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RPCC Pharmacy Forum

Special Interest Articles:

- Homeopathic Teething Products
- Nuplazid
- COPD Bronchodilators

Did you know?

The first drug to ever reach $1 billion in sales, Valium, was introduced in 1963. At the height of Valium's popularity in 1978, Americans consumed more than two billion units stamped with the trademark "V". After a heart attack killed Elvis Presley in 1977, autopsy reports revealed that he had ingested huge quantities of Valium (along with other drugs).

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FDA Laboratory Analysis of Homeopathic Teething Products

FDA has issued their findings in a laboratory analysis of homeopathic teething tablets marketed by CVS and Hyland's Inc. FDA states that their testing found that the belladonna alkaloids content and coffea cruda (caffeine) content is not consistent among the manufactured tablets. The levels found far exceeded the amount stated on the products' labels. FDA issued the following statement, "Inconsistency in levels of belladonna, a toxic substance, signals a poorly controlled manufacturing process and poses an unnecessary risk to infants and children under two years of age." The company has not agreed to conduct a recall at this time. The FDA recommends discontinuing use of these products marketed by Hyland's immediately and dispose of any in the home. Symptoms that may be seen with a belladonna exposure include seizures, lethargy, excessive sleepiness, muscle weakness, skin flushing, constipation, difficulty urinating or agitation.

References

1. Pharmacy Today. *FDA confirms elevated levels of belladonna in certain homeopathic teething products*. 30 January 2017. http://www.pharmacist.com/article/fda-confirms-elevated-levels-belladonna-certain-homeopathic-teething-products. (Accessed January 30, 2017).
2. United States Food and Drug Administration. *FDA confirms elevated levels of belladonna in certain homeopathic teething products.* 27 January 2017. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm538684.htm. (Accessed January 30, 2017).

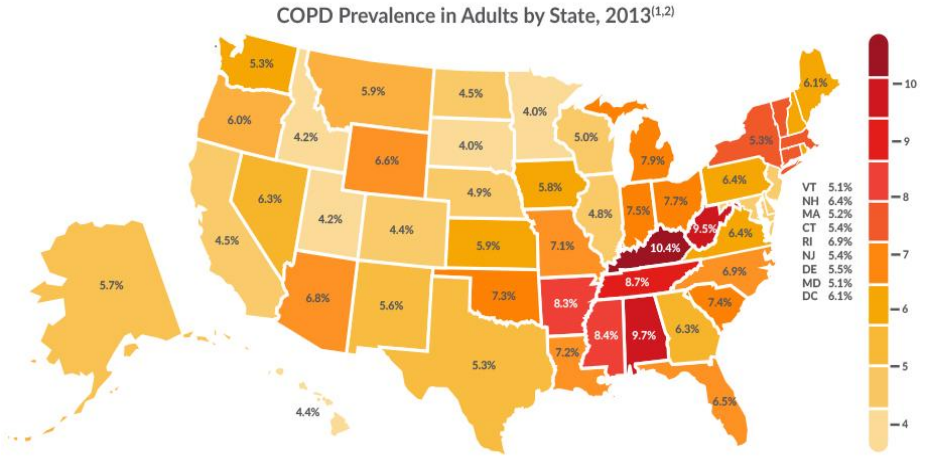
Medication Approved for Treatment of Psychosis in Parkinson's Disease

Nuplazid®(pimavanserin) is the first and only medication approved by the U.S. Food and Drug Administration (FDA) for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. Psychosis is common in Parkinson's in part because the medications used to improve tremors and stiffness may cause hallucinations and delusions. National Parkinson Foundation states that about one million people in the United States and from four to six million people worldwide suffer from Parkinson's disease. An estimated 40 percent of these patients have Parkinson's disease psychosis, a crippling condition that is characterized by hallucinations and delusions. This condition is associated with significant caregiver hardship, and is a major reason for nursing home placement among Parkinson's patients. Pimavanserin's mechanism of action is not fully understood, it may be mediated through inverse agonist and antagonist activity at serotonin 5-HT(2A) and serotonin 5-HT(2C) receptors. Concentration-dependent QTc interval prolongation has also been reported with pimavanserin use. In studies, QTc interval prolongation (maximum mean change from baseline: 13.5 msec) occurred after pimavanserin dose of twice the therapeutic dose.

References

1. National Parkinson Foundation. *Aware in Care Parkinson's Disease Fact Sheet*.http://www.parkinson.org/pd-library/fact-sheets/aic-fact-sheet (Accessed February 1, 2017).
2. Acadia Pharmaceuticals. *Nuplazid*. http://www.acadia-pharm.com/product/. (Accessed January 31, 2017)
3. *Parkinson's Disease: Nuplazid. Pharmacist's Letter/Prescriber's Letter. 2016; Vol 32 (08).*

Chronic Obstructive Pulmonary Disease Bronchodilators



"Unfortunately, the symptoms of chronic obstructive pulmonary disease cannot be completely eliminated with treatment and the condition usually worsens over time."

COPD is the third leading cause of death in the United States. Millions of people may have the disease and do not know it. More than 11 million people have been diagnosed with COPD in the United States. COPD causes serious long-term disability and early death. Unfortunately, the symptoms of chronic obstructive pulmonary disease cannot be completely eliminated with treatment and the condition usually worsens over time. However, treatment can control symptoms and can sometimes slow the progression of the disease.
Bronchodilators are a mainstay of COPD treatment and include β-adrenergic agonists, anticholinergics, and methylxanthines. β-adrenergic agonists are effective in alleviating symptoms and improving exercise capacity, and they can produce significant increases in FEV_1.

