

Major New Drugs

Part 2

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Goals and Objectives

Goals:

To provide the pharmacist with information about recently approved major new drug entities introduced in the United States.

Objectives:

After completing this article, the pharmacist should be familiar with the:

1. Pharmacology of each new drug.
2. Pharmacokinetic profile of each new drug.
3. Major use(s) of each new drug.
4. Therapeutic efficacy of each new drug.
5. Adverse effects of each new drug.

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Universal Program Number 406-000-06-008-H01.
The expiration date for this program is 7/31/09.



Acamprosate – Campral – Forest

Acamprosate is a synthetic taurine derivative structurally similar to gamma-amino-butyric acid (GABA) that is used orally to maintain abstinence from alcohol. Acamprosate exerts its effects by decreasing glutamatergic transmission and modulating neuronal hyperexcitability during withdrawal from alcohol.

Acamprosate has low bioavailability, reaches peak plasma levels within eight hours, is not metabolized, is eliminated via renal pathways and has a half-life of 24+ hours.

Adverse effects associated with the use of acamprosate include diarrhea, several minor gastrointestinal effects, headache and rash. Suicidal ideation has occurred. Acamprosate is teratogenic in animals, but does not appear to have potential for abuse or dependence. Acamprosate interacts with naltrexone.

The usual maintenance dose of acamprosate is 2 tablets (666 milligrams) three times a day.

Meningococcal Vaccine – Menactra – Sanofi-Pasteur

This is a conjugated polysaccharide vaccine used for protection against disease caused by *Neisseria meningitidis*. This vaccine is composed of 4 micrograms of meningococcal polysaccharide from each of four serogroups conjugated to diphtheria toxoid protein.

The most common adverse effects associated with this vaccine have been headache, malaise, and fatigue. The vaccine should not be used in individuals who have hypersensitivity to any of its components or to latex, which is used in the vial stopper.

The vaccine is administered as a single intramuscular injection.

Ibandronate – Boniva – Roche/Gsk

Ibandronate is an oral bisphosphonate used once a month for prevention and treatment of postmenopausal osteoporosis.

Ibandronate is poorly absorbed and must be taken after an overnight fast. To avoid esophageal irritation, ibandronate must also be taken while in an upright position with 8 ounces of water. After taking ibandronate, the patient must not eat or drink anything and remain upright for an hour. Antacids and other medications containing cations may interfere with the absorption of ibandronate and must be taken at a different time.

Adverse effects associated with the use of ibandronate include gastrointestinal disturbances (e.g., heartburn, esophageal irritation, diarrhea) and, rarely, ocular inflammation.

The usual dose for ibandronate is a 150 milligram tablet monthly.

Pramlintide – Symlin – Amylin

Pramlintide is a synthetic analog of human amylin that is used as adjunctive treatment for patients with type 1 or type 2 diabetes who inject insulin at mealtimes and have failed to achieve control of their diabetes. Amylin is synthesized by pancreatic beta cells and secreted with insulin.

Pramlintide is administered subcutaneously, achieves peak levels within 30 minutes, is eliminated and metabolized via renal systems, and has a half-life of less than one hour.

Adverse effects associated with the use of pramlintide include nausea, vomiting, anorexia and headache. Pramlintide slows gastric emptying; therefore, it may decrease the rate and extent of absorption of orally administered drugs. Consequently, other drugs should not be administered one hour before or two hours after administering pramlintide.

The dose for pramlintide is individualized, but typically ranges from 60 micrograms to 120 micrograms before meals.

Exenatide – Byetta – Amylin/Lilly

Exenatide is a synthetic peptide that stimulates release of insulin from pancreatic beta cells and is used as adjunctive therapy for patients with type 2 diabetes who do not have control of their disease with non-insulin therapy. Exenatide is not indicated for use with insulin.

Exenatide potentiates insulin secretion, inhibits glucagon secretion, and slows gastric emptying, which results in a modest lowering of fasting glucose and a significant reduction in postprandial levels.

Exenatide is administered subcutaneously, achieves peak levels in about two hours, has a half-life of approximately 4 hours, is not metabolized and is eliminated via the kidney.

Adverse effects associated with the use of exenatide include gastrointestinal effects (e.g., nausea) and in combination with oral antidiabetic drugs has caused hypoglycemia. Exenatide is teratogenic in animals, which results in it being contraindicated in pregnancy. Since exenatide causes an increase in gastric emptying time, other drugs should not be administered concurrently.

