

## New Drug Update 2010

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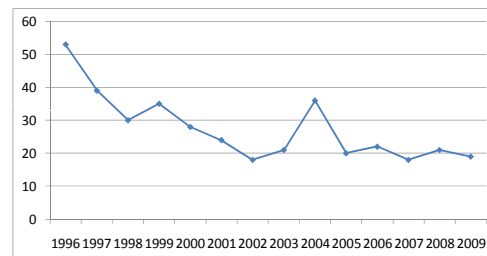
## Objectives

- Identify the new drugs and dosage forms approved in 2010 by the FDA with a focus on: mechanism of action, pharmacokinetics, FDA-approved indications, ADR's, drug interactions, dosing.
- Determine advantages, disadvantages, and overall place in therapy of the new drugs in relation to existing drugs.
- Discuss changes in labeling for several currently marketed drugs.
- Identify drugs in the development pipeline.

## FDA Approvals in 2009

- 19 New Molecular Entities
- 6 New Biologics
- 43 New Dosage Forms
- 1 Withdrawal

## FDA New Molecular Entities Approvals by Year



## FDA Approvals Thus Far in 2010

- 12 New Molecular Entities
- 4 New Biologics
- 18 New Dosage Forms
- 1 Withdrawal

## 2010 FDA Withdrawals

- Gemtuzumab ozogamicin (Mylotarg™)—Pfizer
  - Indicated for treatment of acute myeloid leukemia (AML ) approved in May 2000
  - Post-approval clinical trial begun in 2004 to determine whether adding gemtuzumab ozogamicin to standard chemotherapy would result in an improvement in clinical benefit (survival time) to AML patients
    - Recently stopped early when no improvement in clinical benefit was observed and a greater number of deaths

2010  
Significant New Molecular Entities,  
Biologics, Dosage Forms

Cardiovascular Drugs

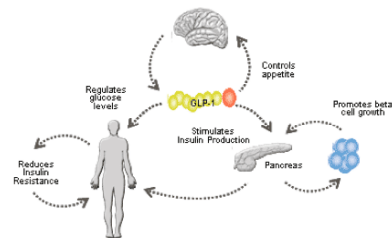
New Generics Approved  
Losartan (Cozaar™) and Losartan/HCTZ  
(Hyzaar™)

- First angiotensin receptor blocker (ARB) to go generic on 4/6/10
- Cost:
  - Losartan 25mg: \$139.99/100 tabs (vs. \$175.50)
  - Losartan 100mg/HCTZ 25mg: \$295.51 (vs. \$355.51)

Endocrine Drugs

Liraglutide (Victoza™)  
Novo Nordisk

- 2<sup>nd</sup> approved glucagon-like peptide 1 (GLP-1) agonist (incretin mimetic) to improve glucose control for type 2 DM (1<sup>st</sup> approved in 2005 was exenatide [Byetta™])
  - GLP-1 is an incretin hormone which stimulates the pancreas to increase insulin secretion in response to high blood glucose levels, inhibits the release of glucagon after meals, and slows gastric emptying
    - Liraglutide shares 97% amino acid sequence of GLP-1
  - Liraglutide is associated with appetite suppression and weight loss as well possibly due to a central effect



[http://www.clinidibet.com/es/infodiabetes/noticias/2009/images/07\\_en.gif](http://www.clinidibet.com/es/infodiabetes/noticias/2009/images/07_en.gif)

### Liraglutide (Victoza™) Novo Nordisk

- FDA-approved for type 2 DM used alone or in addition to oral drugs such as metformin or sulfonylureas
- LEAD-6 (Lancet 2009;374:39 Epub 2009 Jun 8)
  - Metformin and/or sulfonylurea
    - + liraglutide 1.8mg: -1.12% A1C (and more patients reached A1C goal <7%), -3.24kg
    - + exenatide 10mcg BID: -0.79% A1C, -2.87kg, severe hypoglycemia in 2 patients and more minor hypoglycemia

### Liraglutide (Victoza™) Novo Nordisk

- ADR's:
  - GI: nausea (28.4%, but < 10% in 6 weeks), diarrhea (17.1%), vomiting (10.9%), constipation (9.9%)
  - Hypoglycemia: severe hypoglycemia (monotherapy N=7, combo with sulfonylurea N=6)
  - Anti-liraglutide antibody formation (8.6%)
  - Boxed warning: thyroid C-cell carcinomas in rats; thyroid C-cell hyperplasia in trials in humans
  - Rare: Pancreatitis

### Liraglutide (Victoza™) Novo Nordisk

- Dosing
  - 0.6mg QD x 1 week SC, then 1.2mg QD SC. If further glucose lowering required after 1 more week, then 1.8mg QD SC
  - Administered SC in abdomen, thigh, upper arm
  - Give at consistent time of the day and can be given without regard to meals
  - Use with caution in renal dysfunction, limited experience

### Liraglutide (Victoza™) Novo Nordisk

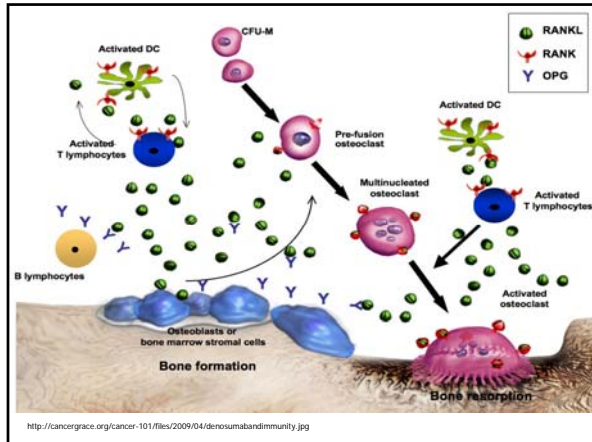
- Cost
  - 6mg/ml in 3ml prefilled pen
  - Victoza™ \$280-\$386 / month
  - Byetta™ \$264-\$272 / month
- Long acting exenatide (Bydureon™) weekly coming

### Denosumab (Prolia™) Amgen

- A RANK ligand (RANKL) inhibitor for osteoporosis
  - A human IgG2 monoclonal antibody with affinity and specificity for human RANKL (receptor activator of nuclear factor kappa-B ligand)
  - FDA-approved for the treatment of postmenopausal women with osteoporosis at high risk for fracture

### Denosumab (Prolia™) Amgen

- MOA:
  - Binds to RANKL, a transmembrane or soluble protein essential for the formation, function, and survival of osteoclasts, the cells responsible for bone resorption
  - Prevents RANKL from activating its receptor, RANK, on the surface of osteoclasts and their precursors.
  - Prevention of the RANKL/RANK interaction inhibits osteoclast formation, function, and survival, thereby decreasing bone resorption and increasing bone mass and strength in both cortical and trabecular bone



## Denosumab (Prolia™) Clinical Trials

- FREEDOM
  - 7,808 women with postmenopausal osteoporosis
  - 60mg subcutaneous injection every six months, compared with placebo at three years
  - 68% reduction in vertebral fractures (4.8 % ARR)
    - new spine fractures incidence of 2.3% with denosumab vs. 7.2% placebo
  - 40% reduction in hip fractures (0.3% ARR)
    - Incidence of hip fractures of 0.7% with denosumab vs. 1.2% placebo

Product information for Prolia. Amgen Inc. Thousand Oaks, CA 91320. June 2010

## Denosumab (Prolia™) Clinical Trials

- FREEDOM
  - 20% reduction in non-vertebral fractures (1.5% ARR).
    - Incidence of non-spine fractures of 6.5% with denosumab vs. 8% placebo
  - Significant bone density increases at all key sites measured (8.8% lumbar spine, 6.4% total hip, 5.2% femoral neck)

