

Major New Drugs

Part 2

Biologics — 2006 & First Trimester 2007

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Goals and Objectives

Goals:

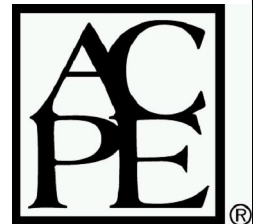
To provide the health care practitioner with knowledge on the new molecular entities approved by the Food and Drug Administration (FDA) in 2006.

Objectives:

After completing this lesson, for each new drug described the pharmacist should be able to:

1. List the generic and brand name, and manufacturer/distributor
2. Explain the agent's major therapeutic use(s)
3. Outline the mechanism of action
4. Describe the pharmacokinetic profile and common drug-interactions
5. Discuss adverse effects and contraindications
6. Describe the dosage schedule, route of administration, strengths, and any storage issues
7. Outline monitoring parameters

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Alglucosidase alfa, IV infusion (Myozyme — Genzyme)

Myozyme is IV infusion enzyme replacement therapy for the treatment of Pompe disease, a rare genetic disorder caused by a deficiency in acid alpha-glucosidase (GAA) which is needed to break down glycogen, a stored form of sugar used for energy. The drug is produced through recombinant DNA technology and works by degrading glycogen by catalyzing hydrolysis of the glycosidic linkages.

Myozyme has been shown to improve ventilator-free survival in patients with infantile-onset disease.

The drug may cause serious hypersensitivity reactions. Other adverse events include reactions at the infusion site, fever, diarrhea, rash, vomiting, cough, otitis media, pneumonia, upper respiratory tract infections, and gastroenteritis.

Myozyme is infused over four hours with the usual dose 20 mg/kg every two weeks. The product is available in 50 mg vials, with refrigerator storage.

Hepatitis B immune globulin (HepaGam B — Cangene)

HepaGam B is an immune globulin for the treatment of acute exposure to blood containing HBsAg, perinatal exposure of infants born to HBsAg-positive mothers, sexual exposure to HBsAg-positive persons and household exposure to persons with acute HBV infection. It is also used to prevent HBV recurrence after liver transplantation in HbsAg-positive individuals. HepaGam is not used to treat active HBV infection and it is ineffective in treatment of chronic active HBV.

HepaGam is a nonpyrogenic sterile solution containing IgG specific to the Hepatitis B surface antigen (HbsAg). It provides 3-6 months of post-exposure prophylaxis with a 17-25 day half life.

Adverse events include hypersensitivity. HepaGam should be used with caution in individuals with thrombocytopenia or coagulation disorders and IgA deficiency. The formulation contains maltose which may cause high glucose readings in individuals using certain glucose testing equipment .

The IM injection is given at 0.06ml/kg in adults as soon as possible after exposure (within 24 hours of needlestick or 14 days of sexual exposure.) For

perinatal exposure, 0.5 ml is given IM within 12 hours of birth.

The product is available as a .5% solution in 1 ml and 5 ml vials.

Human immune globulin, SQ injection (Vivaglobin — ZLB Behring)

Vivaglobin is a subcutaneous injection used to treat primary immune deficiency (PID). It is an immune globulin replacement therapy of IgG antibodies against bacteria and viral agents.

Vivaglobin is 73% bioavailable and reaches peak plasma concentration in 2.5 days.

It is contraindicated in patients with hypersensitivity to immune globulin or a history of anaphylactic reactions to immune globulin preparations. Adverse events include headache, fever, rash, nausea, diarrhea, sore throat, weakness, cough, and injection site reactions. Vivoglobin may decrease the immune response to live vaccines so their administration should be avoided during therapy.

For PID, the usual dosage is 100-200 mg/kg SQ infusion each week at a rate of no more than 20mL/hour.

Vivoglobin is available as a refrigerated injection solution in 3mL, 10mL, and 20mL vials with 160mg/mL of IgG.

Idursulfase injection (Elaprase — Shire)

Elaprase is an IV enzyme replacement therapy for the treatment of Hunter's Syndrome. It is human iduronate-2-sulfatase produced by recombinant DNA technology and causes the catabolism of accumulated glycosaminoglycans that result from the enzyme deficiency.

Elaprase has a half-life of 44-48 minutes.

The product may cause serious hypersensitivity reactions, including respiratory distress, hypoxia, hypotension, angioedema, and seizure. Adverse events include headache, fever, rash, itching, redness, hypertension, joint pain, limb pain, malaise, and visual problems.

Elaprase is administered via IV infusion over 1-3 hours with a usual dose of 0.5 mg/kg weekly. It comes as a 6mL vial with a 2mg/mL concentration that must be diluted before administration. It is stored in the refrigerator.

