Tanta University
College of Pharmacy
Drug Information &
Poison Control Center

Drug & Poison Information Bulletin

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Call us for any drug related questions on: 01008070516

Medical & Pharmaceutical News

FDA allows marketing of the first test to assess risk of developing acute kidney injury

Acute kidney injury (AKI) is a sudden decline in kidney function, often without early signs or symptoms, following an injury to the kidney caused by a co-existing disease, infection, or other condition. AKI can cause fluid to build up in the body, chest pain, muscle weakness, and permanent kidney damage or chronic kidney disease. Critically ill patients are the most at risk for AKI, particularly patients who meet certain factors such as advanced age, diabetes and high blood pressure. **N.B.** Current laboratory tests can only assess whether a patient may *already have AKI;* often, the patient has progressed to moderate to severe AKI before the test results confirm the clinical diagnosis.

New Test : NephroCheck®

NephroCheck® is a urine test being developed by Astute Medical for assessing risk of acute kidney injury (AKI) in the critically ill patients. ***NephroCheck®*** Test System is intended to be used in conjunction with clinical evaluation in patients who currently have or have had within the past 24 hours acute cardiovascular and or respiratory compromise and are ICU patients as an aid in the risk assessment for moderate or severe acute kidney injury (AKI) within 12 hours of patient assessment.

NephroCheck® detects the presence of insulin-like growth-factor binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinase (TIMP-2) in the urine, which are associated with acute kidney injury. Within 20 minutes, the test provides a score based on the amount of the proteins present that correlates to ***the patient's risk of developing AKI within 12 hours of the test*** being performed.

N.B. - No other tests currently on the market are FDA-approved or cleared to assess ***the risk of developing*** AKI in at-risk patients.
- ***NephroCheck®*** is intended to be used in patients ≥21 years.

Source: www.medicalnewstoday.com (8 September 2014), www.fda.com

Hibiscus in pregnancy?

Hibiscus is an annual plant. Parts of the flower are used to make a popular drink in Egypt called Karkade .
Hibiscus seems to be safe for most people, but the possible side effects of hibiscus are not known. Hibiscus is **UNSAFE** to take during **pregnancy**. There is some evidence that hibiscus might start menstruation, and this could cause a miscarriage. Not enough is known about the safety of taking hibiscus during breast-feeding. **Stay on the safe side, and avoid use.**

Source: www.webmd.com

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Medical & Pharmaceutical News

WHO welcomes Swissmedic approval of Ebola vaccine trial

The World Health Organization (WHO) welcomes the approval by ***Swissmedic*** (the Swiss regulatory authority for therapeutic products) for a trial with an ***experimental Ebola vaccine*** at the Lausanne University Hospital (CHUV). This marks the latest step towards bringing safe and effective Ebola vaccines for testing and implementation as quickly as possible.

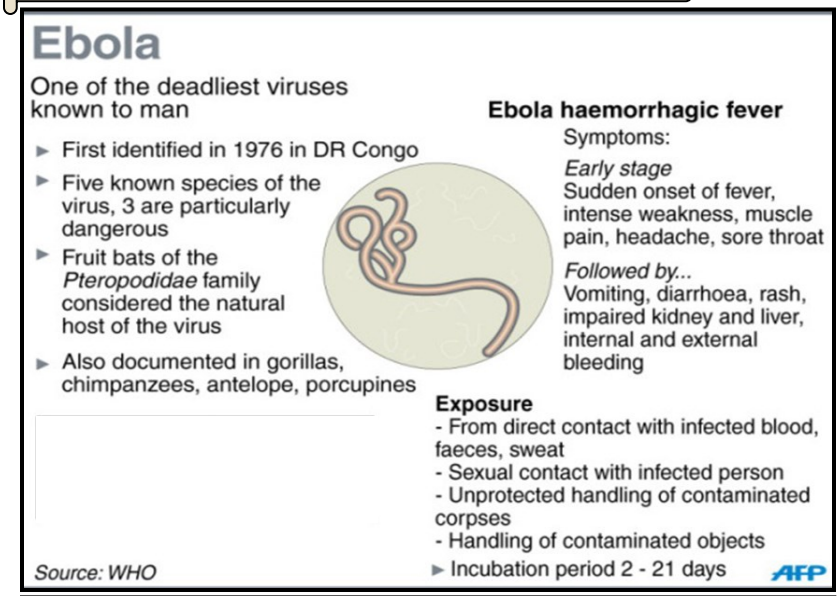
Approval means that: The vaccine can be used on approximately 120 individuals in Lausanne. The trial, which is receiving support from WHO, is the latest in a series of trials that are ongoing in Mali, the United Kingdom, and the United States.