## Denosumab (Prolia™) Amgen

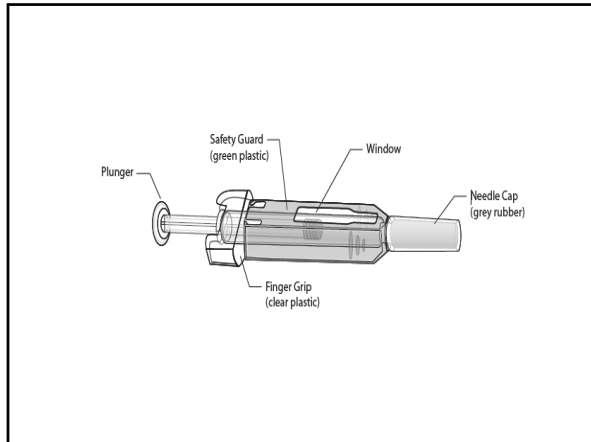
- ADR's
  - Most common ADR's (> 5%): back pain, pain in extremity, hypercholesterolemia, musculoskeletal pain, and cystitis
  - pancreatitis has been reported in clinical trials
- Contraindications
  - Hypocalcemia
- Warnings/Precautions:
  - Infections (including skin), osteonecrosis of jaw, dermatologic reactions, suppressed bone turnover

## Denosumab (Prolia™) Amgen

- Dosing:
  - Administered by a healthcare professional
  - Administer 60 mg every 6 months as a subcutaneous injection in the upper arm, upper thigh, or abdomen
  - Instruct patients to take calcium 1000 mg daily and at least 400 IU vitamin D daily
  - Renal impairment: No dose adjustment is necessary in patients with renal impairment. Patients with creatinine clearance < 30 mL/min or receiving dialysis are at risk for hypocalcemia. Supplement with calcium and vitamin D and consider monitoring serum calcium

## Denosumab (Prolia™) Amgen

- Availability/Storage
  - Single-use prefilled syringe containing 60 mg in a 1 ml solution
  - Single-use vial containing 60 mg in a 1 ml solution
  - Store in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton. Do not freeze.
  - Prior to administration, may be allowed to reach room temperature (up to 25°C/77°F) in the original container.
  - Once removed from the refrigerator, must not be exposed to temperatures above 25°C/77°F and must be used within 14 days. If not used within the 14 days, should be discarded.



## Denosumab (Prolia™) Amgen

- Cost
  - \$825/60mg Injection

## Urology Drugs

## New Generic Approved Tamsulosin (Flomax™)

- The first selective alpha-blocker for benign prostatic hyperplasia (BPH) to go generic
- Cost: \$120 per 30 caps (\$142 for brand Flomax™), but price should drop with additional generics coming on the market
- Dosing: 0.4mg/d to 0.8mg/d

## Hexaminolevulinate (Cysview™) Photocure ASA

- An optical imaging agent indicated for use in the cystoscopic detection of non-muscle invasive papillary cancer of the bladder among patients suspected or known to have lesion(s) on the basis of a prior cystoscopy
  - To be used with the Karl Storz D-Light C Photodynamic Diagnostic (PDD) system to perform cystoscopy with the blue light setting (Mode 2) as an adjunct to the white light setting (Mode 1)
  - Not a replacement for random bladder biopsies or other procedures used in the detection of bladder cancer
  - Not for repetitive use

## Hexaminolevulinate (Cysview™) Photocure ASA

- ADR's:
  - Most common ADR is bladder spasm (occurring in < 3% of patients)
  - Others: dysuria, hematuria, bladder pain, procedural pain, urinary retention and headache, all occurring in ≤ 2% of patients
- Contraindications:
  - porphyria, gross hematuria, BCG immunotherapy or intravesical chemotherapy within the past 90 days, or known hypersensitivity to hexaminolevulinate or aminolevulinate derivatives

### Hexaminolevulinate (Cysview™) Photocure ASA

- Availability:
  - Kit containing a 10 mL glass vial containing 100 mg powder of Cysview (hexaminolevulinate hydrochloride) for Intravesical Solution
  - A polypropylene vial containing 50 mL diluent
  - One Luer Lock catheter adapter
  - Once reconstituted, the solution contains 2 mg/mL (8mmol/L) of hexaminolevulinate hydrochloride

### Hexaminolevulinate (Cysview™) Photocure ASA

- Administration
  - Training in blue light cystoscopy with the Karl Storz D-Light C PDD system is essential prior to the use of Cysview
  - Reconstitute powder with all 50 mL of supplied diluent under aseptic conditions
  - Use solution shortly after reconstitution. If unable to use, the solution may be stored for up to 2 hours in a refrigerator at 2°-8°C (36°-46°F) in labeled syringe. Discard after 2 hours

### Hexaminolevulinate (Cysview™) Photocure ASA

- Administration
  - Instill 50 mL of reconstituted solution into the emptied bladder via an intravesical catheter. Retain in the bladder for 1 hour before evacuating and performing cystoscopic examination
  - First perform a complete cystoscopic examination of the entire bladder under white light and then repeat the examination of the entire bladder under blue light. Record and document information about location and appearance of suspicious lesions and areas seen under both white and blue light

### New Dosage Form Dutasteride/Tamsulosin (Jalyn™)--GSK

- A combination of dutasteride (5 $\alpha$ -reductase inhibitor) and tamsulosin (alpha-adrenergic antagonist)
  - FDA-approved for the treatment of symptomatic benign prostatic hyperplasia (BPH) in men with an enlarged prostate

### New Dosage Form Dutasteride/Tamsulosin (Jalyn™)--GSK

- ADR's
  - The most common ADR's reported in  $\geq 1\%$  of patients: ejaculation disorders, impotence, decreased libido, dizziness, and breast disorders
- Drug Interactions
  - Metabolized by both CYP3A4 and CYP2D6
  - Concomitant use with known inhibitors can cause a marked increase in plasma levels resulting in an increased rate of ADR's
  - Use with ketoconazole and paroxetine is not recommended

### New Dosage Form Dutasteride/Tamsulosin (Jalyn™)--GSK

- Dosing
  - Take one capsule daily approximately 30 minutes after the same meal each day
  - Swallow capsule whole
- Availability
  - Each capsule contains 0.5mg dutasteride and 0.4mg tamsulosin hydrochloride

**New Dosage Form**  
**Vardenafil (Staxyn™)—GSK/Schering**

- A phosphodiesterase 5 (PDE5) inhibitor indicated for the treatment of erectile dysfunction
  - Orally disintegrating tablet
  - Not interchangeable with vardenafil (Levitra™) 10 mg film-coated tablets
  - Provides higher systemic exposure compared to vardenafil 10 mg film-coated tablets
  - $T_{max}$  1.5h

**New Dosage Form**  
**Vardenafil (Staxyn™)—GSK/Schering**

- Dosing
  - Take as needed, orally, approximately 60 minutes before sexual activity
  - The maximum recommended dosing frequency is one tablet per day
  - Placed on the tongue where it will disintegrate. It should be taken without liquid
  - May be taken with or without food
- Availability
  - 10 mg: White, round, orally disintegrating tablets

**Psychiatry Drugs**

**New Dosage Form**  
**Trazodone (Oleptro™)**  
**Labopharm**

- Extended-release formulation for depression
- Starting dose: 150 mg once daily. May be increased by 75 mg per day every three days. Maximum dose: 375 mg per day
- Dosing at the same time every day in the late evening, preferably at bedtime, on an empty stomach
- Availability: 150mg and 300mg tablets

**ID Drugs**

**New Dosage Form**  
**Aztreonam (Cayston™)—Gilead**

- Inhaled monobactam antibiotic for improving respiratory symptoms in cystic fibrosis patients with *Pseudomonas aeruginosa*
- Safety and effectiveness have not been established in pediatric patients below the age of 7 years, patients with FEV1 <25% or >75% predicted, or patients colonized with *Burkholderia cepacia*

### New Dosage Form Aztreonam (Cayston™)—Gilead

- Dosing:
  - Lyophilized aztreonam (75 mg/vial)
  - Diluent (0.17% sodium chloride): 1 mL/ampule
  - Administer one dose (one single use vial and one ampule of diluent) 3 times a day for 28 days
  - Administer only with the Altera® Nebulizer System

### New Dosage Form Miconazole (Oravig™)—Strativa Pharma

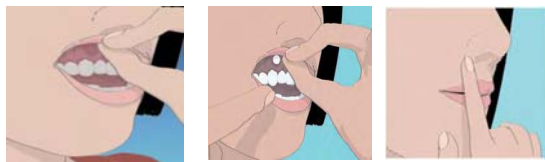
- An azole antifungal FDA-approved for the local treatment of oropharyngeal candidiasis in adults
  - Buccal tablet formulation
- Available in many dosage forms historically: cream, ointment, powder, solution, suppository, aerosol

### New Dosage Form Miconazole (Oravig™)—Strativa Pharma

- ADR's
  - Most common ADR's: diarrhea, headache, nausea, dysgeusia, upper abdominal pain, and vomiting
- Efficacy was compared to clotrimazole troche and miconazole gel

### New Dosage Form Miconazole (Oravig™)—Strativa Pharma

- Dosing
  - Application of one 50 mg buccal tablet to the gum region once daily for 14 consecutive days
  - Instruct patients not to crush, chew, or swallow tablets
- Availability
  - 50 mg buccal tablets



Product information for Oravig™. Strativa Pharma. Woodcliff Lake, NJ. April 2010

### Meningococcal Vaccine (Menveo™) Novartis

- Vaccine to prevent meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y, and W-135 in persons 11-55yo

### Meningococcal Vaccine (Menveo™) Novartis

- ADR's:
  - Most frequently occurring ADR's: pain at the injection site (41%), headache (30%), myalgia (18%), malaise (16%) and nausea (10%)
- Contraindications:
  - Severe allergic reaction (anaphylaxis) after a previous dose of Menveo™, any component of this vaccine, or any other CRM197, diphtheria toxoid or meningococcal-containing vaccine is a contraindication

### Meningococcal Vaccine (Menveo™) Novartis

- Dosing:
  - Administer 0.5 mL intramuscular injection after reconstitution
  - Consists of a liquid vaccine component (MenCYW-135 liquid conjugate component) and a lyophilized vaccine component (MenA lyophilized conjugate component)
  - Reconstitute the MenA lyophilized conjugate component with the MenCYW-135 liquid conjugate component immediately before administration

### Meningococcal Vaccine (Menveo™) Novartis

- Storage:
  - Store refrigerated, away from the freezer compartment, at 36°F to 46°F (2°C to 8°C)
  - Protect from light. Vaccine must be maintained at 36°F to 46°F during transport
  - Do not use after the expiration date. The reconstituted vaccine should be used immediately, but may be held at or below 77°F (25°C) for up to 8 hours

### Pneumococcal 13-valent Conjugate Vaccine (Prevnar 13™)--Wyeth

- Vaccine approved for use in children 6 weeks through 5 years of age (prior to the 6<sup>th</sup> birthday).
  - FDA-approved for active immunization for the prevention of invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.
  - Also approved for the prevention of otitis media caused by *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F. No otitis media efficacy data are available for serotypes 1, 3, 5, 6A, 7F, and 19A

### Pneumococcal 13-valent Conjugate Vaccine (Prevnar 13™)--Wyeth

- ADR's:
  - The most commonly reported solicited adverse reactions (≥20 %): redness, swelling and tenderness at the injection site, fever, decreased appetite, irritability, increased sleep, and decreased sleep
- Contraindications:
  - Severe allergic rxn (anaphylaxis) to Prevnar 13, Prevnar (Pneumococcal 7-valent Conjugate Vaccine [Diphtheria CRM<sub>197</sub> Protein]) or any diphtheria toxoid-containing vaccine

### Pneumococcal 13-valent Conjugate Vaccine (Prevnar 13™)--Wyeth

- Dosing:
  - The 4-dose immunization series consists of a 0.5 mL intramuscular injection administered at 2, 4, 6, and 12-15 months of age
  - 0.5 mL suspension for intramuscular injection, supplied in a single-dose pre-filled syringe
- Storage
  - Store refrigerated at +2°C to +8°C (36°F to 46°F).

## Neurology Drugs

### Dalfampridine (Ampyra™) Acorda Therap

- First oral drug approved for patients with multiple sclerosis
  - FDA approved to improve walking in patients with multiple sclerosis
  - Also known as fampridine and 4-aminopyridine, available from compounding pharmacies
- MOA:
  - Potassium channel blockade that has been shown to increase action potential conduction in demyelinated axons

### Dalfampridine (Ampyra™) Acorda Therap

- Clinical Trials
  - 2 trials evaluating Timed 25-foot walk
  - Significantly greater number of patients demonstrated faster walking speed (20%) compared to placebo (35% and 43% vs. 8% and 9%)

Product information for Ampyra. Acorda Therapeutics, Inc. Hawthorne, NY 10532. January 2010  
Goodman AD, et al. Lancet 2009;373:732-8.

### Dalfampridine (Ampyra™) Acorda Therap

- ADR's: seizures (dose-related), urinary tract infection, insomnia, dizziness, headache, nausea, weakness, back pain, balance disorder, swelling in the nose or throat, constipation, diarrhea, indigestion, throat pain, and burning, tingling or itching of skin

### Dalfampridine (Ampyra™) Acorda Therap

- Renal impairment:
  - Contraindicated in patients with moderate or severe renal impairment (CrCl  $\leq$  50ml/min)
  - The risk of seizures in patients with mild renal impairment (CrCl 51-80ml/min) is unknown (plasma levels may approach those seen at a dose of 15 mg twice daily, a dose that may be associated with an increased risk of seizures)

### Dalfampridine (Ampyra™) Acorda Therap

- Dose: 10mg PO BID, reevaluate in 2-6 weeks
  - Tablets (extended release) should only be taken whole; do not divide, crush, chew, or dissolve
  - Availability: through specialty pharmacies coordinated by Ampyra™ Support Services network
  - Cost: \$13,000/y
- 2 other oral MS agents (immune modulators which can decrease relapses and slow disability) coming soon: cladribine, fingolimod

New Dosage Form  
Pramipexole (Mirapex ER™)  
Boehringer Ingelheim

- Extended-release formulation for Parkinson's disease
- Dosing: Starting dose is 0.375 mg given once daily; dose may be increased gradually, not more frequently than every 5 to 7 days, first to 0.75 mg per day and then by 0.75 mg increments up to a maximum recommended dose of 4.5 mg per day. Assess therapeutic response and tolerability at a minimal interval of 5 days or longer after each dose increment.

New Dosage Form  
Pramipexole (Mirapex ER™)  
Boehringer Ingelheim

- Patients may be switched overnight from immediate-release pramipexole tablets to Mirapex ER™ tablets at the same daily dose, but dose adjustment may be needed in some patients

New Dosage Form  
Pregabalin (Lyrica™ Oral Solution)—Pfizer

- Oral solution formulation of pregabalin FDA-approved for:
  - Neuropathic pain associated with diabetic peripheral neuropathy (DPN)
  - Post herpetic neuralgia (PHN)
  - Adjunctive therapy for adult patients with partial onset seizures
  - Fibromyalgia

New Dosage Form  
Pregabalin (Lyrica™)—Pfizer

- ADR's
  - Most common ADR's (≥ 5% and 2x placebo): dizziness, somnolence, dry mouth, edema, blurred vision, weight gain and thinking abnormal (primarily difficulty with concentration/attention).

