Gender-Specific Dosing of Zolpidem

In January 2013, the Food and Drug Administration (FDA) required the manufacturers of zolpidem products to lower the recommended dose of immediate release (IR) zolpidem (Ambien®, Ambien CR®, and Zolpimist®) due to safety concerns. Most notably, gender-specific dosing is now recommended due to evidence of decreased zolpidem clearance in women.1,2

Several automotive collision reports involving zolpidem were submitted to the FDA, as well as evidence that zolpidem blood levels above 50 ng/mL can impair driving sufficiently to cause a motor vehicle accident. Driving simulation and laboratory studies found that when given a dose of 10 mg zolpidem, 3% of men and 15% of women had zolpidem concentrations above 50 ng/mL eight hours post-dose. Clinical trials also found that a dose of 12.5 mg extended-release zolpidem resulted in zolpidem concentrations >50 ng/mL eight hours post-dose in 33% of women and 25% of men.2

Support for gender-specific dosing was provided through a crossover pharmacokinetics study comparing one dose of 3.5 mg sublingual zolpidem to one dose of 10 mg IR zolpidem in 33 patients (n=19 males). Zolpidem clearance was greater in males compared to females. After normalizing values in correlation to body weight, males still had greater clearance, but the difference between genders was not as large. The authors concluded that the data supported gender-specific dosing for zolpidem with a lower recommended dose for women.3 This recommendation is consistent with current dosing of Intermezo®, a lower dose zolpidem product indicated for middle-of-the-night awakenings which already recommends a lower dose for women.4 Limitations of the kinetics study include a small sample size, linearly scaled doses, and exclusion of patients who had any type of sleep disorder.3

As of April 2013, the recommended initial dose of zolpidem IR (Ambien®, Edluar®, and Zolpimist®) is 5 mg for women and either 5 or 10 mg for men taken once daily before bedtime. Patients taking zolpidem CR (Ambien CR®) should start with 6.25 mg for women and either 6.25 or 12.5 mg for men also taken once daily before bedtime. The lowest effective dose of zolpidem should be used, but patients may increase to a maximum daily dose of 10 mg zolpidem IR or 12.5 mg zolpidem CR.1,5

References:
1. A. Gazo, Sanofi, written communication, July 1, 2013.

By Laura Vigil, PharmD Candidate

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Inside this issue:

Breo Ellipta® for COPD 2
Patient Information: “Base Tanning” 3
Patient Information: Erectile Dysfunction from Propecia® 4

We welcome any comments and suggestions for future newsletter topics.

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Breo Ellipta® (fluticasone furoate/vilanterol) was recently approved for treating airflow obstructions and reducing exacerbations associated with chronic obstructive pulmonary disease (COPD). Breo Ellipta® also improved lung function when compared to placebo. Unlike current inhaled corticosteroid/long-acting beta agonist (ICS/LABA) combinations, Breo Ellipta® is dosed once daily. In clinical studies, Breo Ellipta® significantly reduced exacerbations and was as effective at improving lung function as Advair® (fluticasone propionate/salmeterol).1,2

Significant reductions in COPD exacerbations were seen with Breo Ellipta® when compared to vilanterol alone.2 Two similar, randomized, double-blind studies compared various doses of fluticasone furoate and vilanterol (FF/VI) to vilanterol alone in 3255 patients with moderate to severe COPD. Patients then received either a combination of 25 mcg vilanterol and one of three doses of fluticasone furoate (50, 100, 200 mcg) or 25 mcg vilanterol alone once daily for 52 weeks. The primary endpoint was the rate of moderate (worsening COPD symptoms ≥2 consecutive days) or severe exacerbations (defined as symptoms requiring hospitalization). Secondary endpoints were time to first exacerbation and rate of exacerbations requiring corticosteroid use.2

Significantly fewer exacerbations were seen in all three FF/VI groups in the pooled data from both studies. Times to first moderate or severe exacerbation were significantly longer in both the 100/25 and 200/25 mcg groups compared to vilanterol. Adverse events were more common in the FF/VI groups. Bone fractures and pneumonia occurred almost twice as often in the FF/VI groups. Withdrawal rates were similar in all four groups; however, more patients in the FF/VI groups dropped out due to adverse events. The authors concluded that FF/VI compared to vilanterol alone significantly reduced COPD exacerbation rates. The results are limited by the lack of health status or quality of life evaluation. And the lack of comparison to another ICS/LABA combination.2

Breo Ellipta® was as effective as Advair® in improving lung function.3 A randomized, double-blind, double-dummy study enrolled patients with moderate to severe COPD. Patients received either 100/25 mcg FF/VI once daily plus placebo twice daily (n=266) or 50/500 mcg salmeterol/fluticasone propionate twice daily and placebo once daily (n=262) for 12 weeks. The primary endpoints were the change from baseline in the weighted mean FEV1 scores after 12 weeks, time to improvements in FEV1 scores by 100 mL, and trough FEV1 scores.3

FF/VI treatment improved FEV1 scores and produced improvement faster than salmeterol/fluticasone treatment. However, no statistical differences were found between the treatments in any of the endpoints. Headache was the most frequently reported adverse event in both groups. Local corticosteroid effects were more commonly seen in the salmeterol/fluticasone group; however, more cardiovascular events occurred in the FF/VI group. The authors concluded that FF/VI had similar efficacy in improving lung function compared to Advair®. One limitation was that only Caucasians and Asians participated in the study; therefore, extrapolation to other ethnicities may be limited. Also, the study was only available as a poster presentation, and a full evaluation of the results was not possible.3

