylera™, a patented 3-in-1 capsule for the eradication of *H. pylori*. Pylera™, the only product of its kind, combines the strength of three ingredients in one capsule: bismuth subcitrate potassium (140 mg), metronidazole (125 mg) and tetracycline hydrochloride (125 mg). Pylera™ capsules, taken in combination with omeprazole, are indicated for the treatment of patients with *H. pylori* infection and duodenal ulcer disease (active or history of within 5 years). This innovative product has simplified traditional quadruple therapy by providing a shorter duration of therapy (10 days vs. 14 days) and a simplified dosing regimen (reduced pill burden 140 vs. 252). Clinical studies have confirmed that Pylera™ is not only as effective as other therapies for the eradication of *H. pylori*, but is as well-tolerated.


According to Loren Laine, MD, Professor of Medicine, University of Southern California (Los Angeles, CA), peptic ulcers in the stomach and duodenum are two of the most important conditions to benefit from Pylera™. “These are relatively common disorders that are said to have lifetime prevalence in the US of up to 10 percent. Ulcers typically present as

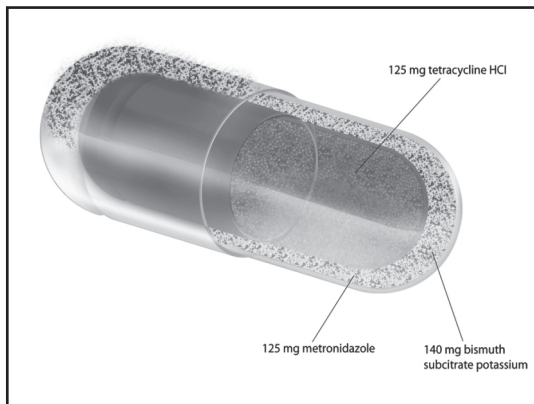
pain, but can occasionally have life-threatening complications. Getting rid of the *H. pylori* is the key to managing these conditions.” Previous ulcer treatments have led to high recurrence rates: gastric and duodenal ulcers recur in up to 80 percent of patients within a year after having received short-term treatment with acid suppression therapy. Studies have shown that the recurrence rate of peptic ulcers after one year is generally less than 5 percent in patients in whom the organism has been eradicated.<sup>2</sup>

Dr. Laine explains the benefits of a “test-and-treat” strategy, which has been recommended for most patients suffering from dyspepsia. “With this approach, patients undergo a test for *H. pylori* infection. If positive, the patients can be treated with eradication therapy, preventing the need for further diagnostic testing in

some patients, thereby decreasing costs.” As to other serious conditions associated with *H. pylori*, Dr. Laine adds, “there is no doubt that *H. pylori* infection is an important risk factor for gastric cancer. At this point, it hasn’t been clearly documented that getting rid of *H. pylori* in adults will prevent the development of gastric cancer, but there is certainly discussion about it. Gastric MALT lymphoma has also been shown to be linked to the

presence of *H. pylori*, and there is evidence demonstrating that when you get rid of *H. pylori* in most of these cases, the disease resolves. That’s quite striking.”

The Phase III North American trials conducted with 275 patients with a history of duodenal ulcer compared the Pylera™ regimen given in combination with two daily doses of 20 mg of omeprazole (OBMT), to the widely used OAC triple therapy (20 mg of omeprazole, 1 g of amoxicillin and 500 mg of clarithromycin, all given twice a day). On an intent-to-treat basis, the eradication rates, although not statistically significant, were 87.7 percent and 83.2 percent, respectively, in favor of Pylera™.<sup>3</sup> These results confirmed that Pylera™ can be used as a first-line therapy for the eradication of *H. pylori*. 



### About Axcan Pharma Inc.

Axcan Pharma Inc. is a leading multinational specialty pharmaceutical company focused on gastroenterology. The company develops and markets a broad line of prescription products to treat a range of gastrointestinal diseases and disorders such as inflammatory bowel disease, irritable bowel syndrome, cholestatic liver diseases and complications related to pancreatic insufficiency.

