new rules, new drugs, new problems

5-15 years (drug lag)

$800 million - $3.4 billion from beginning the NDA to marketing
I-STOP bill, will require all prescriptions to be transmitted in electronic format, except for emergency situations and other limited circumstances, by no later than March 27, 2016.

*List of 12 situations that do not apply...think compounding and complicated
Changes moving forward..no more pregnancy categories are being assigned to newly approved drugs..They are being assigned a "risk factor" related to fertility, pregnancy and lactation. 81 drugs have this rating now.

8.1 Pregnancy

Risk Summary

ENTRESTO can cause fetal harm when administered to a pregnant woman. Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.
*Fast track….drugs for potentially serious diseases that show promise in phase III and offer therapy not yet available

*Break through status….drugs that show promise in phase II and would treat serious disease and for which current therapy is not available

*New categories

*Anthim…oblitoxaximab for treatment of inhalational anthrax with appropriate antibiotics; IV over 1.5 hours risk of anaphylaxis, pretreat with diphenhydramine

*Only completed Phase 1 studies….approved for stockpiling….not ethical or available human subjects

*New drug for anthrax

ladipasvir/sofosbuvir (Harvoni)...
394,500/12 wk

sofosbuvir/velpatasvir (Epclusa) for six forms of hepatitis B
574, 760/12 weeks, all genotypes, no additional drugs

sofosbuvir/sofosbuvir (Sivaddi/Pakhtcr)...
$147,000/12 wk

sofosbuvir/daclatasvir (Sovaldi/Daklinza)...
$147,000/12 wk

elbasvir/grapiprevir (Zapatier)...
$54, 400/12 wk

dasabuvir, ombitasvir, paritaprevir/retonivir (Viekira Pac also Viekira XR)
$ 83,320/12 wk

2016 warning of causing hepatic impairment
Zapater highly effective with genotype 1 or 4; safer with renal impairment, not for use with moderate to severe hepatic impairment.

Harvoni can be used with hepatic impairment
*New Antibiotics*

- ceftazidime/avibactam (Avycaz) complicated intra-abdominal and given with metronidazole for complicated UTIs...IV q8-12 hours over 2 hours
- ceftolozane/tazobactam (Zerbax) complicated UTI and intraabdominal infections...IV q18h over one hour. *C diff* very common effect
- tobramycin (Bethkis) inhalation for cystic fibrosis patients with *pseudomonas*
- finafloxacin (Xtoro) topical for treatment of swimmer’s ear

*New antibiotics*

- vancomycin...IV for life threatening infections, orally for *C diff*
- televancin (Vibativ)...IV only, gram-positive strains, complicated skin infections
  - dalbavancin (Dalvance) susceptible strains in adults with skin infections...IV, culture first
- oritavancin (Orbactiv). Skin infections, interferes with warfarin. BB warning
  - BB warning of serious fetal risk; prolonged QT interval; foamy urine; nephrotoxicity; red-man syndrome risk during infusion
  - Bactericidal cause the death of the bacteria by disrupting the cell membrane

*Lipoglycopeptides*
*Drugs affecting Blood coagulation*

- Local vasoconstriction seals off small injury
- Platelet aggregation forms a platelet plug
- Hageman factor is activated
- Intrinsic pathway converts prothrombin to thrombin to seal system
- Extrinsic pathway clots the blood that has leaked out of the vascular system
**Actions of Anticoagulants**

- Antiplatelets
  - Alter the formation of the platelet plug
- Anticoagulants
  - Interfere with the clotting cascade and thrombin formation
- Thrombolytic drugs
  - Break down the thrombus that has been formed by stimulating the plasmin system

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**Platelet inhibitors**

- abciximab (ReoPro): IV only, cardiac events
- anagrelide (Agrylin): PO, thrombocytopenia
- aspirin (generic): reduction of CV event risks
- cilostazol (PlaFlex): oral, intermittent claudication
- clopidogrel (Plavix): reduction of CV event risks
- congloril (Kengrall): reduction of CV events during procedures; cannot be combined with clopidogrel, prasugrel
- dipyridamole (Persantine): prevention of CV events
- eptifibatide (Integrilin): PO, going for percutaneous procedures; BB warning for serious to fatal bleeding
- epifibatide (Integrilin): acute coronary syndrome
- ticagrelor (Brilinta): severe risk of bleeding, if combined with aspirin, aspirin dose should be kept between 75-100
- ticlopidine (Ticlid): reduction of strokes with TIA
- tirofiban (Aggrastat): acute coronary syndrome
- vorapaxar (Zontivity): protease activated receptor antagonist

**BB** warning bleeding and death
Heparin...natural compound...must be injected...rapid onset
Protamine sulfate ...direct reversal agent

Low molecular weight heparins...