Breo Ellipta® will be available as a 100/25 mcg inhaler and should be administered at the same time once daily.4 As with other ICS-containing inhalers, patients should be instructed to rinse their mouths without swallowing to avoid oral candidiasis. Nasopharyngitis, upper respiratory tract infections, headache, and oral candidiasis were the most frequently reported adverse events in clinical trials. Potentially fatal pneumonia occurred more frequently in patients taking Breo Ellipta®.2,4 Increased bone fractures were also seen in various studies, possibly due to the long-term effects of inhaled corticosteroid use. Patients at a high risk for bone fractures should have their bone mineral densities assessed before starting Breo Ellipta® and periodically monitored.4

Breo Ellipta® is efficacious in reducing COPD exacerbations and improving lung function, with similar efficacy to Advair®. Breo Ellipta® will be available as a once daily maintenance treatment for COPD later this year. The novel once daily dosing may potentially increase compliance and subsequently clinical outcomes. However, further studies assessing adherence and outcomes comparing Breo Ellipta® to other ICS/LABA combinations are needed before routinely utilizing the once-daily inhaler.

By Chris Chong, PharmD Candidate

REFERENCES:
PATIENT INFORMATION:
The Good, the Bad, and the Ugly Facts About Base Tans

Many people go to a tanning salon to develop a tan prior to spending time in the sun; this is called a “base tan.” The belief is that a base tan will prevent a sunburn.

The GOOD
Getting a base tan from a tanning salon can provide a sun protection factor (SPF) of 4 at most. An SPF of 4 means that someone can stay in the sun 4 times longer than they normally could without burning. For example, a person who burns in the sun within 15 minutes can lengthen this time period to a maximum of 60 minutes (15 minutes X SPF 4 = 60 minutes) with a base tan.

The BAD
There are several problems with any kind of tan because a tan means that the skin was injured by ultraviolet (UV) rays. Since skin cells are damaged with any type of tanning, there is no such thing as a safe tan. Going to a tanning salon is even more harmful than spending time in the sun because the UV rays used in tanning beds can be 15 times stronger than UV rays from the sun.

The UGLY
Anytime someone gets a tan or sunburn, the risk increases for early skin aging, eye damage, and skin cancer. Early skin aging can be seen in the form of wrinkles, dark spots, and leathery skin. UV rays can also weaken the immune system which could lead to sickness. People who use tanning beds are 75% more likely to develop melanoma which is the deadliest form of skin cancer. This risk increases with each tan. Frequent tanning is one reason why skin cancer is becoming more common in younger people in the US. It is the second most common type of cancer for women in their 20s and the third most common for men in their 20s.

HOW TO STAY SAFE
Instead of base tanning, use sunscreen with an SPF of 15 or higher and apply it 30 minutes before going in the sun. Reapply sunscreen every two hours or after being in the water. Wear protective clothing, sunglasses, and a wide-brimmed hat to shield skin from UV rays. Try to stay in the shade between 10 am and 4 pm because this is when the sun’s rays are the strongest.

To get a glowing tan without the cancer risk, sunless tanning is an option. A sunless tan uses lotions or sprays to color the skin for a few days. This is a safe way to darken skin without increasing the risk of cancer. Spray-on tanning is also available at some salons, but accidentally breathing in the spray may not be safe. Many sunless tanning products provide no protection from the sun, and sunscreen should be used with sunless tanning products to avoid burning.

By Laura Vigil, PharmD Candidate

REFERENCES:
Concerns of Erectile Dysfunction Associated with Propecia®

For men taking Propecia® (finasteride 1 mg) to treat male pattern baldness, developing erectile dysfunction (ED) is a valid concern. In one particular instance, a healthy 24-year-old developed persistent ED after taking finasteride for 1 month. Within 2-5 days of starting finasteride, he experienced a decreased sex drive and complete failure to achieve an erection. He continued taking finasteride for an additional month, but these side effects continued. After stopping finasteride, the sexual dysfunction persisted despite treatment with ED medications such as Viagra® (sildenafil). Although one reported case of persistent ED is not considered statistically significant, patients should be aware of the “worst case scenario” of developing ED from finasteride use.

Propecia® is a prescription medication that targets the chemical known for causing male pattern baldness. The medication works by decreasing the amount of testosterone that is converted into a steroid chemical (DHT) linked to male pattern baldness. Speculation by clinicians and data from trials provide conflicting information about developing ED from finasteride due to a decrease in DHT levels. Patients taking finasteride should be fully informed about the possibility of developing ED from its use.

Erectile dysfunction is listed as a possible side effect for Propecia®. Throughout a one-year safety trial, ED was more common in men treated with finasteride than in men treated with placebo. In addition, more men on finasteride discontinued treatment due to ED. Erectile dysfunction was usually temporary and did not persist when the medication was stopped. In men who continued taking finasteride, the symptoms of ED typically resolved. The researchers of this safety trial found no clear association between the development of ED and finasteride use.

Another clinical trial also found no clear evidence that finasteride caused ED. One hundred and eighty-six males were evaluated for ED before and after taking finasteride for 4-6 months. Eight cases of ED were reported in this study, but the researchers concluded that no statistically significant changes in the health of these men was caused by finasteride.

Government drug regulation agencies in the US and UK have ordered the manufacturer of finasteride to expand the side effect warnings to include ED. In 2012, the FDA ordered Merck to revise their drug label to include a statement about patients developing ED from Propecia®. Previous users of Propecia® have reported persistent ED after discontinuing this medication.

The incidence of ED caused by finasteride is minimal and not greater than that seen with placebo. However, men should be assessed throughout treatment to track their sexual health and determine if ED develops while taking finasteride. If any changes in sexual health occur, the medication should be stopped, and patients should speak with their physician or pharmacist immediately.

By Dustin Cavanaugh, PharmD Candidate

REFERENCES:


