

PharmSTAT

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New Year's Resolutions

Written By: Leslie Johnson, PharmD.

'Tis that time of year again. Time for old acquaintance to be forgotten and bad habits to be broken. Along with the start of the new year comes resolutions. Reports indicate that the majority of the resolutions made are health related. People's desire to improve their lifestyle offers the healthcare team many opportunities for information, assistance, therapy, support, and encouragement. One of the most popular resolutions made at the start of the new year is smoking cessation.

For many years the common belief was that quitting "cold turkey" was the only way tobacco use could cease. This created a great deal of frustration and anxiety for patients and their families. There was also a high relapse rate associated with abrupt cessation of tobacco. For many, the side effects of weight gain, irritability, and headache were excuses not to quit. However, the healthcare team now understands that it is possible to help a patient quit by using a variety of methods. Along with non-pharmacologic options like hypnosis and acupuncture, there are a number of pharmaceutical options. Most products are available by prescription only. However, two of the most popular methods, the nicotine patch and the nicotine gum, are available without a prescription.

Nicotine replacement products work by providing the patient the nicotine that their body is dependent upon via non-tobacco means. Dosage forms include a transdermal patch, gum, oral inhaler, and nasal spray. Currently only the oral inhaler and nasal spray require a physician's prescription.

The nicotine patch is a daily transdermal system that is worn for 24-hours and then discarded. This provides a steady level of nicotine within the body. The nicotine patch is available in 3 strength, 7-mg, 14-mg, and 21-mg. The starting dose is determined by the number of cigarettes a

patient smokes daily. Patients who smoke 25 or more cigarettes per day should begin with the 21-mg patch; those who smoke fewer than 25 cigarettes per day should begin with the 14-mg patch. The initial strength is continued daily for 6 weeks and then the dose is decreased. The patient then "steps down" to the next lowest strength. For example, a patient that begins with the 21-mg patch would step down to a 14-mg patch; the 14-mg patch would be worn for 2 weeks, and then finally the 7-mg patch would be worn for 2 weeks. The patch should be applied to a hair free area on the upper body. Only one patch should be worn at a time. Skin irritation at the site of administration is possible and may be due to the nicotine or the patch adhesive. Patches should not be cut or torn. Patients should be instructed to store the patches in an area not accessible to children or pets. Remind patients that used patches still contain nicotine; a used patch should be disposed of in way that it cannot be obtained by children or animals. Patients should not smoke while using the patch because nicotine overdose is possible.

The nicotine gum is another smoking cessation aid. This dosage form employs a matrix delivery system to provide the nicotine dose to the patient. The nicotine gum provides on demand nicotine. Blood levels of nicotine fluctuate similarly to smoking. The gum is available in 2-mg and 4-mg pieces and the starting dose is based upon the number of cigarettes smoked daily. Patients should be instructed to place a piece of the gum in their mouth, bite it repeatedly until a tingling sensation is felt, and then place the gum between their cheek and gum. The patient will continue to experience a slight tingling or burning sensation as the nicotine is released and absorbed. When the tingling stops the gum should be bitten again to release more nicotine. The gum should be discarded when the tingling is no longer felt. The patient should be instructed not to chew the gum. Patients can use the gum as frequently as they feel necessary. It is recommended that patients use a scheduled dose of gum and then have additional pieces that may be used to treat nicotine cravings. It is recommended that patients gradually decrease the number of pieces of gum used daily.

The nicotine oral inhaler and nasal spray both require a prescription. The oral inhaler is the only therapy that mimics the activity of smoking and may be appropriate in patients for whom the act of inhaling is a key part of the addiction. Patients place a nicotine cartridge into the inhaler and puff intermittently for 20 minutes. This delivers the nicotine equivalent to smoking two cigarettes. Most patients require between 6 and 16 cartridges initially. They should be instructed to gradually decrease the number of cartridges used daily. The nasal spray is administered nasal daily on an as needed basis. No more than 5 sprays per hour or 40 sprays per day should be used. Nasal and throat irritation are

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common side effects of nasal nicotine replacement. There is no set tapering regimen recommended for either of the prescription products; however, the usual duration of therapy is 3 months.

Bupropion, marketed as Zyban™, is used as an adjunct method for smoking cessation. Bupropion is an antidepressant that is a weak inhibitor of serotonin and norepinephrine reuptake and an inhibitor of neuronal dopamine reuptake in the CNS. The exact mechanism of action in smoking cessation is unknown, but it is believed that the effects on neurotransmitters play a key role. Bupropion is dosed as 150-mg once daily for 3 days and then increased to twice daily. Drug steady-state is reached after 1 week of treatment, and decreased nicotine intake should not be initiated until this time. Treatment should be continued for 7-12 weeks. Patients may continue to smoke while taking the drug, however decreasing daily nicotine use is necessary for complete cessation. Bupropion is not a nicotine replacement product and should be used as an adjunct to a total smoking cessation program that includes behavior and lifestyle modifications to be successful.