Warfarin...blocks the use of vitamin K in liver cells...vitamin K is the base for the clotting factors...can be taken orally 2-3 day onset...impact on liver leads to multiple drug interactions

*New oral anticoagulants*

dabigatran etexilate mesylate  Pradaxa
Direct thrombin inhibitor  To reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation. Tx of DVT, PE in a parenteral anticoagulant, prevention of recurrent DVT, PE in previously treated patients and prevention of DVT, PE after hip replacement Capsules should not be chewed, broken or opened... Risk of thrombotic events when stopping suddenly. Risk of bleeding, monitor accordingly. Not to be combined with rifampin. Gastritis may occur. Keep in original package, blister packs preferred. Do not stop suddenly...no screening test...first new one to have a reversal agent

rivaroxaban  Xarelto
* Factor Xa inhibitor
* Prophylaxis and treatment of deep vein thrombosis, which may lead to pulmonary embolism in patients undergoing knee or hip replacement surgery; prevention of stroke with nonvalvular AF; reduce the risk of recurrent DVT, PE
* 10 mg/day PO without regard to food: start dosing within 6-10 hr of surgery, continue for 35 days following hip replacement, 12 days following knee replacement
* Do not stop drug abruptly, rebound increased risk of stroke or CV event; no testing, no antidote
*apixaban* *Elliquis* activated thrombin inhibitor

*Prevention of stroke with AF; prevention and treatment of DVT after knee/hip surgery; reduction of risk of recurrent DVT, PE*  
*Do not stop drug abruptly, rebound increased risk of stroke or CV event; no testing, no antidote*

*edoxaban* (Savaysa) oral thrombin inhibitor  
*treatment of nonvalvular AF; tx of DVT, PE after 5-10 days of parenteral therapy (not recommended with hepatic impairment)*  
*Warnings added: serious to fatal rebound thrombotic events with stopping of drug; serious to fatal bleeding*

Praxibind..idarucizumab..direct antidote for dabigatran..risk of thrombotic events, IV monoclonal antibody, emergency use..have to start another anticoagulant to prevent rebound clotting

Warfarin..  
Vitamin K..2-3 days to see effect or prothrombin complex concentrate *(Kcentra, Octaplex)*

*Reversing oral anticoagulants*
Herbs that interfere with blood coagulation

- angelica
- cat's claw
- chamomile
- chondroitin
- feverfew
- garlic
- gingko
- goldenseal
- grape seed extract
- green leaf tea
- horse chestnut seed
- psyllium
- fish oil
- vitamin E
- turmeric
**Cellular Production of Cholesterol**

- Enter circulation as tightly packed cholesterol, triglycerides, and lipids
- Carried by proteins that enter circulation; broken down for energy or stored for future use as energy
- High-density lipoproteins (HDL)
  - Enter circulation as loosely packed lipids
  - Used for energy; pick up remnants of fats and cholesterol left in the periphery by LDL breakdown

**Lipoproteins Produced in the Liver**

*Low-density lipoproteins (LDL)*
- Enter circulation as tightly packed cholesterol, triglycerides, and lipids
- Carried by proteins that enter circulation; broken down for energy or stored for future use as energy

*High-density lipoproteins (HDL)*
- Enter circulation as loosely packed lipids
- Used for energy; pick up remnants of fats and cholesterol left in the periphery by LDL breakdown

**Lipid Blood Level Treatment Guidelines**

- Patients who have cardiovascular disease:
  - Patients with an LDL, or “bad” cholesterol level of 190 mg/dL or higher;
  - Patients with Type 2 diabetes who are between 40 and 75 years of age; and
  - Patients with an estimated 10-year risk of cardiovascular disease of 7.5 percent or higher who are between 40 and 75 years of age (the report provides formulas for calculating 10-year risk).
- In terms of clinical practice, prescribers can use risk assessment tools in some cases to determine which patients would most likely benefit from statin therapy, rather than focusing only on blood cholesterol to determine which patients would benefit.
- High lipid levels are not on with risk list for CAD...Framingham or metabolic syndrome
Drugs Used to Treat Hyperlipidemia

* Bile acid sequestrants
* HMG-CoA inhibitors
* Fibrates
* Niacin
* Cholesterol absorption inhibitors
* Other: triglyceride transfer inhibitor, oligonucleotide inhibitor