New Dosage Form  
Pregabalin (Lyrica™)—Pfizer

- Dosing
  - DPN Pain: Administer in 3 divided doses/day; Begin dosing at 150 mg/day, may be increased to a maximum of 300 mg/day within 1 week
  - PHN: Administer in 2 or 3 divided doses/day; begin dosing at 150 mg/day, may be increased to 300 mg/day within 1 week, maximum dose of 600 mg/day

New Dosage Form  
Pregabalin (Lyrica™)—Pfizer

- Dosing
  - Adjunctive Therapy for Adult Patients with Partial Onset Seizures: Administer in 2 or 3 divided doses/day; begin dosing at 150 mg/day, maximum dose of 600 mg/day
  - Fibromyalgia: Administer in 2 divided doses/day; begin dosing at 150 mg/day, may be increased to 300 mg/day within 1 week, maximum dose of 450 mg/day

**New Dosage Form  
Pregabalin (Lyrica™)—Pfizer**

- Availability
  - Oral Solution: 20 mg/mL
  - Store at room temperature, 59°F to 86°F (15°C to 30°C) in its original package.
  - Must be used within 45 days of first opening the bottle

**New Dosage Form  
Memantine (Namenda XR™)**

- An uncompetitive antagonist of the N-methyl-D-aspartate (NMDA) type of glutamate receptors
  - FDA-approved for the treatment of moderate to severe dementia of the Alzheimer's type
  - Extended release formulation of memantine

**New Dosage Form  
Memantine (Namenda XR™)**

- ADR's
  - The most commonly observed ADR's occurring at a frequency of at least 5% and greater than placebo: headache, diarrhea and dizziness

**New Dosage Form  
Memantine (Namenda XR™)**

- Dosing
  - Initial Dose: 7 mg once daily
  - Maintenance Dose: 28 mg once daily
  - A minimum of 1 week of treatment with the previous dose should be observed before increasing the dose
  - A target dose of 14 mg once daily is recommended in patients with severe renal impairment
  - (Regular release tabs: 5mg/d to 10mg BID)

**New Dosage Form  
Memantine (Namenda XR™)**

- Availability
  - Extended-release capsule: 7 mg, 14 mg, 21 mg, 28 mg

**New Dosage Forms  
Lacosamide (Vimpat™)--UCB**

- Oral solution formulation of lacosamide (also available as injection and tablet)
- FDA-approved for partial-onset seizures
  - Tablets and oral solution are indicated for adjunctive therapy in patients ≥17 years
  - Injection is indicated as short term replacement when oral administration is not feasible in these patients.

### New Dosage Forms Lacosamide (Vimpat™)--UCB

- Dosing
  - Initially, give 50 mg twice daily (100 mg/day). The dose may be increased, based on clinical response and tolerability, at weekly intervals by 100 mg/day given as two divided doses to a daily dose of 200 to 400 mg/day.
- Availability
  - 10 mg/mL oral solution (465ml)
  - Store at room temperature
  - Discard after 7 weeks of opening

### Sedative/Hypnotics/Pain Drugs

### New Dosage Form Hydromorphone (Exalgo™)--Covidien

- Opioid agonist indicated for once daily administration for the management of moderate to severe pain in opioid tolerant patients requiring continuous, around-the-clock opioid analgesia for an extended period of time
  - The first extended-release hydromorphone (Palladone™) was taken off the market because alcohol caused the drug to release too fast

### New Dosage Form Hydromorphone (Exalgo™)--Covidien

- Dosage: 8 mg to 64 mg once daily in clinical trials
- Availability: Tablets: 8 mg, 12 mg and 16 mg dosage strengths

### New Dosage Form Oxycodone (Oxycontin™)—Purdue Pharma

- New formulation that is harder to crush or dissolve
- Turns into a gel when dissolved in liquid

### New Dosage Form Oxycodone (Oxycontin™)—Purdue Pharma

- Per FDA:
  - The reformulated OxyContin™ is intended to prevent the opioid medication from being cut, broken, chewed, crushed or dissolved to release more medication.
  - The new formulation may be an improvement that may result in less risk of overdose due to tampering, and will likely result in less abuse by snorting or injection; but it still can be abused or misused by simply ingesting larger doses than are recommended

**New Dosage Form  
Buprenorphine (Butrans™)—  
Purdue Pharma**

- FDA-approved for the management of moderate to severe chronic pain in patients requiring a continuous, around-the-clock opioid analgesic for an extended period of time
- MOA: partial mu opioid receptor agonist (also weak kappa antagonist, delta agonist, partial agonist at ORL-1 (nociceptin) receptors)

**New Dosage Form  
Buprenorphine (Butrans™)—  
Purdue Pharma**

- ADR's:
  - Most common ADR's (≥5%): nausea, headache, application site pruritus, dizziness, constipation, somnolence, vomiting, application site erythema, dry mouth, and application site rash.

**New Dosage Form  
Buprenorphine (Butrans™)—  
Purdue Pharma**

- Dosing:
  - Each patch is intended to be worn for 7-days
  - In opioid-naive patients, the initial dose should always be 5 mcg/hour
  - For patients already receiving opioids, consult conversion instructions
  - Do not increase the dose until the patient has been exposed continually to the previous dose for 72 hours
  - After removal, wait a minimum of 3 weeks before applying to the same site
  - When no longer required by the patient, taper the dose as part of a comprehensive treatment plan

**New Dosage Form  
Buprenorphine (Butrans™)—  
Purdue Pharma**

- Availability
  - Transdermal system: 5 mcg/hour, 10 mcg/hour, and 20 mcg/hour

**New Dosage Form  
Doxepin (Silenor™)—Somaxon Pharma**

- FDA-approved for the treatment of insomnia characterized by difficulties with sleep maintenance
  - MOA for sleep is thought to be antagonism of histamine H<sub>1</sub> receptors
  - Efficacy trials compared to placebo
  - Historically used for depression (tricyclic antidepressant), anxiety, pruritis, urticaria, but at larger doses

**New Dosage Form  
Doxepin (Silenor™)—Somaxon Pharma**

- ADR's
  - The most common treatment-emergent ADR's (reported in ≥ 2% of patients): somnolence/sedation, nausea, and upper respiratory tract infection

### New Dosage Form

#### Doxepin (Silenor™)—Somaxon Pharma

- Dosing
  - Initial dose: 6 mg, once daily for adults and 3 mg once daily for the elderly
  - Take within 30 minutes of bedtime. Total daily dose should not exceed 6 mg
  - Should not be taken within 3 hours of a meal
- Availability
  - 3 mg and 6 mg tablets
  - tablets not scored

### New Dosage Form

#### Ketorolac (Sprix™)—Roxro Pharma

- NSAID FDA-approved for short term (up to 5 days) management of moderate to moderately severe pain
  - Nasal spray formulation of ketorolac
  - PKs vs. IM ketorolac: similar  $t_{1/2}$ ,  $t_{max}$ , BA 60%
  - Compared to placebo in trials

### New Dosage Form

#### Ketorolac (Sprix™)—Roxro Pharma

- ADR's
  - The most common ADR's (incidence > 2%): nasal discomfort, rhinalgia, increased lacrimation, throat irritation, oliguria, rash, bradycardia, decreased urine output, increased ALT and/or AST, hypertension, and rhinitis

### New Dosage Form

#### Ketorolac (Sprix™)—Roxro Pharma

- Dosing
  - For adult patients < 65 years of age: 31.5 mg (one 15.75 mg spray in each nostril) every 6 to 8 hours. The maximum daily dose is 126 mg.
  - For patients ≥ 65 years of age, renally impaired patients, and patients less than 50 kg (110 lbs): 15.75 mg (one 15.75 mg spray in only one nostril) every 6 to 8 hours. The maximum daily dose is 63 mg
  - Has not been shown to be safe and effective in pediatric patients
  - Should be discarded within 24 hours of taking the first dose, even if the bottle still contains some medication.

