Tegaserod Maleate (Zelnorm™) Tablets
Manufacturer: Novartis, East Hanover, NJ
Indications: A drug used for the short-term treatment of irritable bowel syndrome (IBS) in women whose primary bowel symptom is constipation.

Drug Class: A 5-hydroxytryptamine (5-HT₄) receptor partial agonist that binds with high affinity at human 5-HT₄ receptors, whereas it has no appreciable affinity for 5-HT₃ or dopamine receptors. It has moderate affinity for 5-HT₁ receptors.

Uniqueness of Drug: Tegaserod maleate, by acting as an agonist at neuronal 5-HT₁ receptors, triggers the release of further neurotransmitters, such as calcitonin gene-related peptide, from sensory neurons. The activation of 5-HT₁ receptors in the gastrointestinal tract stimulates the peristaltic reflex and intestinal secretion and also inhibits visceral sensitivity. Tegaserod increases the movement of stools (fecal matter) through the bowels. It does not cure IBS and does not treat diarrhea-predominant IBS. Tegaserod reduces pain and discomfort in the abdominal area and reduces bloating and constipation.

Precautions: Tegaserod maleate should not be initiated in patients who are currently experiencing or who frequently experience diarrhea. The drug should be discontinued immediately in patients with new or sudden worsening of abdominal pain. The following list of adverse effects have been possibly related to tegaserod maleate: pain, flushing, facial edema, hypotension, angina pectoris, arrhythmia, vertigo, ovarian cyst, miscarriage, irritable colon, fecal incontinence, back pain, cramps, breast carcinoma, asthma or pruritus, attempted suicide, increased appetite, emotional lability, anxiety, sleep disorder, depression, increased creatine phosphokinase, and increased micturition.

Dosage: The recommended dose of tegaserod maleate is 6 mg twice daily taken orally with a glass of water just prior to a meal. The maximum duration of treatment is 12 weeks, and treatment should be discontinued after four weeks if no response has occurred. No dosage adjustment is necessary in patients with mild to moderate renal or liver impairment. The drug is not recommended in patients with severe renal or liver impairment. No dosage adjustment is needed in elderly patients.

P&T Committee Considerations: Tegaserod maleate is the first drug to receive approval by the Food and Drug Administration (FDA) for short-term treatment of IBS in women with the primary bowel symptom of constipation. It differs from alosetron, a drug recently removed from the market, which treats diarrhea-predominant IBS in women. The safety and effectiveness of the drug in men have not been established. FDA based its decision to approve the drug on the results of three randomized, double-blind, placebo-controlled clinical studies, each lasting 12 weeks. The efficacy of tegaserod maleate beyond 12 weeks has not been studied.

The adverse event reported most often associated with tegaserod maleate, compared to placebo, was diarrhea, which usually occurred within the first week of treatment. Typically, diarrhea resolved without patients having to discontinue tegaserod maleate therapy. It is recommended that tegaserod maleate tablets be placed on the hospital formulary as an effective treatment of women with constipation-associated IBS. The average wholesale price of the drug is unknown because the drug has not been officially placed on the market as of this writing.

Alprostadil for Injection (Intracavernosal Use) (Caverject Dual Chamber System)
Manufacturer: Pharmacia and Upjohn, Kalamazoo, MI
Indications: Used for the treatment of erectile dysfunction caused by neurogenic, vasculogenic, or mixed-etiologic disorders.

Drug Class: Alprostadil is the naturally occurring form of prostaglandin E₁ (PGE₁).

Uniqueness of Drug: Alprostadil (dose range 2.5–60 mcg) is injected in smaller doses directly into the corpus cavernosum of the penis, where erections form. Injection therapy produces erections in about five to 20 minutes by relaxing the smooth muscle within the penis, and this action allows blood to become trapped in the shaft of the penis in a natural way. Generally, the erection lasts about one hour. The drug is known to cause an erection by relaxing the smooth muscle within the penis, and this action allows blood to enter and to become trapped in the penis.

Warnings: Prolonged erection, lasting more than four hours and up to six hours in duration, occurred in 4% of 1,861 patients treated up to 18 months with alprostadil sterile powder. The incidence of priapism (erections lasting more than six hours in duration) was 0.4% with the same length of use. Pharmacologic intervention and/or aspiration of blood from the corpus cavernosum were performed in two of seven patients with priapism. To minimize the chances of prolonged erection or priapism, alprostadil for injection should be titrated slowly to the lowest effective dose (see Dosage). The patient must be instructed to immediately report to his prescribing physician or, if he or she is unavailable, to seek immediate medical attention for any erection persisting longer than four hours. If priapism is not treated immediately, penile tissue damage and permanent loss of potency can result.

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The following precautions should be heeded with alprostadil for injection: possible penile fibrosis, increased peripheral blood concentrations of PGE1, and excess bleeding in patients receiving warfarin. Alprostadil should not be used in combination with other vasoactive drugs, and patients should not reuse or share needles.

**Dosage and Administration:** The dosage of alprostadil for injection should be individualized for each patient by careful titration under supervision of a physician. In patients with erectile dysfunction of vasculogenic, psychogenic, or mixed etiology, dosage titration should be initiated at 2.5 mcg of alprostadil. If there is a partial response, the dose may be increased by 2.5 mcg to a dose of 5 mcg and then in increments of 5 to 10 mcg, depending on erectile response, until the dose that produces an erection suitable for intercourse and not exceeding a duration of one hour is reached. If there is no response to the initial dose of 2.5 mcg, the second dose may be increased to 7.5 mcg, followed by increments of 5 to 10 mcg. The patient must stay in the physician’s office until complete detumescence has occurred. If there is no response, the next higher dose may be given within one hour. If there is a response, there should be at least a one-day interval before the next dose is given.