HMG-CoA Inhibitors

* atorvastatin (Lipitor)
* fluvastatin (Lescol)
* lovastatin (Mevacor)
* pravastatin (Prevachol)
* rosuvastatin (Crestor) risk with Asian-Americans
* simvastatin (Zocor)

Research is indicating increased risk of developing diabetes, dementia......stress that healthy people should not take them just because their “numbers” are high
* Peroxisome proliferator receptor alpha activator
  * Fenofibric acid (Trilipix)
  * Activates hepatic receptors to increase breakdown of lipids, eliminate triglyceride rich particles from the plasma and reduces the production of an enzyme that naturally inhibits lipid breakdown
  * Gallstones, rhabdomyolysis with statins, increased bleeding with anticoagulants
  * Recent study showed no benefit with use...on the pricey side

* Lomitapide (Juxtapid) with diet and exercise for patients with homozygous familial hypercholesterolemia only...BB warning: risk of severe liver toxicity, pregnancy category X..only available through limited access program, triglyceride transfer protein inhibitor
* Etoricoxib (Fenbid) weekly subcutaneous injection, with diet and exercise for patients with homozygous familial hypercholesterolemia only...BB warning: risk of severe liver toxicity, pregnancy category X..only available through limited access program..inhibits formation of apoprotein B
* Alirocumab (Praluent) Adjunct to diet and exercise for tx of heterozygous familial hypercholesterolemia with maximal tolerance to statin therapy or clinical atherosclerotic CV disease. Subcut once every 2 wk proprotein conversion inhibiting antibody
* Evolocumab (Repatha) Adjunct to diet and exercise for tx of heterozygous familial hypercholesterolemia with maximum tolerated statin or other lipid lowering therapy or clinical atherosclerotic CV disease subcut once every 2 wk; or three injections given in 30 min subcut once/month proprotein conversion inhibiting antibody
* Newer drugs deemed way too expensive vs benefit
* Omega-3-carboxylic acids (Epanova) with diet and exercise to reduce triglycerides...swallow whole...no evidence of change in CV risks or events or pancreatitis (omega-3-acid ethyl esters (Lovaza) lower very high triglyceride levels)

* Treatment of HF
**Congestive Heart Failure (CHF)**

*Definition*

- Condition in which the heart fails to effectively pump blood around the body. Imbalance between right and left heart function, one side “fails” to do its job leading to congestion in the blood vessels.

*Primary treatment*

- Helping the heart muscle to contract more efficiently to restore system balance

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**Natriuretic peptide**: One of the peptides that causes natriuresis, the excretion of an excessively large amount of sodium in the urine. The natriuretic peptides are produced by the heart and vasculature:

- A-type natriuretic peptide is secreted largely by the atrial myocardium in response to dilation.
- B-type natriuretic peptide is manufactured mainly by the ventricular myocardium and/or the brain.
- C-type natriuretic peptide is produced by endothelial cells that line the blood vessels.

Elevations of B-type natriuretic peptide is useful in the diagnosis of heart failure. The finding of a low level of B-type natriuretic peptide tends to exclude heart failure.
**Treatments for Heart Failure**

- **Vasodilators (ACE inhibitors and nitrates)**
  - Decrease workload of overworked cardiac muscle
- **Diuretics**
  - Decrease blood volume, which decreases venous return and blood pressure
- **Beta-adrenergic agonists**
  - Stimulate the beta-receptors in the sympathetic nervous system, increasing calcium flow into the myocardial cells and causing increased contraction

**Cardiac Glycosides: digoxin**

- **Actions**
  - Increase intracellular calcium, allowing more calcium to enter the myocardial cell during depolarization; cause positive inotropic effect, increasing renal perfusion with a diuretic effect and decreasing renin release; and slow conduction through the AV node
- **Problems:** increases MVO₂ and “steals” oxygen
  - Very low margin of safety

**Phosphodiesterase Inhibitor: milrinone**

- **Classification**
  - Second class of drugs that act as cardiotonic (inotropic) agents
- **Type**
  - Milrinone (Primacor): short-term management of CHF in patients who are receiving other drugs
**New Drugs for HF**

* Ivabradine (Corlanor)...hyperpolarization activated cyclic nucleotide-gated channel blocker (reduces heart rate by changing ...slowing...repolarization) oral agent for adults with compensated chronic HF in sinus rhythm at over 70...no negative inotropic effects.