### New Dosage Form

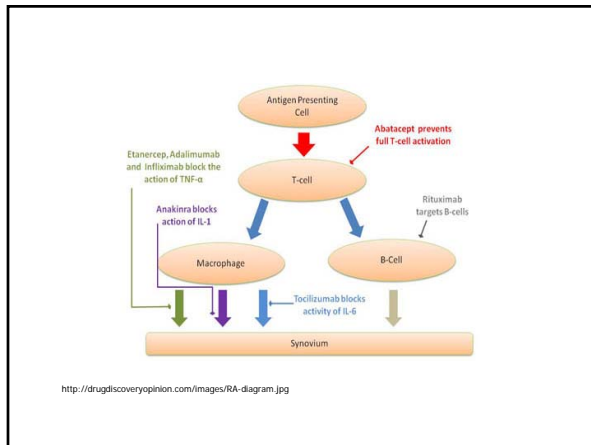
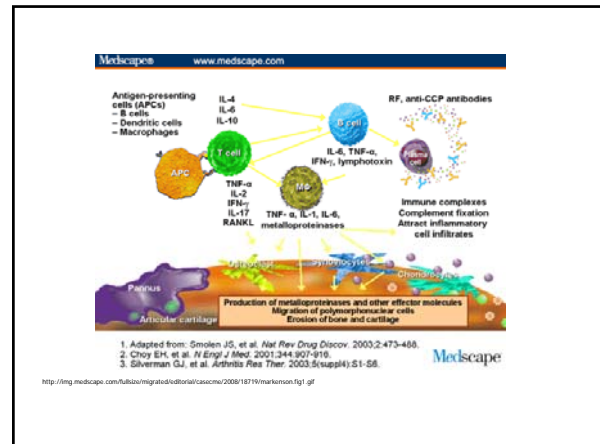
#### Ketorolac (Sprix™)—Roxro Pharma

- Availability
  - Nasal spray: 15.75 mg of ketorolac tromethamine in each 100 μL spray
  - Each 1.7 g bottle contains 8 sprays

## Rheumatology Drugs

## Tocilizumab (Actemra™) Genentech

- Humanized monoclonal antibody representing a new class of meds for RA
  - FDA-approved for IV administration of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to tumor necrosis factor (TNF) inhibitors
- MOA
  - Competitively inhibits the binding of IL-6 to its receptors
  - IL-6 is a pro-inflammatory cytokine overproduced in RA patients that contributes to joint destruction



## Tocilizumab (Actemra™) Clinical Trials

- OPTION
  - Double-blind
  - 623 patients with moderate to severe RA not adequately controlled on methotrexate received IV tocilizumab 8 mg/kg, 4 mg/kg or placebo every 4 weeks in addition to methotrexate
  - 24 weeks: ACR20 response in 59%, 48% and 26% of patients ( $p < 0.0001$ )
  - ACR50 and ACR70 responses in 44%, 31% and 11% and 22%, 12% and 2% of patients

JS Smolen et al. *Lancet* 2008; 371:987-97.

## Tocilizumab (Actemra™) Genentech

- TOWARD
  - 24-week randomized double-blind trial
  - 1220 patients who continued to have active disease despite treatment with DMARDs
  - Tocilizumab 8 mg/kg IV vs. placebo every 4 weeks
  - Patients continued to take methotrexate (75%) or another DMARD (25%).
  - ACR20, ACR50 and ACR70 response rates:
    - Tocilizumab: 61%, 38%, and 21%
    - Placebo: 25%, 9% and 3%

MC Genovese et al. *Arthritis Rheum* 2008; 58:2968-80

## Tocilizumab (Actemra™) Genentech

- RADIATE
  - 24-week double-blind trial
  - 499 patients not adequately controlled on weekly methotrexate and failed to respond to at least one TNF inhibitor
  - Tocilizumab 8 mg/kg, 4 mg/kg or placebo every 4 weeks, in addition to continuing methotrexate
  - ACR20 response: 50%, 30% and 10% ( $p < 0.001$ )
  - ACR50 response: 29%, 17% and 4%
  - ACR70 response: 12%, 5% and 1%

P Emery et al. *Ann Rheum Dis* 2008; 67:1516-23. Epub 2008 Jul 14.

### Tocilizumab (Actemra™) Genentech

- ADR's: infections, increased LFT's, HTN, URI's, increased LDL, GI perforation, hematologic
  - Monitor CBC, LFT's every 4-8 weeks
    - Do not administer if ANC < 2000, PLT < 100,000
    - Do not administer if LFT's > 1.5x
  - Monitor lipids 4-8weeks after start then every 6 months
- Drug Interactions
  - *In vitro* may reverse IL-6-mediated suppression of CYP1A2, 2B6, 2C9, 2C19, 2D6 and 3A4
  - Potentially decreasing levels of other drugs taken concurrently (OC's, simvastatin, omeprazole)

### Tocilizumab (Actemra™) Genentech

- Dosing
  - 4mg/kg every 4 weeks IV over 1 hour
  - Can be increased to 8mg/kg every 4 weeks
  - 80mg/4mg, 200mg/10ml, 400mg/20ml single use vial
- Due to safety concerns, use after TNF drugs and other biologics and not recommended for use with other biologics
- Comparison to other biologics?
- Cost: \$13,000-\$26,000/y

### New Dosage Form Naproxen/Esomeprazole (Vimovo™)— AstraZeneca

- NSAID/PPI combination
  - FDA-approved for relief of signs and symptoms of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID associated gastric ulcers

### New Dosage Form Naproxen/Esomeprazole (Vimovo™)— AstraZeneca

- Dosing
  - One tablet twice daily.
  - Not recommended in moderate/severe renal insufficiency or in severe hepatic insufficiency.
  - Consider dose reduction in mild/moderate hepatic insufficiency
- Availability
  - Delayed release tablets: 375 mg/20 mg or 500 mg/20 mg of naproxen and esomeprazole magnesium

### Respiratory Drugs

### New Dosage Form Mometasone/Formoterol (Dulera™)— Schering

- Combination product containing a corticosteroid and a long-acting beta2-adrenergic agonist FDA-approved for:
  - Treatment of asthma in patients 12 years of age and older
  - Not indicated for the relief of acute bronchospasm
- Formoterol currently available in combination with budesonide (Symbicort™)

New Dosage Form  
Mometasone/Formoterol (Dulera™)—  
Schering

- ADR's
  - Most common ADR's (reported in  $\geq 3\%$  of patients): nasopharyngitis, sinusitis and headache

New Dosage Form  
Mometasone/Formoterol (Dulera™)—  
Schering

- Dosing
  - For oral inhalation only
  - Treatment of asthma in patients  $\geq 12$  years: 2 inhalations twice daily 100 mcg/5 mcg or 200 mcg/5 mcg
  - Starting dosage is based on prior asthma therapy

New Dosage Form  
Mometasone/Formoterol (Dulera™)—  
Schering

- Availability
  - Inhalation aerosol containing a combination of mometasone furoate and formoterol fumarate dihydrate (100mcg/5 mcg or 200mcg/5mcg) per actuation (13gm or 120 inhalations per canister)

Oncology Drugs

Cabazitaxel (Jevtana™)  
Sanofi-Aventis

- A microtubule inhibitor for advanced prostate cancer
  - FDA-approved for in combination with prednisone for the treatment of patients with metastatic hormone-refractory prostate cancer (mHRPC) previously treated with a docetaxel-based treatment regimen

