Alogliptin is an oral dipeptidyl peptidase-IV (DPP-IV) inhibitor used to treat type 2 diabetes mellitus. DPP-IV inhibitors prevent the breakdown of glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP), which are secreted by the small intestine immediately after food ingestion. GLP-1 and GIP increase insulin secretion and decrease glucagon secretion, resulting in lowered plasma glucose levels. Alogliptin (Nesina®) is the fourth gliptin available in the U.S. and was approved by the FDA in January 2013.

Alogliptin treatment resulted in greater changes from baseline in hemoglobin A1c (HbA1c) and fasting glucose levels than placebo. A double-blind, randomized, multicenter study compared alogliptin to placebo in 329 patients with poorly controlled type 2 diabetes and an HbA1c >7%. The mean change in HbA1c was significantly higher in patients receiving alogliptin 12.5 mg (-0.56%) or 25 mg (-0.59%) compared to placebo (-0.02%; p<0.001). Reductions in plasma glucose were also greater for patients treated with alogliptin versus the placebo group (p<0.001). The incidence of adverse events (70%), dropouts due to adverse events (2%), and mild hypoglycemia (2%) were similar across all three patient groups, and none of the groups experienced significant weight gain. A limitation of the study was failure to compare the effect of alogliptin with other DPP-4 inhibitors.

Since 2009, the FDA has required cardiovascular safety testing before and after approval of all new diabetes drugs. Incidence of cardiovascular events in high-risk patients taking alogliptin was studied in the EXAMINE trial. Over 5000 patients with type 2 diabetes and acute coronary syndrome received either alogliptin or placebo along with their existing diabetes and cardiovascular therapy. The primary endpoint was a composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke. A primary endpoint event occurred in 305 of 2700 patients assigned to alogliptin (11.3%) and in 316 of 2679 patients assigned to placebo (11.8%; HR, 0.96; upper boundary of the one-sided repeated confidence interval, 1.16; p<0.001 for noninferiority). The principal secondary endpoint included urgent revascularization due to unstable angina and was not significantly different between the treatments (12.7% and 13.4%; HR, 0.95; upper boundary of the one-sided repeated CI, 1.14). HbA1c levels were significantly lower with alogliptin than with placebo (mean difference −0.36%; p<0.001). Incidences of hypoglycemia, cancer, pancreatitis, and angioedema were similar with alogliptin and placebo. The authors concluded that alogliptin did not increase risk of cardiovascular events. The study was criticized for not reporting the incidence of heart failure, since the SAVOR-TIMI 53 trial found that patients taking saxagliptin had an increased risk for hospitalization for heart failure compared to placebo (3.5% vs. 2.8%; HR, 1.27; p=0.007). Common adverse effects reported in up to 4.4% of patients treated with alogliptin were headache, nasopharyngitis, and upper respiratory tract infection. A pooled analysis showed that the tolerability of alogliptin was similar in younger and elderly patients. In post-marketing reports, hypersensitivity, pancreatitis, and hepatic failure have occasionally occurred. Alogliptin has been evaluated as monotherapy or in combination with other antidiabetic agents. When added to metformin, glipizide, glyburide, pioglitazone, or insulin, alogliptin did not increase the risk of hypoglycemia, and changes in HbA1c levels seen with drug combinations were additive.

An advantage of alogliptin is that it is an oral drug dosed once a day, with or without meals. Alogliptin does not undergo substantial metabolism, and most of the dose is excreted unchanged in the urine. Patients with normal kidney function (CrCl ≥ 60 mL/min) should receive a 25 mg...
You experience heartburn, otherwise known as gastroesophageal reflux disease (GERD) or acid reflux, when stomach acid flows back into the esophagus (muscular tube that carries food and liquid from the mouth to the stomach). The muscle that acts like a valve between the stomach and esophagus becomes weak and does not close properly allowing stomach acid to irritate the esophagus.

Causes
- Obesity
- Pregnancy
- Smoking (or second-hand smoke)
- Certain medications (asthma medications, calcium channel blockers, antihistamines, pain killers, sedatives, and antidepressants)
- Large food portion sizes
- Hiatal hernia (part of the upper stomach slips through the diaphragm [muscle separating lungs from the stomach] and moves into the chest).

Symptoms
- Burning feeling in the chest or the upper part of the abdomen
- A sore throat, hoarseness, or laryngitis (swelling and irritation of the voice box)
- Difficulty swallowing or painful swallowing
- Nausea and/or vomiting
- Wheezing, asthma, and recurrent pneumonia
- Tooth erosion and bad breath

Treatment
The treatment for heartburn or GERD may involve multiple tools. Depending on the severity of the situation patients may need lifestyle changes, medications, or surgery.

Lifestyle changes
- Avoid foods that trigger heartburn such as citrus fruits; spicy, fatty, and fried foods; alcohol; caffeine and carbonated beverages; orange juice; chocolate; peppermint; and vinegar
- Eat smaller meals
- Avoid eating close to bedtime; try not to lay down for at least 3 hours after a meal
- Raise the head of your bed 6-8 inches while resting
- Lose weight if needed
- Wear loose-fitting clothes
- If you smoke, quit smoking

Medications
If the lifestyle modifications mentioned above do not improve symptoms, medications may be needed. There are many over-the-counter medications available to help treat GERD without a prescription; however, patients should still talk to their doctor before starting a medication.

Over-the-counter medications include antacids, H2 blockers, and proton pump inhibitors (PPIs).
- Antacids are first line options for heartburn and GERD. Examples are Tums®, Alka-Seltzer®, Maalox®, Mylanta®, Rolaid®, and Riopan®.
  - Doses greater than 500 mg at one time do not increase benefit of antacids
  - Side effects include diarrhea or constipation
- H-2 receptor antagonists reduce stomach acid production. Examples are ranitidine (Zantac®), cimetidine (Tagamet®), and famotidine (Pepcid®). They can also help heal the esophagus. These medications should only be used for a short period of time (up to 2 weeks) unless prescribed otherwise by your doctor.
  - Side effects include headache, dizziness, nausea, vomiting and diarrhea
- Proton pump inhibitors (PPIs) block acid production and are the most commonly prescribed medication for GERD. Examples are pantoprazole (Protonix®), omeprazole (Prilosec®, Zegrid®), lansoprazole (Prevacid®), rabeprazole (Aciphex®) and esomeprazole (Nexium®). PPIs can heal the esophagus (better than H2 blockers) and are prescribed long term in many patients; however, typical treatment is only recommended for 2 weeks unless otherwise indicated by your doctor.
  - Long term use increases the risk for bone fractures
  - Take on an empty stomach, 30-60 minutes before a meal so that stomach acid can activate the medication

Complications
Serious complications can occur if GERD is untreated for a long period of time. Complications include:
- Inflammation or irritation of the esophagus and can cause bleeding or ulcers
- Difficulty swallowing
- Some respiratory problems like trouble breathing, asthma, chronic cough, or pulmonary fibrosis may be aggravated by GERD
- Barrett’s esophagus where cells lining the esophagus have abnormal shape and color; this can lead to cancer if not treated

By Mackenzie Clark, PharmD Candidate

References on Page 4
PATIENT INFORMATION:
Tooth Whiteners

Have you ever wanted to whiten your teeth but never knew which whitener kit to buy? Many whitening products are available to purchase; however, the variety of kits makes it difficult to decide. This guide will help in choosing the best whitening product as well as offer information and tips.

Selecting a product:
In general, there are two available forms of whitening treatments: bleaching and non-bleaching.

Bleaching products are the most effective treatments. These products bleach teeth with hydrogen peroxide. People may see carbamide peroxide on some product labels, but this eventually breaks down into hydrogen peroxide when applied. Better whitening is more likely to be achieved with products containing a higher percentage of hydrogen peroxide. Over-the-counter bleaching products contain no more than 20% hydrogen peroxide, whereas one-hour professional dental cleanings have concentrations up to 50% hydrogen peroxide.

Systems containing gel with a tray, or mouthpiece, to personally fit teeth work better than whitening strips. Strips work better than gels that are applied directly to teeth without a tray. Rinses, such as mouth washes, are the least effective option for whitening and should be avoided.

Over-the-counter bleaching products are generally used for two weeks. The application time varies anywhere from 30 minutes to overnight depending on the product. Prolonged and improper use of bleaching products may result in gum damage. Read directions carefully with each product, and do not use for longer than the recommended amount of time without talking to your dentist.

Tooth sensitivity is the most common side effect of bleaching. Steps to prevent tooth sensitivity are discussed later.

Non-bleaching treatments are limited to whitening toothpastes. These products work best in combination with bleaching treatments. Whitening toothpastes are also great for maintaining whiteness and dental health after treatment with a bleaching product.

Look for whitening toothpastes approved by the American Dental Association.

Will tooth whiteners work?
Many people have unrealistic expectations regarding teeth whitening systems. Generally, individuals with healthy teeth will benefit most from whitening. Tooth discoloration is a combination of stains and materials on the surface of teeth. Tooth enamel is the outside layer of teeth that is affected by whitening products. Tooth enamel is partially see-through; therefore, dentin, the part of the tooth underneath the enamel, must appear white in order for teeth to whiten. Clean teeth may not appear white if the dentin is not white.

Certain colors of teeth respond best to whitening treatment:
- Yellow teeth have the best response to treatment
- Brown teeth respond less to treatment
- Blue-gray teeth may not respond to treatment

What are ways to decrease tooth sensitivity during whitening?
1. Shorten the amount of time the whitening product is in contact with teeth (for example, apply trays or strips for 30 minutes instead of the sixty minutes stated on the directions).
2. Stop whitening for 2-3 days to allow teeth to whiten and adjust to the product.
3. Ask your dentist for a fluoride product to help strengthen teeth. The fluoride-containing product should be applied for 4 minutes prior to and following whitening.
4. Brush teeth with a toothpaste designed for sensitive teeth (e.g., Sensodyne®).

How to decide between all the whitening kits?
1. Ask friends and family members who have used whitening products.
2. If using a tray or mouthpiece product, choose a kit with a mouthpiece that can be molded to custom fit your teeth.

3. Speak with your dentist regarding the best option.

Overall, tooth whitening systems are vast in number and variety. Gaining the opinion of friends and your dentist will help when deciding which product to purchase. Whitening trays with moldable mouthpieces offer the best results, followed by strips and gels. Non-bleaching products such as whitening toothpastes are best used for maintaining whiteness after bleaching treatments. If tooth sensitivity persists or discoloration of gums occurs during treatment, stop the product immediately and see your dentist.

By Max Whitney, PharmD Candidate

REFERENCES:
Alogliptin (cont. from page 1)

The dose of alogliptin is 12.5 mg for patients with moderate renal impairment (CrCl between 30 and 60 mL/min) and 6.25 mg for patients with severe renal impairment (CrCl <30 mL/min) or on dialysis. Alogliptin is Pregnancy Category B and may be secreted in breast milk. Like other gliptins, alogliptin is an expensive drug with moderate effects on plasma glucose levels. Although it decreases HbA1c levels, there is no evidence that it decreases the risk of heart attacks and strokes in patients with type 2 diabetes. Alogliptin will be used most often in patients likely to be harmed by hypoglycemic events, such as the elderly and those with congestive heart failure, renal failure, and liver disease. Head-to-head trials and longer duration safety trials are needed to assess the superiority and safety of alogliptin compared to other DPP-IV inhibitors.

By Diane DeCamp, PharmD Candidate

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Heartburn (cont. from page 2)

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College of Health Professions and Biomedical Sciences
Drug Information Service
The University of Montana
Skaggs School of Pharmacy
32 Campus Drive
Phone: 406-243-5254
Fax: 406-243-5256
Email: druginfo@umontana.edu