* Sacubitril/valsartan (Entresto)...oral combo of an ARB and a neprilysin inhibitor (blocks the breakdown of natriuretic peptide leading continued high levels and with the blocking of angiotensin II effects drops BP and decreases aldosterone release) oral agent for adults with stable, chronic HF...often used in place of an ARB or ACE...decreases hospitalizations and deaths.

**BiDil**

* Fixed combination drug: isosorbide, hydralazine ...for self-identified black patients to improve function and decrease hospital admissions.
**OTC cold/flu/allergy medicines contraindicated under the age of 4...pushing for 6, lack of therapeutic effectiveness is unbalanced by the adverse effects**

Humidifier, fluids, nasal saline, pain medication as needed, hot shower, avoidance of respiratory irritants

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**ragweed pollen (Rupwitek)**
*Timothy grass pollen (Grastek)**
*grass pollen (Oralair)**
*Phase III...peanut allergies, dust mite allergies

Sublingual allergen extracts to act like allergy shots...exact mechanism not understood...start 12-16 wks before and continue through the season...must observe patient for at least 30 min after first dose...used daily; always prescribe an Epi-pen with this prescription

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*Allergen extracts...*
**Bronchodilators**

- Xanthines: aminophylline (Truphylline), caffeine, dyphylline (Dilor), theophylline (Slo-Bid, Theo-Dur)
- Sympathomimetics: albuterol (Proventil), arformoterol (Brovana), ephedrine, epinephrine (Sus-Phrine), formoterol (Foradil), isoetharine, isoproterenol (Isuprel), levalbuterol (Alupent), pirbuterol (Maxair), salmeterol (Serevent), olodaterol (Striverdi Respimat), terbutaline (Brethaire) and indacaterol (Accopta Neohaler). **BB warning. LABAs cannot be used without inhaled corticosteroids. Risk of death**

**Sympathetic side effects**

- Blood pressure and heart rate increase
- Respiratory efficiency also increases
- Bronchi are dilated and respiratory rate increases
- Pupils dilate
- Piloerection
- Blood is diverted from the GI tract
- Blood is diverted from internal organs
### Anticholinergics:
- ipratropium (Atrovent)
- tiotropium (Spiriva)
- aclidinium (Tudorza Pressair)
- imeclidinium (Incruse Ellipta) long acting anticholinergic
- olodaterol/tiotropium (Stiolto Respimat)
- glycopyrrolate (Seebri Neohaler) COPD, anticholinergic
- glycopyrrolate/formoterol (Bevespri Aerosphere)

### Results of Parasympathetic Nervous System Blocking
- Decreased motility and secretions in the GI tract
- Increased heart rate and contractility
- Relaxation of the bronchi, with decreased secretion
- Constriction of the GI and urinary bladder sphincters
- Pupillary constriction blocked

### Other Medications
- mepolizumab (Nucala) subcutaneous; severe asthma w eosinophilic phenotype (interleukin antagonist)
- resizumab (Cinqair) IV once every 4 wk with severe asthma still not controlled with traditional therapy (decreases eosinophils) BB warning for anaphylaxis; interleukin antagonists; risk of malignancy, helminthic infection
- omalizumab (Xolair), has received expanded approval from the FDA for the treatment of moderate to severe persistent asthma in patients 6 to 11 years old who have in vitro reactivity or a positive skin test to airborne allergens. Xolair was previously indicated for the treatment of allergic asthma patients who are at least 12 years old and for unresponsive chronic urticaria. Monoclonal antibody to IgE antibodies..made from Chinese Hamster ovary cell..prevents the IgE binding to the mast cells and basophils
*Antinflammatory agents
  * Inhaled steroids: beclomethasone (Beclovent), budesonide (Pulmicort), Ciclesonide (Alvesco), fluticasone (Flovent), triamcinolone (Azmacort) fluticasone fumate (Arnuity Ellipta)
  * Leukotriene receptor antagonists: montelukast (Singulair), zafirlukast (Accolate), zileuton (Zyflo)

* Indacaterol (Arcapta) - oral inhalant bronchodilator, beta agonist - long term once daily; not for use in asthma, caution with CV disease
  * roflumilast (Daliresp) oral to reduce exacerbations of COPD in pts with severe disease with chronic bronchitis. phosphodiesterase 4 inhibitor. increases lung cell AMP to increase function and prevent damage
  * alpha, proteinase inhibitor (Glassia) IV for chronic augmentation and maintenance therapy in adults with congenital alpha, proteinase deficiency. IV weekly