Cabazitaxel (Jevtana™)  
Sanofi-Aventis

- TROPIC Trial
  - 755 patients with mHRPC previously treated with a docetaxel-containing treatment regimen
  - Results: 30% [HR=0.70 (95% CI: 0.59-0.83);  $P < 0.0001$ ] reduction in risk of death from mHRPC among patients taking cabazitaxel in combination with prednisone compared with an active chemotherapy regimen consisting of a standard dose of mitoxantrone and prednisone

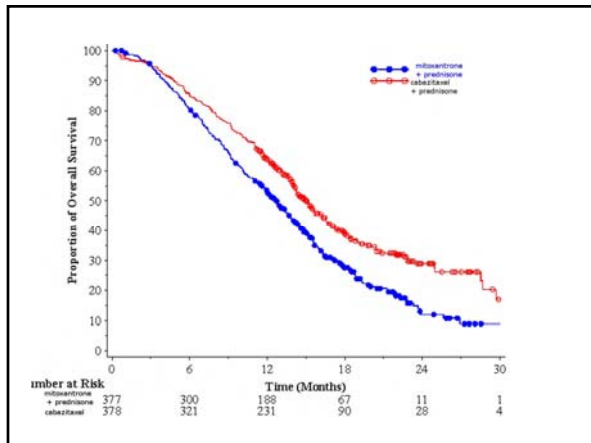
Product information for Jevtana. Sanofi-Aventis. Bridgewater, NJ. June 2010

## Cabazitaxel (Jevtana™) Sanofi-Aventis

- TROPIC Trial
  - Investigator-assessed tumor response rates using Response Evaluation Criteria in Solid Tumors (RECIST) were 14.4% and 4.4% for cabazitaxel-treated and mitoxantrone-treated patients respectively,  $p=0.0005$

## Cabazitaxel (Jevtana™) Sanofi-Aventis

- TROPIC Trial
  - An improvement in median overall survival of 15.1 months for cabazitaxel combination arm versus 12.7 months in the mitoxantrone and prednisone control arm
  - Patients treated with the cabazitaxel combination also experienced a significant improvement in progression-free survival of 2.8 months compared to 1.4 months in the control arm ( $p<0.0001$ )
  - No complete responses were observed on either arm



## Cabazitaxel (Jevtana™) Sanofi-Aventis

- ADR's:
  - Neutropenia, anemia, leukopenia, thrombocytopenia, diarrhea, fatigue, nausea, vomiting, constipation, asthenia, abdominal pain, hematuria, back pain, anorexia, peripheral neuropathy, pyrexia, dyspnea, dysgeusia, cough, arthralgia, and alopecia
- Contraindications:
  - History of severe hypersensitivity reactions to cabazitaxel or to other drugs formulated with polysorbate 80

## Cabazitaxel (Jevtana™) Sanofi-Aventis

- ADR's (cont):
  - The most common ADR's leading to treatment discontinuation: neutropenia and renal failure
  - Treatment discontinuations due to ADR's occurred in 18% of cabazitaxel and 8% of mitoxantrone patients
  - Deaths due to causes other than disease progression within 30 days of last study drug dose were reported in 18 (5%) cabazitaxel patients and 3 (less than 1%) mitoxantrone-treated patients.
  - Most common fatal ADR's in cabazitaxel patients were infections ( $n=5$ ) and renal failure ( $n=4$ ). One death was due to diarrhea-induced dehydration and electrolyte imbalance.

## Cabazitaxel (Jevtana™) Sanofi-Aventis

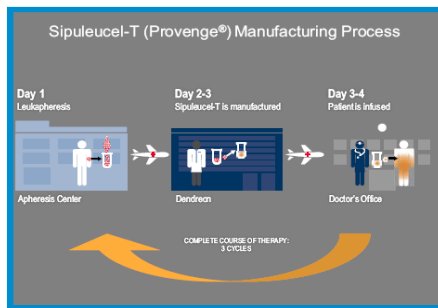
- Dosing:
  - Single use vial 60 mg/1.5 mL, supplied with diluent (5.7 mL)
  - 25 mg/m<sup>2</sup> administered every 3 weeks as a 1-hour IV infusion in combination with oral prednisone 10 mg administered daily throughout cabazitaxel treatment; dose modify if neutropenia or diarrhea
  - Requires 2 dilutions prior to administration
  - Use the entire contents of the accompanying diluent to achieve a concentration of 10 mg/mL
  - PVC equipment should not be used

## Cabazitaxel (Jevtana™) Sanofi-Aventis

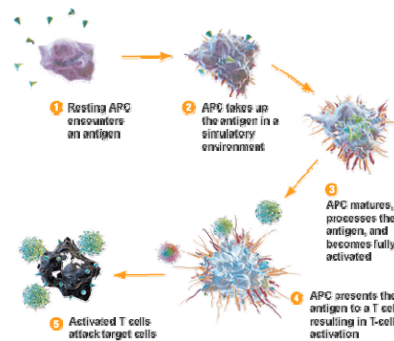
- Premedication Regimen: Administer intravenously 30 minutes before each dose
  - Antihistamine (dexchlorpheniramine 5 mg or diphenhydramine 25 mg or equivalent antihistamine)
  - Corticosteroid (dexamethasone 8 mg or equivalent steroid)
  - H2 antagonist (ranitidine 50 mg or equivalent H2 antagonist)
  - Antiemetic prophylaxis (oral or intravenous) is recommended as needed.

## Sipuleucel-T (Provenge™) Dendreon

- New “therapeutic vaccine” to treat advanced prostate cancer—helps stimulate the body's immune response to prostate cancer cells
  - An autologous cellular immunotherapy indicated for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer
  - Patient's own WBC's are harvested via leukapheresis 3 days prior to the infusion date and then combined with a prostate cancer cell antigen
  - These activated cells are then infused back into the patient



[http://www.prostate-cancer.org/advocacy/img/VoiceRaisedFDA\\_Fig1.gif](http://www.prostate-cancer.org/advocacy/img/VoiceRaisedFDA_Fig1.gif)

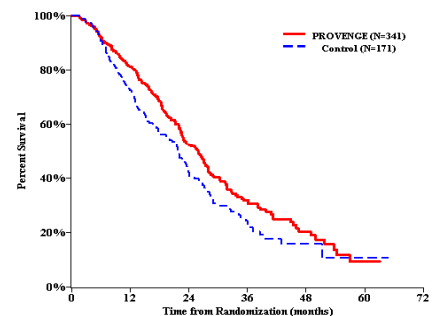


[http://www.pharmaveblog.com/wp-content/uploads/2008/09/img\\_provenge\\_moa.gif](http://www.pharmaveblog.com/wp-content/uploads/2008/09/img_provenge_moa.gif)

## Sipuleucel-T (Provenge™) Dendreon

- Efficacy
  - 512 patients with metastatic hormone treatment refractory prostate cancer
  - Randomized, double-blind, placebo-controlled, multicenter trial
  - Increase in overall survival of 4.1 months (25.8 months, as compared to 21.7 months for those who did not receive the treatment) (p=0.032)

Product information for Provenge. Dendreon Corp. Seattle, WA. 2010



## Sipuleucel-T (Provenge™) Dendreon

- ADR's
  - Most common adverse reactions (incidence  $\geq$  15%) are chills, fatigue, fever, back pain, nausea, joint ache, and headache
  - Serious adverse reactions:
    - Acute infusion reactions (24%)
    - CVA's (3.5%)

## Sipuleucel-T (Provenge™) Dendreon

- Administration/Dosing
  - For Autologous Use Only
  - Administer 3 doses at approximately 2-week intervals
  - Premedicate patients with oral acetaminophen and an antihistamine such as diphenhydramine
  - Before infusion, confirm that the patient's identity matches the patient identifiers on the infusion bag
  - Do not initiate expired infusion
  - Infuse IV over 60 minutes
  - Do Not Use a Cell Filter
  - Interrupt or slow infusion for acute infusion reactions, depending on the severity of the reaction

## Sipuleucel-T (Provenge™) Dendreon

- Administration/Dosing
  - The infusion bag must remain within the insulated polyurethane container until the time of administration. Do not remove the insulated polyurethane container from the outer cardboard shipping box.
  - Confirm Product Release Before Infusion
  - Do not infuse PROVENGE until confirmation of product release has been received from Dendreon. Dendreon will send a Cell Product Disposition Form containing the patient identifiers, expiration date and time, and the disposition status (approved for infusion or rejected), to the infusion site.