About the vaccine: The vaccine is based on a genetically modified chimpanzee adenovirus ("ChAd-Ebola"; Chimpanzee-Adenovirus chAD3-ZEBOV). The trial will test the safety of the vaccine and its capacity to induce an immune response. Results from the CHUV trial will – together with the results of other centres involved – provide the basis for planning subsequent trials involving several thousand participants & for choosing vaccine dose-level for efficacy trials.

Developed by the US National Institute of Allergy and Infectious Diseases (NIAID) and pharmaceutical company GlaxoSmithKline. The application, submitted at the end of September 2014, was handled as a priority, given the dimensions of the Ebola epidemic in West Africa.

Source: www.who.int (Statement 28 October 2014)

What should I know about Ebola virus



Ebola is not spread through the air or by water, or in general, by food.

- However, in Africa, Ebola may be spread as a result of handling bushmeat (wild animals hunted for food) and contact with infected bats.
- There is no evidence that mosquitos or other insects can transmit Ebola virus.
- Only a few species of mammals (ex: humans, bats, monkeys, and apes) have shown the ability to become infected with and spread Ebola virus.

No FDA-approved vaccine or medicine is available for Ebola. Experimental vaccines and treatments for Ebola are under development.

The following basic interventions, when used early, can significantly improve the chances of survival:

- Providing I.V. fluids & balancing electrolytes.
- Maintaining oxygen status and blood pressure.
- Treating other infections if they occur.

Recovery from Ebola depends on good supportive care and the patient's immune response & People who recover from Ebola infection develop antibodies that last for ***at least 10 years***, possibly longer.

It isn't known if people who recover are immune for life or if they can become infected with a different species of Ebola. Some people who have recovered from Ebola have developed long-term complications, such as joint and vision problems.

Source: www.cdc.gov

Personalized Medicines

Mepolizumab as personalized medicine in asthma

Background:

- Patients with severe asthma often require high doses of steroid-based treatments that can significantly impair their quality of life. These high doses can cause debilitating side effects including mood swings, diabetes, bone loss, skin bruising, cataracts and hypertension.
- Some patients with severe asthma have frequent exacerbations associated with ***persistent eosinophilic inflammation*** despite continuous treatment with high-dose inhaled glucocorticoids with or without oral glucocorticoids.
- These specific types of patient with severe asthma have an overabundance of a particular type of white blood cell ***(eosinophil)*** present in their sputum.
- These patients often suffer from the most severe asthma symptoms and can only be treated through steroid-based medications such as prednisone.

What's New ???

A new study published in *New England Journal of Medicine* on September 2014 and presented at the European Respiratory Society (ERS) congress recruited the largest number of participant to investigate using ***a new, antibody-based drug for this group of patients***, this drug was named **Mepolizumab**.

This study was not the only but there was more studies published in the same journal and in the Lancet proving that:

► **Mepolizumab** can replace traditional, steroid-based treatments for a specific subset of patients, resulting in improved outcomes and reduced side effects.

► This new drug is the only therapy that has been proven to be effective in well-established clinical trials to help reduce doses of steroid-based treatments such as prednisone for those with severe asthma.

► Additionally Mepolizumab reduced sputum and blood eosinophil counts and was shown to be safe for up to 12 months.

Mepolizumab is a biologic agent developed to treat asthma. It represents a humanized monoclonal antibody of IgG1 κ type, which targets human IL-5 and thus prevents its interaction with the α-chain of the IL-5 receptor. Several studies have suggested some therapeutic benefit across a spectrum of eosinophil-related disorders.

N.B.

- This is an exciting example of personalized medicine for asthma.
- By using a simple blood or sputum eosinophil count, we can identify which asthma patients can benefit from this new treatment.
- Mepolizumab is not commercially available at present, although it is under review by regulatory agencies.
- GSK is progressing towards global filings of Mepolizumab for severe eosinophilic asthma by the end of 2014.