All of the smoking cessation products are widely available, although the OTC products tend to be favored by patients. These products tend to be easier to obtain and the patient can begin the smoking cessation regimen without first having to see a physician. The nicotine patch may be preferred to the gum because of the once daily administration. Currently the only smoking cessation products on the Palmetto Health Formulary are the nicotine patch and the nicotine gum. Bupropion is available on formulary as Wellbutrin, but not as Zyban. While many prescription plans cover bupropion as an antidepressant (Wellbutrin or Wellbutrin SR), some plans do not cover bupropion for smoking cessation (Zyban). This may be a consideration when trying to determine whether to use this method for patients. Individual insurance plans should be contacted to determine if and which smoking cessation products are covered.

Kava and Liver Toxicity?

Written By: Jarrett R. Amsden, PharmD.

Kava, sometimes known as Kava Kava, "Intoxicating Pepper" or *Piper methysticum* has recently generated some news in Germany and Switzerland. Kava extracts have been linked to approximately 25 cases of liver toxicity. Some of the reported liver toxicities include hepatitis, cirrhosis, liver failure, and even a case requiring a liver transplant. Already, Switzerland has prohibited the sales of kava-containing products and Germany has proposed the same. Currently the United States is asking all physicians to review their cases of hepatic toxicity and report any that may be linked to kava-containing products.

Kava has been used for centuries and is the ceremonial beverage to induce relaxation in the South Pacific. Kava has traditionally been used to treat anxiety disorders, stress, insomnia, and restlessness. It has also been used in the treatment of seizures, psychosis, and depression. Kava extracts work on the central nervous system and produce

anxiolytic, sedative, anticonvulsant, spasmolytic, local anesthetic and analgesic effects. Although the mechanism is not completely understood, kava is not believed to work on GABA, but produces its motor sedation without altering the respiratory process. The applicable part of the kava plant is the root/rhizome. The pharmacological activity comes from the kava-lactones contained in the root. In nature the dried kava root provides 3.5% kava-lactones whereas commercially available products contain 30-70% kava-lactones. The kava-lactones competitively inhibit monoamine oxidase B (MAO-B), antagonize strychnine and can have antithrombotic effects on platelets by inhibiting cyclo-oxygenase and decreasing thromboxane 2 production.

The oral use of kava can cause GI disturbances, oculomotor and accommodation disturbances, headache, dizziness, enlarged pupils and rare allergic skin reactions. Normal doses of kava have been noted to cause "Driving Under the Influence" citations due to its potent CNS effects. Kava should not be used in combination with any other sedative herbs or dietary supplements. Kava's effect may be amplified when taken with benzodiazepines, alcohol, CNS depressants, barbituates, or any other sedative drug. Kava may also decrease the effectiveness of levodopa when given concomitantly. There have also been reports of death associated with overdose of sedatives when used in combination with kava.

Clinical trials have suggested that 70% kava-lactone is more effective than placebo in the treatment of anxiety disorders. The typical dose used was 100mg (70mg kava-lactones) three times a day. Studies have shown doses of 60-120mg of kava-lactones to be effective for nervousness, stress, and anxiety. Kava is also available as a tea that is prepared by boiling 2-4 grams of kava root in 150ml of water for 5-10 minutes. One cup of kava tea is used three times a day.

Kava is not standardized by the FDA and therefore the amount of kava-lactone may vary by product and lot. Due to its lack of understanding and case reports of liver toxicity, caution is advised and doctor supervision is recommended before and during the use of any kava-containing product. Physicians should be aware of all other medications (prescription, over the counter, and herbal) that patients are taking prior to and during a patient's use of a kava-containing supplement.

Saw Palmetto

Written By: Leslie Johnson, PharmD.

Scientific Name: Serenoa repens

Common Names: Saw Palmetto, Sabal, American Dwarf Palm Tree, Cabbage Palm

Uses: Tea made from saw palmetto berries has been used to manage genitourinary problems, increase sperm production, increase breast size, and increase sexual vigor. Today, saw palmetto is being reported to improve the symptoms associated with an enlarged prostate.