## Sipuleucel-T (Provenge™) Dendreon

- Administration/Dosing
  - Not routinely tested for transmissible infectious diseases and may transmit diseases to health care professionals handling the product. Universal precautions should be followed.

## Sipuleucel-T (Provenge™) Dendreon

- Availability
  - Each dose of PROVENGE contains a minimum of 50 million autologous CD54 cells activated with PAPGM- CSF, suspended in 250 mL of Lactated Ringer's Injection, USP in a sealed, patient-specific infusion bag
  - The potency is determined by measuring the increased expression of the CD54 molecule, also known as ICAM-1, on the surface of APCs after culture with PAP-GM-CSF.

## Sipuleucel-T (Provenge™) Dendreon

- Cost:
  - \$93,000

New Dosage Form  
Ondansetron (Zuplenz™)—Strativa Pharma

- An oral soluble film formulation for prevention of nausea and vomiting
- Available as 4 mg and 8 mg oral soluble films
- Similar dosing as oral tablets

Transplant Drugs

Everolimus (Zortress™)  
Novartis

- Immunosuppressant
  - FDA-approved for prophylaxis of organ rejection in adult patients at low-moderate immunologic risk receiving a kidney transplant
  - Use in combination with basiliximab and concurrently with reduced doses of cyclosporine and corticosteroids
  - Approved in 2009 as Afinitor™ for advanced renal cancer
  - A kinase inhibitor

Everolimus (Zortress™)  
Novartis

- MOA
  - Inhibits antigenic and interleukin (IL-2 and IL-15) stimulated activation and proliferation of T and B lymphocytes
  - Binds to a cytoplasmic protein, the FK506 Binding Protein-12 (FKBP-12), to form an immunosuppressive complex (everolimus: FKBP-12) that binds to and inhibits the mammalian Target Of Rapamycin (mTOR), a key regulatory kinase
  - Protein synthesis and cell proliferation are inhibited

Everolimus (Zortress™)  
Novartis

- Efficacy
  - 24-month, multi-national, open-label, randomized (1:1:1) trial comparing two concentration-controlled everolimus regimens of 1.5mg/d starting dose (targeting 3 to 8 ng/ml) and 3.0mg/d starting dose (targeting 6 to 12 ng/mL) with reduced doses of cyclosporine and corticosteroids vs. 1.44 gm per day mycophenolic acid with standard doses of cyclosporine and corticosteroids
  - Results: At 12 months indicated everolimus 1.5 mg/d is comparable to mycophenolic acid in terms of efficacy failure, defined as treated biopsy-proven acute rejection, graft loss, death or loss to follow-up

Product information for Zortress. Novartis. East Hanover, NJ. 2010

Everolimus (Zortress™)  
Novartis

- ADR's
  - Most common (incidence ≥20%) ADR's: peripheral edema, constipation, hypertension, nausea, anemia, UTI, hyperlipidemia.

### Everolimus (Zortress™) Novartis

- Drug Interactions
  - CYP3A4 inhibitors and inducers: Strong-moderate inhibitors (such as cyclosporine, ketoconazole, erythromycin, verapamil) and inducers (such as rifampin)
  - Blood concentration monitoring is recommended; consider dose adjustment of everolimus

### Everolimus (Zortress™) Novartis

- Dosing
  - Starting oral dose of 0.75 mg BID
  - Adjust maintenance dose to achieve everolimus trough concentrations within the 3-8 ng/ml target range
  - Administer as soon as possible after transplantation
  - Routine everolimus and cyclosporine therapeutic drug concentration monitoring is recommended
  - Administer consistently with or without food at the same time as cyclosporine
  - Moderate hepatic impairment: Reduce daily dose by half and monitor blood concentrations

### Everolimus (Zortress™) Novartis

- Availability
  - 0.25 mg, 0.5 mg, and 0.75 mg tablets

### OB/GYN Drugs

### Estradiol Valerate/Dienogest (Natazia™) Bayer HealthCare

- A 4-phasic, 28-day oral contraceptive
  - Contains estradiol instead of ethinyl estradiol and contains a new progestin called dienogest, which has anti-androgenic effects like drospirenone (Yaz™, Yasmin™) but without the risk of hyperkalemia
  - Has a unique four-phase dosing regimen whereby estradiol dose steps down and dienogest dose steps up during the cycle to help avoid breakthrough bleeding
  - Possibly less effects on lipids and thrombosis, but more studies needed

### Estradiol Valerate/Dienogest (Natazia™) Bayer HealthCare

- Availability:
  - Each blister pack contains the following tablets (in order)
    - two dark yellow tablets containing 3 mg of estradiol valerate
    - five medium red tablets each containing 2 mg estradiol valerate and 2 mg dienogest
    - 17 light yellow tablets each containing 2 mg estradiol valerate and 3 mg dienogest
    - two dark red tablets each containing 1 mg estradiol valerate
    - two white tablets which are inert

**Estradiol Valerate/Dienogest (Natazia™)  
Bayer HealthCare**

- Administration:
  - Should be started on day 1 (first day of menstruation) of a woman's cycle.
  - Unlike other combined oral contraceptives, need to use a back-up form of contraception for the first 9 (not 7) days of the first cycle
  - The instructions for what to do when a dose is missed are more complex than most other oral contraceptives, with detailed instructions for how to handle missed doses included in the patient package insert

**Dermatology Drugs**

**New Dosage Form  
Adapalene (Differin™)--Galderma**

- A retinoid lotion FDA-approved for the topical treatment of acne vulgaris in patients 12 years and older
  - Currently available as a cream and gel

**New Dosage Form  
Adapalene (Differin™)--Galderma**

- ADR's:
  - Dry skin of mild to moderate severity was the most frequently reported ( $\geq 1\%$ ) treatment related adverse event
  - Erythema, scaling, dryness, burning/stinging also seen during treatment
  - Avoid exposure to sunlight and sunlamps; wear sunscreen

**New Dosage Form  
Adapalene (Differin™)--Galderma**

- Dosing:
  - Apply a thin film to the entire face and other affected areas of the skin once daily, after washing gently with a mild soapless cleanser.
  - Dispense a nickel size amount (3-4 actuations of the pump) to cover the entire face
  - Avoid application to the areas of skin around eyes, lips and mucous membranes

**New Dosage Form  
Adapalene (Differin™)--Galderma**

- Availability
  - Each gram contains 1 mg (0.1%) adapalene in an oil-in water emulsion in 2oz and 4oz bottles

### Ophthalmology Drugs Gatifloxacin (Zymar™)--Allergan

- A quinolone ophthalmic solution
  - FDA-approved for bacterial conjunctivitis
  - 0.5% solution
  - Has been available as 0.3% solution (Zymar™)
- Dosing
  - Day 1: Instill 1 drop into affected eye(s) every 2 hours while awake (maximum: 8 times/day)
  - Days 2-7: Instill 1 drop into affected eye(s) 2-4 times/day while awake

### Miscellaneous

### Polidocanol (Asclera™) BioForm Medical

- Injectable agent for treating small varicose veins
  - FDA-approved to close spider veins (tiny varicose veins less than 1 millimeter in diameter) and reticular veins (those that are 1 to 3 millimeters in diameter)
- MOA: Damages the cell lining of blood vessels, causing the blood vessel to close, and eventually replaced by other types of tissue

### Polidocanol (Asclera™) BioForm Medical

- ADR's: hematoma, bruising, irritation, discoloration, and pain at the injection site
- Availability:
  - 0.5% and 1% solution in 2 mL glass ampules

### Polidocanol (Asclera™) BioForm Medical

- Administration:
  - For intravenous use only. The strength of the solution and the volume injected depend on the size and extent of the varicose veins. Extensive varicosities may require multiple treatment sessions.
  - Spider veins (varicose veins  $\leq 1$  mm in diameter): Use Asclera 0.5%
  - Reticular veins (varicose veins 1 to 3 mm in diameter): Use Asclera 1%
  - Use 0.1 to 0.3 mL for each injection into each varicose vein. The maximum recommended volume per treatment session is 10 mL

### Carglumic Acid (Carbaglu™) Orphan Europe

- A Carbamoyl Phosphate Synthetase 1 (CPS 1) activator
  - FDA-approved as adjunctive therapy for the treatment of acute hyperammonemia and as maintenance therapy for the treatment of chronic hyperammonemia due to the deficiency of the hepatic enzyme N-acetylglutamate synthase

### Carglumic Acid (Carbaglu™) Orphan Europe

- The most common adverse reactions in  $\geq 13\%$  of patients:
  - infections, vomiting, abdominal pain, pyrexia, tonsillitis, anemia, ear infection, diarrhea, nasopharyngitis, and headache
- Precautions:
  - Hyperammonemia: Monitor plasma ammonia levels during treatment

### Carglumic Acid (Carbaglu™) Orphan Europe

- Dosing (Adult)
  - Recommended initial dose range for acute hyperammonemia is 100 mg/kg/day to 250 mg/kg/day (rounded to nearest 100mg); adjust dose to maintain normal plasma ammonia levels based on age
  - Divide the total daily dose into two to four doses to be given immediately before meals or feedings.
  - Each 200 mg tablet should be dispersed in a minimum of 2.5 ml of water and taken immediately

### Carglumic Acid (Carbaglu™) Orphan Europe

- Dosing (Pediatric)
  - Recommended initial dose range for acute hyperammonemia is 100 mg/kg/day to 250 mg/kg/day
  - Divide the total daily dose into two to four doses to be given immediately before meals or feedings
  - Mix each 200 mg tablet in 2.5 ml of water to yield a concentration of 80 mg/mL
  - May be administered orally with an oral syringe or through a nasogastric tube.

### Alglucosidase alfa (Lumizyme™) Genzyme

- A lysosomal glycogen-specific enzyme indicated for patients 8 years and older with late (non-infantile) onset Pompe disease (GAA deficiency) who do not have evidence of cardiac hypertrophy
  - Safety and efficacy have not been evaluated in controlled clinical trials in infantile-onset patients, or in late (non-infantile) onset patients less than 8 years of age

### Alglucosidase alfa (Lumizyme™) Genzyme

- ADR's:
  - The most frequent ADR's ( $\geq 5\%$ ) in clinical trials were infusion reactions and included: anaphylaxis, urticaria, diarrhea, vomiting, dyspnea, pruritus, rash/erythema, pharyngolaryngeal pain, neck pain, hypoacusis, flushing/feeling hot, pain in extremity, fall and chest discomfort

### Alglucosidase alfa (Lumizyme™) Genzyme

- Dosing
  - 20 mg/kg body weight administered every 2 weeks as an intravenous infusion
  - Dosage form: Lyophilized powder for solution for intravenous infusion (5 mg/ml)
  - Available only through a restricted distribution program called the LUMIZYME ACE Program. Only prescribers and healthcare facilities enrolled in the program may prescribe, dispense or administer

### Velaglucerase alfa (VPRIV™) Shire

- A hydrolytic lysosomal glucocerebrosidase-specific enzyme indicated for long-term enzyme replacement therapy for pediatric and adult patients with type 1 Gaucher disease

### Velaglucerase alfa (VPRIV™) Shire

- ADR's
  - Most common adverse reactions during clinical studies were infusion-related reactions
  - Other commonly observed adverse reactions in ≥ 10% of patients were: headache, dizziness, abdominal pain, nausea, back pain, joint pain, upper respiratory tract infection, activated PTT prolonged, fatigue/asthenia, and pyrexia

### Velaglucerase alfa (VPRIV™) Shire

- Dosing
  - 60 Units/kg administered every other week as a 60-minute intravenous infusion
  - Patients currently being treated with imiglucerase for Gaucher disease can be switched to VPRIV. Patients previously treated on a stable dose of imiglucerase are recommended to begin treatment with VPRIV at that same dose when they switch from imiglucerase to VPRIV
  - Physicians can make dosage adjustments based on achievement and maintenance of each patient's therapeutic goals. Clinical trials have evaluated doses ranging from 15 Units/kg to 60 Units/kg every other week

### Velaglucerase alfa (VPRIV™) Shire

- Availability
  - Lyophilized powder to be reconstituted and diluted for infusion
  - Available in 200 Units and 400 Units single-use vials

### Collagenase Clostridium Histolyticum (Xiaflex™) Auxilium Pharm

- FDA-approved for the treatment of adult patients with Dupuytren's contracture with a palpable cord
- MOA
  - A proteinases that hydrolyzes collagen in its native triple helical conformation under physiological conditions, resulting in lysis of collagen deposits



<http://www.med.und.edu/users/jwhilling/duppain.JPG>

Collagenase Clostridium Histolyticum  
(Xiaflex™)  
Auxilium Pharm

- Efficacy
  - N=66, 44% vs. 5% placebo
  - N= 306, 64% vs. 7% placebo

Product information for Xiaflex, Auxilium Pharm, Malvern, PA, Feb 2010.

Collagenase Clostridium Histolyticum  
(Xiaflex™)  
Auxilium Pharm

- ADR's
  - The most common adverse reactions reported in ≥ 25%: peripheral edema (swelling of the injected hand), contusion, injection site reaction, injection site hemorrhage, and pain in the injected extremity

Collagenase Clostridium Histolyticum  
(Xiaflex™)  
Auxilium Pharm

- Dosing
  - Inject 0.58 mg into a palpable Dupuytren's cord with a contracture of a metacarpophalangeal (MP) joint or a proximal interphalangeal (PIP) joint according to the injection procedure
  - Approximately 24 hours following an injection, perform a finger extension procedure if a contracture persists
  - Injections and finger extension procedures may be administered up to 3 times per cord at approximately 4-week intervals
  - Inject only one cord at a time. If a patient has other cords with contractures, inject each cord in sequential order

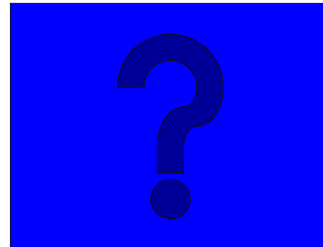
Collagenase Clostridium Histolyticum  
(Xiaflex™)  
Auxilium Pharm

- Availability
  - Single-use glass vials containing 0.9 mg of collagenase clostridium histolyticum as a sterile, lyophilized powder for reconstitution
  - Sterile diluent for reconstitution in a single-use glass vial

### Drugs in the Pipeline

- Cardiovascular
  - Dabigatran (Pradaxa™)—Boehringer Ingelheim
  - Rivaroxaban (Xarelto™)—Bayer
- Hepatitis C (Telaprevir, Boceprevir)
- Alzheimer's Disease (Immune Globulin)
- Multiple Sclerosis (Cladribine, Fingolimod)
- Diabetes (Byetta Once Weekly)
- Systemic Lupus Erythematosus (Belimumab)
- More Generics

### New Drug Update



Bernard J. Dunn School of Pharmacy  
Shenandoah University