* Newer COPD drugs

* intedanib (Ofev), kinase inhibitor for idiopathic pulmonary fibrosis BB warning bleeding, GI perforation, liver toxicity
  * perfenisone (Esbriet), pyridine for idiopathic pulmonary fibrosis BB warning for bleeding, liver toxicity, GI perforation

* Newer pulmonary drugs
Guidelines change rather regularly (?)...mast cell stabilizers out of mix...leukotriene inhibitors in younger patients

CDC.gov has several excellent teaching aids

Current research concerns:

- increased deaths with long term sympathetic agonists...limiting use

BB warning that must be combined with an inhaled corticosteroid

- limiting use of OTC respiratory products in children...not for under 4, caution under 6...pushing for contraindications for under 6

- effects of OTC products on the elderly.

www.nhlbi.nih.gov/guidelines/asthma

*Half way done...jump and shout!!*
Chemical stimulants:
- bisacodyl (Dulcolax)
- cascara
- castor oil (Neolid)
- senna (Senokot)

Bulk stimulants
- lactulose
- magnesium citrate (Citrate of Magnesia)
- magnesium hydroxide (Milk of Magnesia)
- magnesium sulfate (Epsom salts)
- polycarbophil (FiberCon)
- polyethylene glycol-electrolyte solution (Golytely and others)
- psyllium (Metamucil)

Lubricants
- docusate (Colace)
- glycerin (Sani-Supp)
- mineral oil (Agoral Plain)

Lubiprostone (Amitiza) locally acting chloride channel activator that increases the secretion of chloride rich intestinal fluid, leading to increased motility. Treatment of chronic, idiopathic constipation and IBS with constipation in women.

Methylnaltrexone (Relistor) selective antagonist to mu-receptors (cause of the constipation with opioid use). Approved for the treatment of opioid-induced constipation in patients with advanced disease or palliative care on opioids who no longer respond to traditional laxatives.

Crofelemer (FULYZAQ) chloride and calcium channel blocker in the GI tract. TX of HIV drug related non-infectious diarrhea.

Eluxadoline (Viberzi) mu-opioid receptor agonist...adults with IBS/diarrhea.

Rifaximin (Xifaxin) IBS/diarrhea...used for travelers diarrhea, to lower ammonia levels with liver failure.

Naloxegol (Movantik) opioid antagonist for tx of constipation in adults with at least 4wk of continual opioid use for chronic cancer pain...risk of withdrawal symptoms, can’t change pain medication.
Histamine-2 antagonists
cimetidine (Tagamet)
famotidine (Pepcid)
nizatidine (Axid), best with liver disorders
ranitidine (Zantac)

Antacids
aluminum salts (AlternaGEL)
calcium salts (Tums)
magaldrate (Rospam)
magnesium salts (Milk of Magnesia)
sodium bicarbonate (Bell/ans)

Proton pump inhibitors:
dexlansoprazole (Kapidex)
esomeprazole (Nexium)
lansoprazole (Prevacid)
omeprazole (Prilosec)
pantoprazole (Protonix)
rabeprazole (Aciphex)

Protectant
sucralfate (Carafate)

Prostaglandin
misoprostol (Cytotec), used in combination as an abortifacient

Recent study conclusions:
• risk of bone loss
• risk of Clostridium difficile diarrhea
• risk of hypocalcemia
• risk of hypomagnesemia
• risk of pneumonia

Questions being studied
• availability of oral medications
• renal effects
• electrolyte disturbances
• risk vs benefit

* netupitrat/palonosetron (Akynzeo) emetogenic chemotherapy, oral, 1 hour before chemo

* palonosetron (Aloxi) now approved for the prevention of nausea/vomiting in children 1 mo–17 yr (only antiemetic approved for the 1-6 mo group)

* dronanibol (Syndros) oral solution for the tx of weight loss in patients with AIDS or using highly emetogenic chemotherapy when other treatments fail

* granisetron ER injection (Sustol) prevention of chemotherapy-induced nausea and vomiting, effective for 5 days
Duopa (carbidopa/levodopa) enteral suspension for advanced Parkinson's CADD-Legacy 1400 portable infusion pump. Patients should be switched to oral immediate-release carbidopa/levodopa before starting Duopa; the labeling has instructions for conversion from immediate-release tablets to Duopa. The maximum recommended daily dose of levodopa is 2000 mg (1 cassette/day). Patients must also take oral immediate-release carbidopa/levodopa in the evening after disconnecting the pump. The medication cassette should be stored in the refrigerator and removed 20 minutes before administration.