Mechanism of Action: Saw palmetto's proposed mechanism of action involves shifting the altered estrogen/androgen balance seen in benign prostatic hyperplasia (BPH). It is believed that saw palmetto inhibits dihydrotestosterone (DHT) binding at androgen receptors and 5-alpha-reductase activity on testosterone, preventing the conversion of testosterone to DHT. It does not significantly reduce levels of 5-alpha-reductase in the prostatic tissue or circulating levels of testosterone, DHT, and prostate specific antigen (PSA). Saw palmetto may also inhibit growth factors, and exert some anti-inflammatory effects. Overall prostate size is not altered, however the inner prostatic epithelium shrinks with use.

Derived from the ripened berries of the saw palmetto

Contraindications: Saw palmetto is contraindicated in pregnancy and lactation because of its antiandrogen activity.

Safety: The product is likely safe when used orally as directed.

Adverse reactions: Headache and GI disturbances have been reported by patients while using saw palmetto.

Drug Interactions: Concomitant use of saw palmetto may interfere with oral contraceptives and hormone therapy.

Usual dosage: The recommended daily dose for treating the symptoms associated with BPH is 1-2 grams of whole berries or 320mg of a lipophilic extract. A tea may be prepared by simmering 0.5-1 gram of dried berries in 150-ml boiling water for 5-10 minutes and straining before drinking. The tea should be taken three times daily.

Insulin

Written By: Thadd Hirschy, PharmD.

Various types of insulin are currently marketed. There are many patient benefits that arise from each of these insulins. Confusion between insulin types can occur because of all of the new insulin products available. The dose, duration, time of administration and route of administration can vary greatly between products. Some insulins may be given intravenously while others must never be given via this route. Some insulins may be given at any time of the day while others must have a specific scheduled time that they should be taken. A clear understanding of the different varieties of insulin may help to eliminate some of the confusion.

Rapid-acting Insulins

Human lispro insulin (Humalog®)

The name is derived from the switching of two amino acids in the human insulin molecule sequence —lysine and proline. Because of its quick onset, approximately 30 minutes with a peak response seen in 30 to 90 minutes. Lispro insulin can be injected immediately at the beginning of a meal. This allows the patient more freedom with their

diet schedule. Lispro should be administered subcutaneously; it can also be administered intravenously. Lispro may be mixed with NPH and ultralente. Human lispro is currently on the Palmetto Health Formulary.

Insulin aspart (Novolog®)

Insulin aspart is similar to regular insulin but the amino acid aspartic acid replaces proline in the human insulin molecule. Insulin aspart can be mixed with NPH insulin only. The mixing of insulin aspart with zinc containing insulins, like insulin ultralente and lente, should be avoided. Time to onset is about 15 minutes and peaks around 1-3 hours. Insulin aspart is NOT currently on the Palmetto Health formulary.

Regular human insulin (Novolin R®/ Humulin R®)

Regular insulin has a longer onset than lispro insulin. The time to onset is approximately 30 minutes to 1 hour and should be injected about 30 to 60 minutes prior to a meal. Time to peak effect is around 1 to 5 hours. While usually given subcutaneously, regular insulin may also be administered as an IV push or infusion. Regular insulin can also be mixed with other types of insulin (e.g. NPH insulin, ultralente insulin). Regular insulin is currently on the Palmetto Health formulary.

Intermediate-acting Insulins

NPH human insulin (Novolin N®/ HumulinN®)

Neutral protamine hagedore insulin (NPH) provides an onset of approximately 1 to 1.5 hours with a peak effect around 4 to 12 hours. NPH insulin provides a basilar level of insulin with the peak activity usually scheduled to occur around a meal or at a point of known hyperglycemia (e.g. nocturnal hyperglycemia). NPH is a suspension and cannot be given intravenously. NPH should only be administered subcutaneously. NPH can be mixed with regular and lipro insulins. NPH should not be mixed with zinc containing insulins (lente and ultralente insulin). NPH with regular insulin will decrease the number of daily injections the patient has to receive. NPH insulin is on the Palmetto Health formulary.

Lente human insulin (Novolin L®/ Humulin L®)

Lente insulin is the predecessor to NPH insulin. Lente should not be mixed with NPH. Lente insulin can be mixed with regular insulin. Lente insulin contains zinc and can precipitate with other salt forms like calcium phosphate. Onset of action is 1 to 2.5 hours with a peak around 7 to 15 hours. Lente can only be given subcutaneously. The onset of action is about 1 hour with the peak activity seen at 7 hours. Lente is on the Palmetto Health formulary.