### PYLERA™ Safety Overview

**Metronidazole has been shown to be carcinogenic in mice and rats. Unnecessary use of the drug should be avoided.**

To reduce the development of drug-resistant bacteria and maintain the effectiveness of PYLERA™ and other antibacterial drugs, PYLERA™ should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

PYLERA™ therapy is contraindicated in pregnant or nursing women, pediatric patients, in patients with renal or hepatic impairment, and in those with known hypersensitivity to bismuth subcitrate potassium, metronidazole or other nitroimidazole derivatives, or tetracyclines.

### WARNINGS/PRECAUTIONS

#### Bismuth-containing Products

There have been rare reports of neurotoxicity associated with excessive doses of various bismuth containing products. Effects have been reversible with discontinuation of therapy.

Bismuth subcitrate potassium and other bismuth containing products may cause a temporary and harmless darkening of the tongue and/or black stool.

#### Metronidazole

Convulsive seizures and peripheral neuropathy have been reported in patients treated with metronidazole. The appearance of abnormal neurologic signs demands the prompt discontinuation of metronidazole therapy. Metronidazole should be administered with caution to patients with central nervous system diseases.

Metronidazole is a nitroimidazole and should be used with caution in patients with evidence of, or history of, blood dyscrasia. A mild leukopenia has been observed; however, no persistent hematologic abnormalities attributable to metronidazole have been observed.

Known or previously unrecognized candidiasis may present more prominent symptoms during therapy with metronidazole and requires treatment with an antifungal agent.

#### Tetracycline

THE USE OF DRUGS OF THE TETRACYCLINE CLASS DURING TOOTH DEVELOPMENT (LAST HALF OF PREGNANCY, INFANCY, AND CHILDHOOD TO THE AGE OF 8 YEARS) MAY CAUSE PERMANENT DISCOLORATION OF THE TEETH (YELLOW-GRAY-BROWN). TETRACYCLINE HYDRO-CHLORIDE IS A COMPONENT OF PYLERA™ CAPSULES. THEREFORE, PYLERA™ CAPSULES SHOULD NOT BE USED IN THESE PATIENT POPULATIONS.

Tetracycline hydrochloride should not be used during pregnancy. Evidence of embryotoxicity has also been noted in animals treated early in pregnancy. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Photosensitivity, manifested by an exaggerated sunburn reaction, has been observed in some individuals taking tetracycline. Patients apt to be exposed to direct sunlight or ultraviolet light should be advised that this reaction can occur.

Pseudotumor cerebri (benign intracranial hypertension) in adults has been associated with the use of tetracycline. The usual clinical manifestations are headache and blurred vision. While this condition and related symptoms usually resolve soon after discontinuation of the tetracycline, the possibility for permanent sequelae exists.

As with other antibiotics, use of tetracycline hydrochloride may result in overgrowth of nonsusceptible organisms, including fungi.

If superinfection occurs, tetracycline should be discontinued and appropriate therapy should be instituted.

Concurrent use of tetracyclines may render oral contraceptives less effective. Patients should be advised to use a different or additional form of contraception.

### MOST COMMON ADVERSE REACTIONS

The most frequent adverse events (incidence >1%) by treatment group from the North American trial in order of decreasing incidence for the OBMT group are shown below in Table 5. For both treatments, gastrointestinal adverse events (e.g., diarrhea, dyspepsia, abdominal pain, and nausea) are the most commonly reported.

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 or another drug and may not reflect the rates observed in practice.

For more information about Pylera™ or other Axcan Pharma Inc. products, please call 1-800-950-8085 or visit the company's web site at [www.axcan.com](http://www.axcan.com).

### References:

1. Ables, AZ, et al., Update on Helicobacter Pylori Treatment, *American Family Physician* 2007; 75(3).
2. Data on File: Axcan Pharma Inc., 2007.
3. Laine, L., et al. Bismuth-Based Quadruple Therapy Using a Single Capsule of Bismuth Biscalcitrate, Metronidazole, and Tetracycline Given With Omeprazole Versus Omeprazole, Amoxicillin, and Clarithromycin for Eradication of Helicobacter pylori in Duodenal Ulcer Patients: a Prospective, Randomized, Multicenter, North American Trial: *Am J Gastroenterol*, 2003; 98 (3): 562-567.