

# Emerging Drug List

## TEGASEROD

CANADIAN COORDINATING  
OFFICE FOR HEALTH  
TECHNOLOGY ASSESSMENT



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**Generic (Trade Name):** Tegaserod (Zelmac™)

**Manufacturer:** Novartis Pharmaceuticals Inc.

**Indication:** For the treatment of constipation-predominant irritable bowel syndrome (IBS).

**Current Regulatory Status:** Tegaserod is currently under review by Health Canada and the Food and Drug Administration. The product is expected to be launched in Canada late 2001 to early 2002.

**Description:** Irritable bowel syndrome is a disorder characterized by abnormal motor functions, motility patterns and transit times of the gastrointestinal (GI) tract. Typically the mid- and lower gut are affected, leading to a diarrhea or constipation predominant condition. Tegaserod belongs to the chemical class of amino-guanidine indoles. It exerts its action in IBS by acting as a partial agonist at 5-HT<sub>4</sub> receptors, stimulating the release of neurotransmitters involved in the control of gut motility of the gastrointestinal system. This results in a stimulation of the peristaltic reflex and an accelerated colonic transit.

**Current Treatments:** For many patients, the condition can be managed through nonpharmacologic means. Certainly emphasis on a healthy diet with appropriate dietary fiber and avoidance of triggers (e.g. alcohol, caffeine, sorbitol) should be encouraged. Numerous interventions have been explored in the management of IBS, namely those that affect the GI tract. Clinical trials examining the efficacy and safety of these agents punctuate the literature, some indicating success and others not. However, many trials are plagued with deficiencies and problems in design, making the task of evaluating the value of these products difficult. Overall, the data regarding drug therapy for IBS has not always been that convincing. The agents utilized have been aimed at addressing specific aspects of the condition (e.g. pain, depression, abnormal transit time, diarrhea, constipation). Some of the agents that have been tried in the management of IBS that are commercially available in Canada include tricyclic antidepressants (e.g. Elavil®), serotonin reuptake inhibitors (e.g. Prozac®), antidiarrheals (e.g. Imodium®), laxatives [psyllium (Metamucil®)], lactulose (Duphalac®), cholestyramine (e.g. Questran®), dicyclomine (Bentylol®), hyoscamine sulfate (Levsin®), pinaverium bromide (Dicitel®), and trimebutine maleate (Modulon®). Many others are being investigated for their potential value in this disorder (e.g. CCK receptor antagonists, gut-selective calcium channel blockers, NK<sub>2</sub> receptor antagonists, beta<sub>3</sub>-adrenoceptor agonists, gut-selective muscarinic antagonists).

**Cost:** Pricing information is not available at this time.

**Evidence:** Very little of the clinical work regarding tegaserod is published in full in medical journals at this time. Tegaserod has been examined in dose-escalating and dose-ranging trials of 12 to 20 week durations. Tegaserod, dosed 2 or 6 mg twice daily, improved the symptoms associated with constipation predominant IBS (e.g. abdominal discomfort, bloating, constipation) when compared to placebo. When contrasted with placebo, tegaserod (0.5 mg or 2 mg twice daily) diminished the number of days per month that patients experienced significant pain (reduced by 2.3 days), bloating and days without bowel movements (median % change of 29.8, 26.5 and 16.1% respectively). In a dose escalating study, the higher doses (24 mg/day) were not associated with more improvement than lower doses (12 mg/day).



**Adverse Effects:** Common adverse effects reported with the use of tegaserod include diarrhea, which is typically transient; flatulence; abdominal pain; nausea and headache. In a clinical trial involving 24 healthy volunteers, tegaserod (25-100 mg bid) was not associated with clinically significant changes in blood pressure, QRS/QTc interval or pulse rate.

**Conclusion:** Irritable bowel syndrome is a very common condition typically presenting during a patient's youth. It affects up to 15 percent of the population. Its impact is substantial both on the patient, the employer and the health care system. Using U.S. data, it is estimated that the economic impact is \$25 billion annually (1/3 direct costs : 2/3 indirect). Numerous avenues have been explored to help manage this condition, with no one ideal drug being uncovered as of yet. This may be related to the notion that the exact pathophysiology of IBS has not been uncovered, although many theories have been put forth. Tegaserod is a novel agent aimed at managing constipation-predominant IBS. Preliminary data does look favorable in minimizing the symptoms of this condition, however when this data is published in full, it will allow for closer scrutiny. Experience in the general population beyond the formal inclusion criteria used in clinical trials, will give a better sense of the true gains made by this intervention.

- References:**
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  4. Scott LJ, Perry CM. Tegaserod. *Drugs* 1999;58(3):491-6.
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The contents of this bulletin are current as of April 2001.  
The Emerging Drug List highlights drugs not yet approved in Canada that are anticipated to have a significant impact on the health care system. Minimal information is available about these drugs, and they may in future become the subject of an early assessment.

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