In patients with erectile dysfunction of pure neurogenic origin (spinal cord injury), the initial dose titration should be 1.25 mcg of alprostadil. The dose may be increased by 1.25 mcg to a dose of 2.5 mcg and then in 5-mcg increments until the dose that produces an erection suitable for intercourse, and not exceeding one hour, is reached. If there is no response, the next higher dose may be given within the next hour. If there is a response, there should be at least a one-day interval before the next dose is given.

For maintenance use, self-injection therapy by the patient can be started only after the patient is properly trained in the self-injection technique. The dose of alprostadil for injection that is selected for self-injection treatment should provide the patient with an erection that is suitable for intercourse and that is maintained for no longer than one hour. If the duration of erection is longer than one hour, the dose should be reduced.

**P&T Committee Considerations:** Sildenafil citrate was the first drug approved by the FDA for the treatment of male erectile dysfunction. Although the drug is effective, there are many instances of erectile failure, so that another pharmaceutical might be useful to treat vasculogenic, psychogenic, or mixed erectile dysfunctions. A clinical study has provided evidence that alprostadil for injection can produce erections in male patients who failed to respond to sildenafil citrate therapy. Therefore, it is recommended that alprostadil for injection be placed on the hospital formulary to treat patients who do not respond to the orally administered sildenafil citrate. The patient must be closely supervised by the physician in obtaining the effective and safe dose necessary to achieve erection for intercourse. Alprostadil for injection will be supplied as a Dual Chamber Impulse syringe system, 10 mcg powder and diluent, with the price of $39.02 as a single product. The Dual Chamber Impulse syringe system, 20 mcg powder and diluent, costs $50.25 as a single product. The system includes a glass cartridge, which contains sterile, freeze-dried alprostadil in the front chamber and sterile bacteriostatic water for injection in the rear chamber.

**Gabapentin (Neurontin Oral Solution)**  
*Manufacturer:* Pfizer, New York, NY  
*Indications:* Neurontin is indicated for the management of postherpetic neuralgia (PHN) in adults.  
*Drug Class:* Gabapentin, 1-(aminomethyl)cyclohexaneacetic acid, is structurally related to the neurotransmitter GABA (gamma aminobutyric acid) but does not modify GABA_A or GABA_B radioligand binding and does not inhibit GABA uptake or degradation.  
*Uniqueness of Drug:* Gabapentin represents a novel class of antihyperalgesic agents. It decreases substance P activity, and its mechanism might involve stimulation of the neuronal GABAg1,g2 receptors negatively coupled to voltage-dependent calcium channels, thereby lessening pain signals to the brain. However, its mechanism of action is unknown at this time.  
*Precautions:* The total number of subjects treated with gabapentin in controlled clinical trials in patients with PHN was 336, of whom 102 (30%) were between ages 65 and 72, and 168 (50%) were age 75 or older. The most commonly observed adverse effects observed with the use of gabapentin in adults, not observed with equal frequency in placebo-controlled treated patients, were dizziness, somnolence, and peripheral edema. Treatment-emergent side effects, observed in at least 1% of patients with PHN who received gabapentin and more numerous than in the placebo-treated patients, were diarrhea, dry mouth, constipation, vomiting, ataxia, thinking abnormalities, abnormal gait, incoordination, blurred vision, and conjunctivitis. There were no clinically important differences between men and women in the types and incidence of adverse effects.  
*Dosage:* Gabapentin is supplied in capsules of 100, 300, and 400 mg and as an oral solution. It may be initiated as a single 300-mg dose on day 1, 600 mg/day dose on day 2 (divided twice daily), and 900 mg/day dose on day 3 (divided thrice daily). The dose may subsequently be titrated up as needed for pain relief to a daily dose of 1800 mg (thrice daily). In controlled clinical trials, efficacy was observed over a range of doses from 1800 to 3600 mg/day, with comparable effects across the dose range. No additional benefit was demonstrated by using doses greater than 1800 mg/day.

**P&T Committee Considerations:** Gabapentin is an anticonvulsant previously approved as an adjunctive treatment for partial epileptic seizures in adults and children. It is also indicated for the adjunctive treatment of epilepsy and a range of neuropathic pain conditions. It is now approved in the U.S. for the management of PHN. Gabapentin is the first oral medication approved by the FDA for this indication. The pain associated with PHN is extremely intense and, once established, can last for years. In the U.S., there are over one million new cases of herpes zoster each year. PHN is a syndrome of often intractable pain that persists after the resolution of herpes zoster, a condition commonly known as shingles. This intense pain is described as burning, deep aching, tearing, and electric shock–like. Approximately 10% to 15% of all patients with herpes zoster develop PHN, which can persist for years. It is recommended that gabapentin be placed on the hospital formulary for treating patients with PHN. The average wholesale price for the 100-, 300-, and 400-mg capsule are $52.95/100, $132.38/100 and $158.84/100, respectively. The average wholesale price for the 470-ml oral solution is $100.69.