Source: www.medicalnewstoday.com, www.drugs.com, www.uptodate.com

New FDA Approved Drugs

Harvoni® (ledipasvir and sofosbuvir)

Approved ***October 10, 2014*** for the treatment of chronic hepatitis C genotype 1 infection in both treatment-naive and treatment-experienced* adult patients.

Harvoni: Is a fixed-dose combination of 90 mg ***ledipasvir*** "hepatitis C virus (HCV) NS5A inhibitor" and 400 mg ***sofosbuvir*** "an HCV nucleotide analog NS5B polymerase inhibitor".
Dose : One tablet taken orally once daily with or without food.
Side Effects: May include, but are not limited to fatigue & headache.
Treatment duration: Depending on prior treatment experience and the presence or absence of cirrhosis.

Patient Population	Recommended Treatment Duration
Treatment-naïve with or without cirrhosis	**12** weeks
Treatment-experienced without cirrhosis	**12** weeks
Treatment-experienced with cirrhosis	**24** weeks

Note: - Treatment duration of **8** weeks can be considered in treatment-naive patients without cirrhosis who have a baseline HCV RNA level less than 6 million IU/ mL.
- This regimen is the first FDA-approved interferon- and ribavirin-free regimen to treat HCV.

*** Treatment experienced patients*** defined as patients who have failed treatment with either:
↳Peginterferon + Ribavirin
or ↳peginterferon + Ribavirin + HCV protease inhibitor.

Source: www.centerwatch.com, www.hepatitisc.uw.edu

Trulicity ™ (dulaglutide)

Approved ***September 18, 2014*** as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Mechanism of action: It is a ***glucagon-like peptide (GLP-1)**** receptor agonist. It increases intracellular cyclic AMP in beta cells leading to glucose-dependent insulin release, also decreases glucagon secretion & slows gastric emptying.
Dosage & administration : Supplied as a solution for S.C. injection in the abdomen, thigh, or upper arm.

- The recommended initiating dose is **0.75 mg** once weekly.
- The dose may be increased to **1.5 mg** once weekly for additional glycemic control.
- The maximum recommended dose is 1.5 mg once weekly.
- Administer Trulicity once weekly, any time of day, with or without food.

**** GLP-1:*** Is one of the incretin hormones derived from the L-cells of the distal small intestine and large bowel according to the presence of nutrients .It exert several systemic effects, including :

- ♣ Glucose dependent stimulation of insulin secretion by pancreatic ***beta-cells***.
- ♣ Glucose dependent suppression of post-prandial glucagon secretion from pancreatic ***alpha-cells***.
- ♣ Slowing of gastric emptying and enhancement of satiety.

Source: www.centerwatch.com

New FDA Approved Drugs

New FDA approved drugs for the treatment of idiopathic pulmonary fibrosis

Idiopathic Pulmonary fibrosis (IPF): Occurs when lung tissue becomes damaged and scarred. This thickened, stiff tissue makes it more difficult for lungs to work properly with unknown cause (*idiopathic*).

Symptoms: Shortness of breath, dry cough, fatigue, unexplained weight loss & aching muscles and joints.

Complications: Pulmonary HTN, right-sided heart failure (cor pulmonale), respiratory failure & lung cancer.

Treatments: The lung scarring can't be reversed but some treatments may improve symptoms or slow the disease's progress. Because IPF was originally thought to be due to inflammation of the alveoli leading to fibrosis and scarring, antinflammatory drugs may be useful. Treatment options may include:

- Corticosteroid (prednisone), sometimes in combination with other immunosuppressant such as methotrexate or cyclosporine. Adding acetylcysteine to prednisone may slow the disease in some people. None of these combinations has proved very effective over the long run.
- Oxygen therapy.
- Pulmonary rehabilitation.
- Lung transplantation.

New two drugs approved on *October 2014* for the treatment of *IPF*

Ofev (nintedanib)

Ofev: Is a small molecule that inhibits multiple receptor tyrosine kinases (RTKs) & non-receptor tyrosine kinases (nRTKs) that blocks multiple pathways that may be involved in the scarring of lung tissue.

Dosage:

- 150 mg twice daily administered (capsule for oral administration).
- Ofev capsules should be taken with food & swallowed whole with liquid.

Esbriet (pirfenidone)

Esbriet: Is an oral antifibrotic p38 MAP kinase Inhibitor that reduces growth factor signaling. Esbriet acts on multiple pathways that may be involved in the scarring of lung tissue. The mechanism of action of pirfenidone in the treatment of IPF has not been established.