Influenza Virus Vaccine injection (FluLaval — GSK/ID Biomedical)

FluLaval is used to provide active immunity to influenza virus strains contained in the vaccine.

Protective antibody titers are achieved within 2 weeks after vaccination and provide protection for more than 6 months, with the exception of the elderly where protective titers may drop at 4 months.

Adverse events include anaphylaxis, chills, fever, malaise, Guillain-Barre syndrome, headache, tiredness, weakness, in addition to local injection site reactions.

Optimal time for adult vaccination is October-November, but may continue through December and the influenza season.

FluLaval is available as a 0.5mL/dose IM injection with one dose per season. It is stored refrigerated.

Panitumumab IV injection (Vectibix — Amgen)

Vectibix is a recombinant human IgG2 kappa monoclonal antibody that binds to the human Epidermal Growth Factor Receptor (EGFR). It is used to treat EGFR-expressing metastatic colorectal cancer with disease progression following fluoropyrimidine, oxaliplatin, and irinotecan containing chemotherapy.

The drug's half-life is 7.5 days with a range of 4-11 days.

Vectibix can cause severe dermatologic toxicity complicated by infection, including sepsis. Patients should limit sun exposure, and use sunscreen protection. Toxicity to the GI mucosa, eyes, and nails may also occur. Adverse events include infusion reactions, fatigue, abdominal pain, nausea, diarrhea, and hypomagnesemia.

Vectibix is an IV infusion dosed at 6 mg/kg every 2 weeks and is infusion over a one hour time period.

Doses over 1000 mg are administered over 90 minutes. The drug is available in 100 mg vials (20mg/mL) stored refrigerated.

Quadrivalent Human Papillomavirus Injection (Gardasil — Merck)

Gardasil is used to prevent cervical cancer caused by HPV.

The vaccine is contraindicated in patients with known hypersensitivity to HPV or the formulation. Adverse events include fever, dizziness, malaise, nausea, diarrhea, joint pain, and injection site reactions.

The injection is dosed at 0.5mL followed by 0.5mL at 2 and 6 months after initial vaccination in children over 9 years and to adults younger than 26 years. CDC recommends vaccination at 11-12 years of age.

Gardasil is a 0.5mL injection, single-use and is refrigerated.

Ranibizumab injection (Lucentis — Genentech)

Lucentis is a vascular endothelial growth factor A (VEGF-A) inhibitor to treat neovascular wet age-related macular degeneration.

It is an intravitreal injection and low levels of the drug are found in the serum after injection. It has a half-life of 9 days.

Adverse events include conjunctival hemorrhage, eye pain, vitreous floaters, increased intraocular pressure, and inflammation. Other adverse reactions include headache, arthralgia, and nausea.

The usual dosage is 0.5mg (0.05mL) monthly for the first four months, then every three months if monthly injections are not possible. Lucentis comes in a 0.05mL vial with 10 mg/mL.

Rotavirus vaccine, live, oral (RotaTeq — Merck)

RotaTeq is a vaccine for the prevention of rotavirus gastroenteritis in infants and children caused by the serotypes G1, G2, G3, and G4 when administered

as a three-dose series to infants between the age of 6 and 32 weeks.

After injection, a three-fold increase in antirotavirus IgA was noted in 93% to 100% of infants with protection lasting at least 2 years.

Adverse events include fever, diarrhea, vomiting, otitis media, and irritability.

RotaTeq is an oral, live vaccine given in three 2mL doses at 2, 4, and 6 months of age. It is available as an oral suspension, in prefilled, ready-to-use dosing tubes. It is stored refrigerated.

Zoster Vaccine (Zostavax — Merck)

Zostavax is a vaccine to prevent Herpes Zoster and is for use in individuals 60 years of age and older.

After administration, seroconversion is achieved at 6 weeks and protection has been demonstrated for at least 4 years.

Besides injection-site reactions, other adverse events include fever, headache, rhinitis, respiratory infection, and flu-like syndrome.

Zostavax is given 0.65mL subcutaneously by injection. The powder formulation is stored in the freezer with the diluent stored separately at room temperature or in the refrigerator.

Aliskiren (Tekturna — Novartis)

Tekturna is a renin inhibitor to treat hypertension.

The drug provides maximum hypertensive effect within 2 weeks of administration. It has poor absorption, decreased by high-fat meals. It has a half-life of about 24 hours.

Tekturna is contraindicated in patients with a history of idiopathic or hereditary angioedema, bilateral renal artery stenosis, or in pregnancy. Adverse events include dizziness, rash, diarrhea, increased creatine clearance, increased BUN, and cough.