Long-acting Insulins

Ultralente insulin (Humilin U®)

Ultralente insulin is similar to lente insulin but it has a longer duration of action. Like lente insulin, ultralente has a zinc moiety that can precipitate with other heavy metals like calcium phosphate. Ultralente can only be given subcutaneously. Ultralente provides a stable level of insulin

for greater than 36 hours with an onset of action around 4 to 8 hours and a peak of 10 to 30 hours. Ultralente insulin is on the Palmetto Health formulary.

Insulin glargine (Lantus®)

Insulin glargine is one of the newest insulins to enter the market. As with lispro insulin, the structure of insulin glargine has been modified to improve its duration of action. Insulin glargine provides a plateau level of insulin that is constant for a 24-hour period, mimicing the body's natural basilar insulin secretion. Onset of action is around 1 hour with a peak around 5 hours. Insulin glargine is an acidic preparation and therefore cannot be mixed with any type of insulin. When insulin glargine is injected a microprecipitate forms providing a slow release of insulin over 24-hours. Insulin glargine is administered once daily at bedtime. When switching from a twice daily NPH schedule to insulin glargine, the total dose should be decreased by 20%. Insulin glargine is currently on the Palmetto Health formulary.

Combination Insulins

Insulin 70/30 (Novolin 70/30®/ Humulin 70/30®)

Insulin 70/30 is a mixture of 70% of NPH and 30% regular insulin. The combination is administered twice daily with meals. When injected at proper times, the patient will receive a peak of insulin around each major meal (breakfast, lunch and supper) and a peak close to bedtime to prevent nocturnal hyperglycemia. Insulin 70/30 is administered subcutaneously and should never be administered intravenously. Because insulin 70/30 is a combination product it is not possible to independently adjust the amount of NPH or regular insulin administered. Insulin 70/30 is on the Palmetto Health formulary.

Insulin 50/50

Insulin 50/50 is a 50% suspension of NPH and 50% regular insulin. It is very similar to 70/30 only with different concentrations. It allows for higher doses of regular insulin, relative to NPH, for patients who have higher postprandial blood glucose levels. Insulin 50/50 is NOT on the Palmetto Health formulary.

Humalog 75/25®

Humalog 75/25 contains a mixture of 25% **lispro** insulin and 75% protamine **lispro** insulin. Humalog 75/25 is similar to insulin 70/30; however, the patient administers the dose immediately prior to a meal. Protamine insulin lispro is not currently marketed alone but can only be found in the combination product. The product should only be administered subcutaneously. Humalog 75/25 is on the Palmetto Health formulary.

Many advances have been made in the manufacturing and production of exogenous insulin. A wide variety of insulins are now available allowing for individualization of therapy and increased glycemic control.

Insulin	Onset	Time to Peak	IV Route	Mix Insulin
Regular Insulin	30 min to 1hr	1-5 hr	Yes	Yes
Lispro insulin	30 min	30-90 min	Yes	Yes
Aspart insulin	15 min	1-3 hour	Yes	Avoid Zinc containing insulins (U" and L')
NPH insulin	1-1.5hr	4-12 hr	No	Except with U and L
Lente insulin	1-2.5 hr	7-15 hr	No	Except with U and N
Ultralente insulin	4-8 hr	10-30 hr	No	Except with N and L
Insulin 70/30, Insulin 50/50	Regular:30min NPH: 1 hr	Regular: 1 hr NPH: 6 hr	No	NO
Humalog 75/25®	Lispro: 30 min Protamine: 1 hr	Lispro: 30min Protamine:6 hr	No	NO
Insulin glargine	1hr	5 hr	No	NO

* L=lente ** U=ultralente

Medication Safety

The following is an example of a difficult to read order. See if you can interpret order #6 correctly. The intended order can be found at the bottom of this page.

Keep in mind that pharmacy receives the carbon copy of each order. **Never try to correct or write over an order. Always cross out and rewrite.**

START HERE	DATE 12-20-01	TIME 4:25	PROFILED BY: 	FIL
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OCpk = med diff in an
 1 SMA-7 in an
 2 Ck in an take patient
 3 ABG per respity 2 hrs
 4 ABG 6am in SA 21. 2001
 5 (Lulyn 600g 90 IU.
 6

Tips for avoiding medication errors:

- Always write legibly**
Legibility is the number one reason for medication errors!
- Never write over, always cross out and rewrite**
The order above is a great example.
- Always be careful of "carbon copy" forms**
Stray marks can make the carbon difficult to read.
- Never "U", always spell out "units"**
Poorly written "U" can be mistaken for a 0 - leading to a 10 fold overdose.
- Lead with zeros, never trail**
0.1mg is ok but 1.0mg can be confused with 10mg on handwritten orders.