The dose for exenatide is individualized and dependent on the patient, but typical doses are 5 or 10 micrograms before the morning and evening meal.

Micafungin – Mycamine – Astellas

Micafungin is an echinocandin antifungal used for intravenous treatment of esophageal candidiasis and prophylaxis in invasive *Candida* infection in patients undergoing hematopoietic stem cell transplantation.

Micafungin blocks cell wall synthesis, is metabolized primarily by the liver, eliminated in the feces, and has a half-life of more than 15 hours.

Adverse effects associated with the use of micafungin include fever, headache, gastrointestinal disturbances, and leucopenia.

The usual intravenous dose for micafungin is 50 milligrams daily for prophylaxis and 150 milligrams daily for treatment administered as a single dose over one hour.

Entecavir – Baraclude – Bristol-Myers Squibb

Entecavir is a nucleoside analog used to treat adults with active hepatitis B virus infection. Entecavir exerts its effects by inhibiting HBV polymerase.

Entecavir reaches maximum concentrations within two hours, is minimally metabolized, and eliminated primarily unchanged via the kidney.

Adverse effects associated with the use of entecavir include fatigue, headache, dizziness and nausea. Entecavir has been reported to be carcinogenic in rodents.

The usual oral dose for entecavir is 0.5 milligrams daily.

Pegaptanib – Macugen – Pfizer/Eyetech

Pegaptanib is used as an intravitreal injection to treat all subtypes of neovascular age-related macular degeneration. Pegaptanib is a selective vascular endothelial growth factor antagonist, which blocks the activity of this growth factor which results in reducing inflammation that can be produced by this specific compound.

Adverse effects associated with the use of pegaptanib are primarily related to ophthalmic issues and include vitreous floaters and opacities as well as more severe problems, such as retinal detachment.

Pegaptanib is administered once every six weeks by intravitreal injection into one eye.

Ropinirole – Requip – GlaxoSmithKline

Ropinirole is a dopamine agonist that is used to treat Parkinson's disease, but is now used to treat moderate to severe restless leg syndrome. Restless leg syndrome is associated with an urge to move the legs, usually as a result of discomfort. The exact cause of restless leg syndrome is unknown, but dopamine dysfunction may have a role in the problem.

Ropinirole is well absorbed, achieves peak levels in about 2 hours, is metabolized extensively by CYP1A2, is eliminated by the kidney, and has a half-life of about 6 hours.

Adverse effects associated with the use of ropinirole include nausea, somnolence, vomiting, dizziness, and fatigue. Like other drugs in this group, ropinirole may cause hallucinations and compulsive behavior. Ropinirole has been demonstrated to be teratogenic. Since ropinirole is metabolized by CYP1A2, it must be used with caution with drugs that affect 1A2 (e.g., omeprazole, fluvoxamine).

The usual dose for ropinirole in treating restless leg syndrome is 0.5 to 1 milligram daily.

Tigecycline – Tygacil – Wyeth

Tigecycline, the first of a new class of antibiotics known as the glycylcyclines, is a derivative of minocycline used intravenously to treat complicated intra-abdominal and skin and skin-structure infections.

Tigecycline inhibits protein synthesis in the organism, is extensively distributed after administration, is eliminated primarily in the feces and has a half-life of more than 40 hours. Tigecycline is considered to be a bacteriostatic agent.

Tigecycline is similar to the tetracyclines and causes the same types of adverse effects, including nausea, vomiting, photosensitivity, and alterations in some enzymes and BUN.

Tigecycline should not be used in children less than 8 years old and should not be used during pregnancy.

The usual dose for tigecycline is 100 milligrams intravenously initially followed by 50 milligrams every 12 hours administered over 30 to 60 minutes.

Tipranavir – Aptivus – Boehringer Ingelheim

Tipranavir is a protease inhibitor that is administered with ritonavir to treat HIV infection in patients who have ongoing viral replication and have experienced resistance to multiple protease inhibitors.

Tipranavir does not have the typical peptide structure of proteases, which allows for more flexible binding to the HIV protease active site.

Tipranavir is administered orally, is metabolized in the liver by CYP3A4, is eliminated primarily in the feces, and has a half-life of about 6 hours.

Adverse effects associated with the use of tipranavir include abnormal liver enzymes and lipid concentrations and hepatitis. In addition, gastrointestinal dysfunction (e.g., vomiting) may occur. Tipranavir contains a sulfonamide component in its composition; therefore, it should be used with caution in patients with sensitivity to sulfonamides.

