

Update on New Drugs of 2005-2006

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Issues

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- In clinical trials, Exubera® was found to be as effective as short-acting insulin to improve blood glucose levels and had higher patient satisfaction secondary to decreased frequency of injections.
- Rozerem® is a melatonin receptor MT1 and MT2 agonist, and helps maintain circadian rhythms that underlie a normal sleep-wake cycle.

The past two years have brought some interesting new medications. These are just a few of the new agents a physician might see in his or her practice.

Ranexa® (ranolazine)-CV Therapeutics

Ranolazine was approved in January 2006 to treat chronic angina for patients not responding to other anti-anginals. The mechanism of action is not known, but its anti-anginal and anti-ischemic effects are not dependent on heart rate or blood pressure reduction. Common side effects include dizziness, headache, nausea, and constipation. Ranolazine is contraindicated in patients with pre-existing QTC prolongation, hepatic impairment (Child Pugh A, B, and C), and in patients taking potent CYP3A inhibitors. Ranexa® has a few clinically significant drug interactions; it has been shown to increase digoxin concentrations 1.5-fold and can inhibit the metabolism of medications that are metabolized by CYP2D6, notably some tricyclic anti-depressants. Steady-state concentrations are usually seen after three days of twice daily dosing. It is initiated at 500 mg orally twice daily without regard to meals, and increased to 1000 mg twice daily as needed/tolerated. Doses higher than 1000 mg twice daily have shown greater propensity for QTC prolongation and increased risk of torsades de pointes. Patients should be counseled to avoid any medication known to prolong the QTC interval, as well as grapefruit juice, throughout the duration of therapy.

Exubera® (human rDNA insulin)-inhaled-Pfizer

Exubera® was approved in January 2006 for treatment of adults with Type 1 and Type 2 diabetes. Exubera® is inhaled into the lungs where the insulin is absorbed quickly to decrease blood glucose levels. In clinical trials, Exubera® was found to be as effective as short-acting insulin to improve blood glucose levels and had higher patient satisfaction secondary to decreased frequency of injections. Common side effects include hypoglycemia, cough, dry mouth, and chest-pain. Exubera® is available in 1 mg and 3 mg blister packs. The dose is to be determined by the prescriber, and can be calculated

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by using the following formula: patient's weight in kilograms x 0.05 mg per kg equals the pre-meal dose (in milligrams) rounded down to the nearest whole milligram. The 1 mg blister pack is roughly equivalent to 3 international units of subcutaneously injected regular insulin, and the 3 mg pack is roughly equivalent to 8 international units. Patients should be counseled to take Exubera® ten minutes before meals and can be used with other oral hypoglycemics. It is important to note that Exubera® does not replace long-acting insulin products and should not be used in patients with lung disease or who smoke or have stopped smoking within six months prior to initiation of therapy.

Byetta® (exenatide)-Amylin Pharmaceuticals

Byetta® was approved in April 2005 as adjunctive therapy to improve glycemic control for Type 2 diabetics who are taking metformin, a sulfonylurea, or a combination of the two and have not achieved adequate glucose control. Exenatide is an incretin mimetic agent which mimics the enhancement of glucose-dependent insulin secretion, thereby reducing both fasting and post-prandial glucose. Typical adverse events consist of primarily GI disturbances, such as nausea, vomiting, diarrhea, and dyspepsia. Peak plasma concentrations occur around two hours post-dose. Notable drug interactions include antibiotics and oral contraceptives, which should be taken one hour prior to exenatide. Byetta® is initiated at 5 mcg subcutaneously twice daily within sixty minutes prior to morning and evening meals; do not give after meals. After one month of therapy the dose may be increased to 10 mcg twice daily. Patients should be counseled that Byetta® is not a replacement for insulin, and is not approved for Type 1 diabetics. Byetta® has been associated with weight loss in many patients, but should be avoided in any diabetic with severe gastroparesis. The medication is available in a pre-filled syringe containing sixty doses of the medication or a one-month supply.

Januvia® (sitagliptin phosphate)-Merck

Januvia® was approved in October 2006 for treating patients with Type 2 diabetes to improve glycemic control as monotherapy or in combination with metformin or thiazolidinediones when the single agent alone with diet and exercise does not provide adequate control. It should not be used in Type 1 diabetics or to treat diabetic ketoacidosis as the medication would not be effective for these conditions. Januvia® is a DDP-4 inhibitor which slows the inactivation of incretin hormones. It increases insulin release and decreases glucagon levels in the circulation in a glucose-dependent manner. Peak concentrations are seen between 1 to 4 hours post-dose. The recommended dose is 100 mg once daily without regard to meals. Dosage adjustments are required for moderate and severe renal insufficiency. Common side effects of Januvia® include headache, nasopharyngitis, and upper respiratory tract infection. There are no known clinically significant drug interactions or contraindications to sitagliptin therapy. The rates of hypoglycemia with Januvia® used in combination with sulfonylureas or insulin have not been studied. The medication is available in 25 mg, 50 mg, and 100 mg tablets.