The recommended dosage in adults is 150 mg once daily which may be increased to a maximum of 300 mg. Tekturna is available as a 150-mg oral tablet.

Lapatinib (Tykerb — GSK)

Tykerb is an EGFR/HER2 inhibitor for use in combination with capecitabine, for the treatment of advanced or metastatic HER2-positive breast cancer in women who have received prior therapy, including Herceptin (trastuzumab).

The drug is extensively metabolized by the liver through the CYP3A4 and 3A5 pathways, and to a lesser extent by CYP2C19 and 2C8. It has an elimination half-life of 24 hours. It will increase the effect/toxicity of other drugs that inhibit CYP3A4 such as azole antifungals, clarithromycin, diclofenac, doxycycline, erythromycin, and others.

Adverse reactions include fatigue, hand-and-foot syndrome, diarrhea, rash, nausea, vomiting, abdominal pain, mucosal inflammation, stomatitis, dyspepsia, anemia, neutropenia, thrombocytopenia, limb and back pain, dyspnea, and insomnia, among others.

Tykerb is formulated as a 250 mg oral tablet. Tykerb is available at specialty pharmacies through a restricted-access program.

Lisdexamfetamine dimesylate (Vyvanse — Shire)

Vyvanse is a prodrug of dextroamphetamine for the treatment of attention deficit/hyperactivity disorder.

Vyvanse is rapidly absorbed and widely distributed in the plasma. It undergoes non-CYP liver metabolism with an elimination half-life of less than an hour prior to being converted to dextroamphetamine with a 10-13 hour half-life.

Vyvanse is contraindicated in individuals with cardiovascular disease, hypertension, hyperthyroidism, glaucoma, a history of drug abuse and within 2 weeks of using an MAO inhibitor. Adverse events include insomnia, headache, decreased appetite, irritability, dizziness, fever, vomiting, and rash.

Vyvanse is formulated as 30-mg, 50-mg and 70-mg oral capsules with a recommended dose of 30 mg daily with increases in increments of 20mg/day until optimal response is achieved.

Retapamulin ointment

(Altabax — GSK)

Altabax is a topical pleuromutilin antibiotic for the treatment of impetigo.

The drug is extensively metabolized by the liver through the CYP3A4 system and is 94% protein bound. When using topically, however, absorption is low.

Adverse events include headache, itching, eczema, diarrhea, nausea, and local site irritation.

The recommended dosage is to apply to the affected area twice daily for 5 days for adults and children over 9 months.

Altabax is a topical ointment in a 1% formulation in 5 g, 10 g, and 15 g tubes.

New Biologics 2006 & New Molecular Entities through April 2007

Generic Name	Brand Name	Sponsor	Indication	Date Approved
Alglucosidase alfa, IV infusion	Myozyme	Genzyme	Pompe disease	04/28/2006
Hepatitis B immune globulin injection	HepaGam B	Cangene	Immune globulin for acute exposure to blood containing HBsAg, perinatal exposure, exposure to HBsAg-positive persons.	1/27/2006
Human immune globulin, SQ injection	Vivaglobin	ZLB Behring	Primary immune deficiency	1/9/2006
Idursulfase injection	Elaprase	Shire	Hunter Syndrome	7/24/2006
Influenza virus vaccine injection	FluLaval	GSK/ID Biomedical	Influenza immunization for adults	10/5/2006
Panitumumab, IV injection	Vectibix	Amgen	Metastatic colon cancer	9/27/2006
Quadrivalent human papillomavirus types 6,11,16,18 injection	Gardasil	Merck	Cervical cancer prevention caused by HPV	6/8/2006
Ranibizumab, injection	Lucentis	Genentech	Neovascular wet age-related macular degeneration	6/30/2006
Rotavirus vaccine, live, oral	RotaTeq	Merck	Prevention of rotavirus gastroenteritis in infants.	02/03/2006
Zoster vaccine, live, injection	Zostavax	Merck	Herpes Zoster vaccine	5/25/2006
Aliskiren	Tekturna	Novartis	Hypertension	3/5/2007
Lapatinib	Tykerb	GSK	Metastatic HER2-positive breast cancer	3/13/2007
Lisdexamfetamine dimesylate	Vyvanse	Shire	ADHD	2/23/2007
Retapamulin ointment	Altabax	GSK	Impetigo	04/12/2007

Adapted from the FDA (www.fda.gov/cder/rdmt/InternetNDA06.htm) and FDC's Pharmaceutical Approvals Monthly, January 2007 and May 2007 issues.