The combination of these drugs results in potential interactions as they are part of the CYP3A and 2D6 metabolism processes.

The usual dose for tipranavir is 500 milligrams taken twice a day with food.

Ramelteon – Rozerem – Takeda

Ramelteon, an indole derivative that is not a controlled substance, is a melatonin receptor agonist used for treatment of insomnia associated with difficulty falling asleep.

Ramelteon is highly selective for melatonin receptors that inhibit chemicals that result in an inability to fall asleep; therefore, the inhibition of some of these processes results the opportunity to fall asleep easier.

Ramelteon is administered orally, undergoes extensive first-pass metabolism via CYP1A2 and CYP3A4, is eliminated primarily in the urine, and has a half-life of about 2.5 hours.

Adverse effects associated with the use of ramelteon include rebound insomnia, dizziness, nausea, and somnolence. Ramelteon has been shown to be teratogenic in rodents and has been implicated in hyperprolactinemia.

The usual dose for ramelteon is 8 milligrams taken 30 minutes prior to bedtime.

Ziconotide – Prialt – Elan

Ziconotide is a synthetic neuronal N-type calcium channel blocker that is used as an intrathecal infusion for treating severe pain in patients who do not respond to other treatments. Ziconotide binds to N-type voltage sensitive calcium channels and blocks neurotransmitter release from presynaptic primary afferent nerve terminals.

Ziconotide is 100% bioavailable in the CSF, is metabolized in serum and tissues and has a half-life in the CSF of about 5 hours.

Adverse effects include severe psychiatric symptoms as well as other CNS symptoms (e.g., dizziness, confusion, tremor and mental slowing) have occurred. Infections, such as bacterial meningitis have also been encountered with ziconotide. Ziconotide interacts with opioids, which may result in enhanced toxicity for both drugs.

The typical dose for ziconotide is individualized depending on the needs of the patient.

Decitabine – Dacogen – Mgi Pharma

Decitabine is a nucleoside analog designed to disrupt DNA synthesis. This disruptive activity promotes cytotoxic DNA hypomethylation and apoptotic cell death in rapidly dividing cells.

Dacogen is specifically indicated for the treatment of multiple types of myelodysplastic syndromes, including secondary myelodysplastic syndromes and various types of refractory anemia.

Adverse reactions associated with the use of decitabine include neutropenia, cytopenia, anemia, and gastrointestinal tract disorders

Decitabine is supplied as a sterile lyophilized powder, for reconstitution in sterile water and dilution for intravenous injection. Recommended initial dosing is 15 mg/m² via continuous 3-hour intravenous infusion, once every 8 hours for 3 days. Treatment cycles should be repeated every 6 weeks, for a minimum of 4 cycles, barring serious adverse reaction. If adverse reaction occurs, subsequent cycles can be delayed until recovery is achieved. Treatment should be discontinued if evidence of disease progression is observed.

Human Papillomavirus Vaccine – Gardasil -- Merck

Human papillomavirus vaccine is a non-infectious quadrivalent recombinant vaccine, which delivers the major capsid (L1) protein of human papillomavirus (HPV) types 6, 11, 16 and 18 in highly purified virus-like particles, in combination with an aluminum-containing vaccine adjuvant.

The vaccine is specifically indicated for the prevention of conditions caused by HPV types 6, 11, 16 and 18 infections. These include cervical cancer, genital warts, and precancerous or dysplastic lesions. The vaccine exerts its activity by providing HPV-6, -11, -16 and -18 L1 protein, conferring protection against these HPV strains, presumably through induction of humoral immune response. These strains are responsible for the majority of cases of cervical cancer and genital warts.

Adverse events associated with the use of this vaccine may include, but are not limited to, injection site issues (e.g., pain, swelling), fever, nausea, and nasopharyngitis.

The recommended intramuscular dosing regimen is 3 single injections of 0.5 ml of the vaccine, at day 0, 2 months after the first dose, and 6 months after the first dose.

Darunavir – Prezista -- Tibotec

Darunavir is a protease inhibitor that is specifically indicated for the treatment of HIV infections in combination with ritonavir and other antiviral agents in treatment-experienced patients, including patients who have failed prior courses of treatment with other protease inhibitors.

Adverse events associated with the use of darunavir include diarrhea, nausea, headache, rash and potentially severe skin reactions (e.g., Stevens-Johnson Syndrome)

The recommended initial dosing regimen for darunavir is 600 mg twice daily, in combination with 100 mg ritonavir twice daily, with food.