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Rozerem® (ramelteon)-Takeda

Rozerem® was approved in July 2005 for treatment of insomnia characterized by difficulty with sleep onset. Rozerem® is a melatonin receptor MT1 and MT2 agonist, and helps maintain circadian rhythms that underlie a normal sleep-wake cycle. Unlike other sleep agents, ramelteon has not been shown to be habit forming. Peak concentrations occur around 0.75 hours after the oral dose. The dose is 8 mg orally to be taken thirty minutes prior to bedtime. Common side effects include headache, somnolence, and diarrhea. Ramelteon should be avoided in patients with severe hepatic disease or patients currently taking fluvoxamine. Patients should be counseled not to take Rozerem® after high-fat meals, and to contact the prescriber if any sexual side effects occur, as ramelteon has been shown to affect reproductive hormones in adults, specifically decreasing testosterone and increasing prolactin levels.

Bidil® (isosorbide dinitrate [ISDN]/ hydralazine)-NitroMed Inc.

Bidil® was approved in June 2005 for treatment of heart failure as an adjunct to standard therapy (beta blockers & ACE-inhibitors) in self-identified black patients to improve survival, to prolong time until hospitalization for heart failure, and improve functional status. There is little experience with its use in New York Heart Association Class IV heart failure. Bidil® is a combination of ISDN and hydralazine which act as arterial and venous vasodilators. The pharmacokinetic properties of this medication are similar to the individual ingredients. Common adverse events include headache, dizziness, flushing, and hypotension. Bidil® is contraindicated in anyone with a known allergy to nitrates and with current use of phosphodiesterase-5 inhibitors such as sildenafil (Viagra®), vardenafil (Levitra®), and tadalafil (Cialis®). It is available as a fixed-dose of 37.5 mg hydralazine and 20 mg ISDN and should be started at one tablet orally three times a day titrated to a maximum tolerated dose not to exceed two tablets three times a day. If side effects become intolerable, the dose may be decreased to one-half tablet three times a day.

Exjade® (deferasirox)-Novartis Pharmaceuticals

Exjade® was approved in November 2005 for the treatment of chronic iron overload due to blood transfusions in patients two years of age and older. Deferasirox is an iron chelator that binds to Fe³⁺ and forms a stable complex with iron. It is a highly selective binder; some in-vitro studies suggest four to five times the potency of deferoxamine. The normal starting dose is 20 mg per kg orally daily and can be increased to a maximum dose of 30 mg per kg daily. Dosage adjustments can be made every three to six months in 5 to 10 mg per kg increments. Serum ferritin levels should be monitored monthly, and dosage adjustments may be made every three to six months based upon the ferritin trends. Common side effects include GI symptoms, rash, itching, as well as auditory or visual disturbances. Use with caution in patients with hepatic or renal disease as the medication can produce a dose-dependent increase in serum creatinine. Exjade® is available in 125 mg, 250 mg, and 500 mg tablets for oral suspension, and the tablets may be mixed with water, orange juice, or apple juice. Patients should be counseled to take Exjade® on an empty stomach and avoid aluminum-containing antacids as Exjade® can potentially bind to the aluminum instead of iron.

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Tygacil® (tigecycline)-Wyeth Pharmaceuticals

Tygacil® was approved in June 2005 for the treatment of bacterial infections in patients eighteen years of age and older caused by susceptible organisms. Tygacil® is specifically indicated for complicated skin and skin structure infections as well as complicated intra-abdominal infections. This is a new class of antimicrobial called glycylcycline which inhibit bacterial protein translation. Tigecycline has extensive anti-microbial coverage: gram-positives including MRSA, multiple gram-negatives including those that produce ESBL's (extended spectrum beta-lactamases), anaerobes and atypical organisms. However, Tygacil® does not provide coverage against Pseudomonas species. The most common adverse event is nausea, but patients may experience typical tetracycline-like adverse effects, such as photosensitivity, pseudotumor cerebri, and pancreatitis. The initial dose is 100 mg IV followed by 50 mg IV every twelve hours given as a thirty to sixty minute infusion. There is no dosage adjustment necessary in renal impairment, but in severe hepatic impairment the initial dose remains the same, while the maintenance dose is decreased to 25 mg IV every twelve hours. Average duration of therapy is five to fourteen days, depending on the severity of the infection.

Chantix® (varenicline tartrate)-Pfizer

Chantix® was approved in May 2006 as a new therapeutic agent for smoking cessation. Varenicline binds to alpha-4-beta-2 neuronal nicotinic acetylcholine receptors, acting as a nicotine agonist also while blocking nicotine from binding to the alpha-4-beta-2 receptor. Common side effects include nausea (which appears to be dose-dependent), sleep disturbances, constipation, vomiting, and flatulence. Patients should select a date to stop smoking and begin Chantix® one week prior to that date. The dose titration is as follows: an initial dose of 0.5 mg by mouth once daily on days one through three, then increase to twice daily on days four through seven, then 1 mg twice daily from day eight until twelve weeks of therapy have been completed. The use of Chantix® with bupropion (Wellbutrin®) has not been established, but patients should be counseled on other methods of smoking cessation. Advise patients to take the medication after a meal and with a full glass of water. There are no known contraindications to Chantix® therapy.

References Available Upon Request