Bronchodilators that can be used alone or in combination and include the following:

Short- acting Beta2-agonists (SABA) and long-acting Beta2-agonists (LABA)

- Some LABA bronchodilators are twice daily (Formoterol and salmetrol) and some are once daily (indacaterol, oladaterol, vilanterol).

Anticholinergic Drugs- Short–acting (SAAC) (ipratropium) and long-acting (LAAC) (tiotropium)

- Extensive use of this class of agents in a wide range of doses and clinical settings has shown them to be very safe. The main side effect is dryness of mouth.

Combination Bronchodilator Therapy . Combining bronchodilators with different mechanisms and durations of action may increase the degree of bronchodilation with a lower risk of side-effects compared to increasing the dose of a single bronchodilator.

- Combinations of SABAs and SAACs are superior compared to either medication alone in improving FEV1 and symptoms.

Inhaled corticosteroids (ICS)

- ICS in combination with long-acting bronchodilator therapy. In patients with moderate to very severe COPD and exacerbations, an ICS combined with a LABA is more effective than either component alone in improving lung function, health status and reducing exacerbations

References

1. Juvelekian, George. (2012, October). Chronic Obstructive Pulmonary Disease. (Retrieved from http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/pulmonary/chronic-obstructive-pulmonary-disease/),
2. American Lung Association. *How Serious is COPD.* http://www.lung.org/lung-health-and-diseases/lung-disease-lookup/copd/learn-about-copd/how-serious-is-copd.html. (Accessed February 1, 2017).
3. Global Initiative for Chronic Obstructive Lung Disease. *Pocket Guide to COPD Management 2017.* http://goldcopd.org/wp-content/uploads/2016/12/wms-GOLD-2017-Pocket-Guide.pdf. (Accessed February 6, 2017).
4. Han, MeiLan King. (2016, March 17).Chronic Obstructive Pulmonary Disease Overview. (Retrieved from http://www.uptodate.com/contents/chronic-obstructive-pulmonary-disease-copd-treatments-beyond-the-basics).

Bronchodilators Used in COPD

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Medication	Mechanism	Toxicity
Short-acting Bronchodilators "rescue inhaler"		
Short-acting Beta-2 agonist (SABAs): Albuterol (Salbutamol) (*ProAir HFA, Proventil HFA, Ventolin HFA)* Levalbuterol *(Xopenex HFA)* Terbutaline	Bronchiolar smooth muscle relaxation, mast cell membrane stabilization, skeletal muscle stimulation, decreased release of inflammatory cytokines.	Results from over-stimulation of beta-adrenergic activity. In addition, beta-adrenergic selectivity is lost, so beta-1 effects can be seen. Tachycardia, hypertension, tachypnea, tremor, agitation, nausea, vomiting, hypokalemia, and hyperglycemia.
Anticholinergic: Ipratropium *(Atrovent HFA)*	Blocks acetylcholine receptors in bronchial smooth muscle causing relaxation	Extension of anticholinergic effects-xerostomia, urinary retention, constipation, mydriasis, flushing, tachycardia
Combination Short-acting Beta-2 agonist/ Anticholinergic: Albuterol/ipratropium *(Combivent Respimat, DuoNeb)*	Bronchiolar smooth muscle relaxation, mast cell membrane stabilization, skeletal muscle stimulation, decreased release of inflammatory cytokines. Blocks acetylcholine receptors in bronchial smooth muscle causing relaxation	(see albuterol and ipratropium)
Long-acting Bronchodilators "maintenance inhaler"		
Long-acting Beta-2 agonist (LABAs): Formoterol *(Foradil Aerolizer)* Indacaterol *(Arcapta Neohaler)* Olodaterol *(Striverdi Respimat)* Salmeterol *(Serevent Diskus)*	Bronchiolar smooth muscle relaxation, mass cell membrane stabilization, skeletal muscle stimulation, decreased release of inflammatory cytokines.	****Black box warning for asthma related deaths. **** Exert their toxic effects via sympathetic activation via beta adrenergic receptors. (see albuterol)
Long-acting Anticholinergic (LAACs): Aclidinium *(Tudorza Pressair)* Glycopyrrolate *(Seebri Neohaler)* Tiotropium *(Spiriva HandiHaler, Spiriva Respimat)* Umeclidinium *(Incruse Ellipta)*	Blocks acetylcholine receptors in bronchial smooth muscle causing relaxation.	**(see ipratropium)**
Combination LABA/LAAC: Formoterol/Aclidinium Indacaterol/glycopyrrolate *(Utibron Neohaler)* Olodaterol/tiotropium *(Stiolto Respimat)* Vilanterol/umeclidinium *(Anoro Ellipta)*	Bronchiolar smooth muscle relaxation, mast cell membrane stabilization, skeletal muscle stimulation, decreased release of inflammatory cytokines. Blocks acetylcholine receptors in bronchial smooth muscle causing relaxation	****Anoro Ellipta has a black box warning in asthma related deaths. **** Exert their toxic effects via sympathetic activation via beta adrenergic receptors. (see albuterol) **(see albuterol and ipratropium)**
Combination LABA/corticosteroid: Formoterol/budesonide *(Symbicort)* Salmeterol/fluticasone propionate *(Advair Diskus, Advair HFA)* Vilanterol/fluticasone furoate *(Breo Ellipta)* Mometasone/formoterol *(Dulera)*	Bronchiolar smooth muscle relaxation, mast cell membrane stabilization, skeletal muscle stimulation, decreased release of inflammatory cytokines. Decreased cytokine production, increased expression Beta-2 receptors, decreased vascular permeability, decreased mucous secretions, decreased eicosanoid production.	****Black box warning for asthma related deaths. **** asthma adequately controlled on long-term asthma-control medication or low- or medium-dose inhaled corticosteroids; use not recommended