*One month’s supply of Duopa costs $60542; PEG-J tube insertion and administration-related expenses will significantly increase the cost of treatment.*
*Treating hyperglycemia*

“I have metal fillings in my teeth. My refrigerator magnets keep pulling me into the kitchen. That’s why I can’t lose weight!”

“diabetes”

diabetes, glucose, blood, insulin, type, causes, symptoms, diabetes, history, family, people, prevention, risk, form, system, cell, body
Hypoglycemia deemed more dangerous than hyperglycemia...why?

What does that do to guidelines?
**Insulin, inhaled (Afrezza) similar to lispro; one inhalation before meal.**

Warning: Not for pts with asthma, COPD; baseline spirometry before use; risk of lung cancer, acute bronchospasm, lung function deterioration.

- Insulin degludec: Tresiba long acting
- Ryzodeg... insulin degludec and insulin aspart
- Insulin glargine... manufactured (Toujeo) comes with prescribing instructions... not an equivalent to Lantus... must include brand name/concentration, titration directions... tell users never to use a syringe to remove drug from the pen.

*Never share insulin pens or needles*
*Teach proper administration/storage*
*Teach proper disposal of needles and syringes*

*New black box warnings for insulin*

**Site of Action of Drugs Used to Treat Diabetes**
canagliflozin (Invokana) blocks the reabsorption of glucose in the kidney, leading to loss of large amounts of glucose-rich urine...lowers blood glucose...patients also lost weight and lowered systolic BP... bone loss

dapagliflozin (Farxiga)

empagliflozin (Jardiance)

Risk of UTIs, genital fungal infections, hyperkalemia, hypoglycemia, dehydration; warning of ketoacidosis

Sodium-glucose co-transporter 2 inhibitors

DPP-4 inhibitors: slows the breakdown of GLP-1, prolonging the effects of increased insulin secretion, decreasing glucagon release and slowing GI emptying

alogliptin (Nesina)

linagliptin (Tradjenta)

saxagliptin (Onglyza)

DPP-4 inhibitors

Sitagliptin (Januvia)

Warning...development of severe to debilitating joint pain, up to months after discontinuing drug...should stop drug at first sign of severe joint pain, consider not using drug in patients with joint issues

Saxagliptin, alogliptin and all combos new warning of increased risk of HF especially in patients with renal or heart disease

Glucagon-like peptide-1 receptor agonists: mimics normal GLP-1 to enhance glucose-dependent insulin release from beta cells; depresses glucagon release and slows GI emptying; subcutaneous 60 min before morning and evening meals; in combination with other agents

exenatide (Byetta)(Bydureon)

dulaglutide (Trulicity)

abiglutide (Tanzeum)

liraglutide (Victoza)(as Saxenda- approved as a weight loss drug)

Risk of thyroid C-cell tumors, including thyroid medullary carcinoma

* Risk of thyroid C-cell tumors, including thyroid medullary carcinoma
* Lixisenatide (Adlyxin) approved July 30 another glucagon-like peptide-1 agonist

Warnings: not with chronic pancreatitis or type 1 diabetes or with gastroparesis

Injected once daily within one hour of first meal of the day, monitor for pancreatitis, delays gastric emptying, give oral meds one hour before, oral contraceptives one hour before or 11 hours after dose

No warning of thyroid cancer....

* Diazoxide (Proglycem), raises blood sugar level, linked to pulmonary hypertension in baby's whose moms took during pregnancy; suggest not using during pregnancy

**Antidiabetic combos**

* Linagliptin, metformin (Jentaduetos) for type 2 diabetes
* Sitagliptin and metform ER (Janumet ER) for type 2 diabetics
* Sitagliptin and simvastatin (JuviaSync) type 2 diabetics with high lipid levels
* Alogliptin and metformin (Kazano)
* Alogliptin and pioglitazone (Oseni)
* Dapagliflozin/metformin (XigduoXR)
* Canagliflozin/metformin (Invokamet)
* Empagliflozin/linagliptin (Glyxambi)
* Empagliflozin/metformin (Synjord)
Common herbs that interact with antidiabetic drugs:

- juniper berries
- ginseng
- garlic
- fenugreek
- coriander
- dandelion root
- celery

*flibanserin (Addyi)*

* Tx of premenopausal women with hypoactive sexual desire that causes marked distress and interpersonal difficulty
* NOT indicated for post menopausal women, men, or to enhance current sexual performance
* Mechanism of action unknown. It is believed that Addyi helps restore prefrontal cortex control over the brain's motivation/rewards structures, enabling sexual desire to manifest. This is thought to be accomplished by the rebalancing of neurotransmitters that influence sexual desire. Specifically, Addyi increases dopamine and norepinephrine (both responsible for sexual excitement) while transiently decreasing serotonin (responsible for sexual satiety/inhibition) in the brain's prefrontal cortex. ...BB warning: risk of serious hypotension (must be taken before bed), syncope; available by limited access program; depression and suicidality; cannot combine with alcohol, grapefruit juice, many herbs; side effects worse if combined with hormonal contraceptives
* brexipiprazole (Rexulti)
* cariprazine (Vraylar)
  BB warning not for use in dementia-related psychosis, suicidality
  Akathisia, seizures, weight gain, hyperglycemia, dyslipidemia
* aripiprazole: Warning of uncontrollable urges...shopping, eating, sex, already a warning for gambling
* olanzapine, clozapine...both associated with DRESS...drug reaction with eosinophilia and systemic reactions...need to monitor absolute neutrophil count regularly

* Atypical antipsychotics

*The FDA granted breakthrough therapy designation to Janssen's esketamine for the treatment of major depressive disorder with imminent risk for suicide. The drug is a non-competitive and subtype non-selective activity-dependent N-methyl-D-aspartate receptor antagonist that is administered nasally.

* New antidepressant in phase II
brivaracetam (Briviact) oral/IV as adjunct treatment of partial-onset seizures in pts 16 and older...binds to synaptic vesicle protein 2A in the brain, but effects on seizures not understood...daily to three times/day...neurological and psychiatric reactions, suicidality

*n New seizure medication*

*amphetamine (Adzenys XR-ODT) CII

6 yr and older, BB warning abuse, dependence, baseline EKG

methylphenidate ER Aptensio 6 yr and older

*n ADHR drug*

*sugammadex (Bridion)

Reverses neuromuscular blockade induced by rocuronium, vecuronium in adults undergoing surgery (need second method of contraception for 7 days post drug) bradycardia is the big problem, anticholinergic is suggested

*n Anesthesia reversal agent*
*Patiromer (Valtesse)

Oral treatment of hyperkalemia in adults... allow at least 6 h window with other oral drugs... GI effects can be severe

*Potassium lowering drug

*Lesinurad (Zurampic) oral with a xanthine oxidase inhibitor for patients who do not achieve target serum uric acid levels with other treatment...

*BB warning for acute renal failure

*New drug for gout

*Defibrotide (Defitelio) oligonucleotide with profibrinolytic properties for the treatment of any patient with hepatic veno-occlusive disease (sinusoid obstruction syndrome) with renal or pulmonary dysfunction following a hematopoietic stem cell transplant (risk of bleeding, high risk in pregnancy, lactation) IV over 2 h every 6 h for at least 21 days

*Stem cell transplant support
*ibrutinib (Imbruvica) kinase inhibitor that inhibits B cell signaling and cytokine activation. Breakthrough status, success in chronic situations

*Graft vs host disease support

*mifepristone...Mifepr..lower dose...200mg for pregnancy of up to 70 days...previously 49...followed by 800 mcg misoprostol in 1-2 days
*Trying to make availability possible in states that still do not allow the use

*Abortifacient changes

*naloxone...now available in a nasal spray (Narcan Nasal Spray) Evzio available in kit for household use, first responders...OTC in Canada
*Probuphine, the first buprenorphine implant for the maintenance treatment of opioid dependence.

*Opioid antagonist
*darunavir (Prezista) now approved for use in pregnant and postpartum women in combination with an antiretroviral (such as ritonavir)...available as a tablet and as an oral solution

*New indication for HIV drug

*emtricitabine, rilpivirine, tenofovir (Odefsey) ...oral...risk of hepatitis B exacerbations, liver impairment

*New HIV comb drug

*Cholera vaccine...Vaxchora
*Anthrax vaccine...Biothrax
*Quadrivalent flu vaccine Flucelvax
*Quadrivalent

*Scorpion immune globulin
*Prevnar...now approved for all ages, previously over 55, and up to age 1
*Ebola vaccine...up for approval

*New warnings that fainting is a common reaction to vaccines, suggest monitoring patients, administering vaccines lying down

*New biologicals
* necitumumab (Portrazza) nonsmall cell lung cancer
* alecibib (Alzemeo) nonsmall cell lung cancer
* alacezumab (Bexcentris) bladder cancer
* osimertinib (Tagrisso) nonsmall cell lung cancer..mutation specific
* rivocumab (Opdivo) nonsmall cell lung cancer advanced after platinum-based tx
* carfilzomib (Kyprolis) multiple myeloma IV
* cobimetinib (Cotellic) multiple myeloma oral
* daratumumab (Darzalex) multiple myeloma IV
* elotuzumab (Empliciti) multiple myeloma IV
* venetoclax (Venclexia) CLL, genotype specific
* loxazomb (Xarelto) multiple myeloma oral
* obinutuzumab (Gazyva) lymphoma
* talimogene (Tlyov) lesional for unresectable nodal lesions of melanoma
* ipilimumab (Yervoy) and nivolumab (Opdivo) for advanced melanoma
* panobinostat (Farydak) with bortezomib and dexamethasone for multiple myeloma after (no other tx)

* Cancer drugs

* sonidegib (Odonzo) basal cell carcinoma..Hedgehog pathway inhibitor BB warning embryo-fetal toxicity
* trabectedin (tondelis) liposarcoma (rhabdomyolysis, cardiac and hepatic toxicity)
everolimus...also now for neuroendocrine tumors
* palbociclib (Ibrance) breast cancer

* More cancer drugs

* lifitegrast (Xildra) lymphocyte function-associated antigen-1 antagonist ..drops twice a day

* Dry eye ophthalmic drug
*adapalene (Differin Gel) - retinoid, now available as an over the counter acne treatment.

**OTC acne gel**

* orlistat (Xenical, Alli) binds gastric and pancreatic lipase to prevent the breakdown and absorption of fat (black box warning, severe liver toxicity) new warning...blocks the effects of antiretroviral drugs, risk with HIV patients (flatulence, loose and oily stools, incontinence, diarrhea, lack of fat soluble vitamins, Pregnancy category X)

* lorcaserin (Belviq) - selective serotonin agonist...now approved for maintenance as well as weight loss

* phentermine with topiramate (Qsymia)

Latest drugs in combination with diet and exercise only with BMI of ≥ 30 kg/m² or ≥ 27 kg/m² with other comorbidities...cardiac valve problems, CVD problems, GI problems...in studies first year is the biggest loss then drops off...stop in 12 wk if you haven’t lost 5% body weight...contraindicated in pregnancy

**Weight loss agents**
*Weight loss agents have been found to be effective if combined with a low calorie diet and exercise program
*Average weight loss on these agents: 2-3 pounds over 6 mo

* naltrexone/bupropion ER (Contrave) very high BMI...BB suicidality
* Liraglutide (Saxenda)...BB warning thyroid cancer
* Lisdexamfetamine (Vyvanse) treatment of binge eating disorders in adults BB warning...not for weight loss

**Other weight loss drugs**

* Botulinumtoxin...now
  - IncobotulinumtoxinA Xeomin (glabellar lines, blepharospasm, cervical dystonia)
  - AbobotulinumtoxinA Dysport (glabellar line, cervical dystonia)
  - RimabotulinumtoxinB Myobloc cervical dystonia
  - OnabotulinumtoxinA Botox, Botox Cosmetic (glabellar lines, cervical dystonia, axillary hyperhidrosis, blepharospasm, strabismus, upper limb spasticity, migraine, urinary incontinence)
* Warnings of botulism poisoning weeks to days after injection
* Brilinta (vorstoxetine) an antidepressant to Trintellix after name confusion with Brilinta (ticagrelor) an antiplatelet
* Clozapine REMS program hiccups...need to stress risk of infections...monitor WBCs
* Apparent risk of miscarriages if using oral fluconazole during pregnancy (for yeast infections)
* Studies show no link between smoking cessation drugs and suicide
* Zucally sumatriptan patch for severe migraines, pulled after severe burns and permanent scarring...no longer available
* As of July 27, FDA-approved fluoroquinolones (levofloxacin-Levaquin), ciprofloxacin (Cipro), ciprofloxacin extended-release tablets, moxifloxacin (Avelox), ofloxacin and gemifloxacin (Factive) now require a Boxed Warning and revisions to the Warnings and Precautions section of the label about the risk of disabling and potentially irreversible adverse reactions that can occur together. The label also contains new limitations-of-use statements to reserve fluoroquinolones for patients who do not have other available treatment options for acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis and uncomplicated urinary tract infections. The patient Medication Guide that is required to be given to the patient with each fluoroquinolone prescription describes the safety issues associated with these medicines.