Dosage:

- Supplied as a capsule for oral administration.
- The recommended daily maintenance dosage of is 801 mg (three 267 mg capsules) three times a day with food for a total of 2403 mg/day.
- Doses should be taken at the same time each day. Upon initiation of treatment, titrate to the full dosage of nine capsules per day over a 14-day period as follows:

Days 1 through 7	**1 capsule** 3 times a day with food
Days 8 through 14	**2 capsules** 3 times a day with food
Days 15 onward	**3 capsules** 3 times a day with food

Source: www.mayoclinic.com, www.centerwatch.com

Injection Oncolytic Viruses in Melanoma

Background:

⇒ **Melanoma** Is considered the most serious type of skin cancer which develops in the melanocytes, and can also form in the eyes and rarely in internal organs such as intestines.
Normally, skin cells develop in a controlled and orderly way — healthy new cells push older cells toward skin's surface, where they die and eventually fall off. But when some cells develop DNA damage, new cells may begin to grow out of control and can eventually form a mass of cancerous cells. doctors believe exposure to ultraviolet (UV) radiation from the sun and from tanning lamps and beds is the leading cause of melanoma. However, UV light doesn't cause all melanomas.

⇒ **Risk factors** May include: Fair skin, a history of sunburn, excessive ultraviolet (UV) light exposure, living closer to the equator or at a higher elevation, having many moles or unusual moles, a family history of melanoma & weakened immune system.

⇒ **Treatment** For early-stage melanomas usually includes surgery to remove the melanoma and this may be the only treatment needed. If melanoma has spread beyond the skin, treatment options may include: Surgery to remove affected lymph nodes, Chemotherapy, Radiation therapy, Biological therapy & Targeted therapy.

N.B. ♣ Biological therapies used to treat melanoma include ***interferon*** and ***interleukin-2***.
♣ ***Ipilimumab*** (Yervoy) is another drug that uses immune system to fight melanoma & is used to treat advanced melanoma that has spread beyond its original location.
♣ ***Vemurafenib*** (Zelboraf) & ***dabrafenib*** (Tafinlar) are targeted therapy drugs approved to treat advanced melanoma that can't be treated with surgery or that has spread through the body.

Oncolytic virus therapy

Oncolytic virus therapy (OVs) is a type of targeted therapy that is being studied in the treatment of melanoma.

OVs uses a virus that infects and breaks down cancer cells but not normal cells. Radiation therapy or chemotherapy may be given after oncolytic virus therapy to kill more cancer cells.

Injecting melanoma lesions with specific common cold or herpes simplex viruses destroys tumor cells and induces systemic immune responses. The injection of oncolytic viruses directly into lesions is an active area of research in melanoma.

A major goal of OV-mediated immunotherapy is to activate and redirect functional innate and adaptive immune responses toward the tumor.

In addition to direct oncolytic activity, OVs are also very effective at inducing immune responses to themselves and to the infected tumor cells.

OVs encompass a broad diversity of DNA and RNA viruses that are naturally cancer selective or can be genetically engineered.

OVs provide a diverse platform for immunotherapy; they act as in situ vaccines & can be armed with immunomodulatory transgenes or combined with other immunotherapies.

However, the interactions of ***OVs*** with the immune system may affect therapeutic outcomes in opposing fashions: ***negatively*** by limiting virus replication or ***positively*** by inducing antitumor immune responses.

Injection Oncolytic Viruses in Melanoma (Cont.)

OVs have many features that make them advantageous and distinct from current therapeutic modalities in:

- Low probability for the generation of resistance as they use multiple means for cytotoxicity,
- They replicate in a tumor selective fashion and are relatively nonpathogenic and, only minimal systemic toxicity has been detected.
- Virus dose in the tumor increases with time as opposed to classical drug pharmacokinetics that decrease with time .These features should result in a very high therapeutic index.

There have been numerous clinical trials of ***OVs*** for cancer. Most have been phase I with a few phase II trials. Currently, a phase III trial is investigating an oncolytic HSV1- expressing granulocyte macrophage colony-stimulating factor (GM-CSF) for melanoma **(Talimogene laherparepvec, T-Vec)** sponsored by Amgen, Inc.

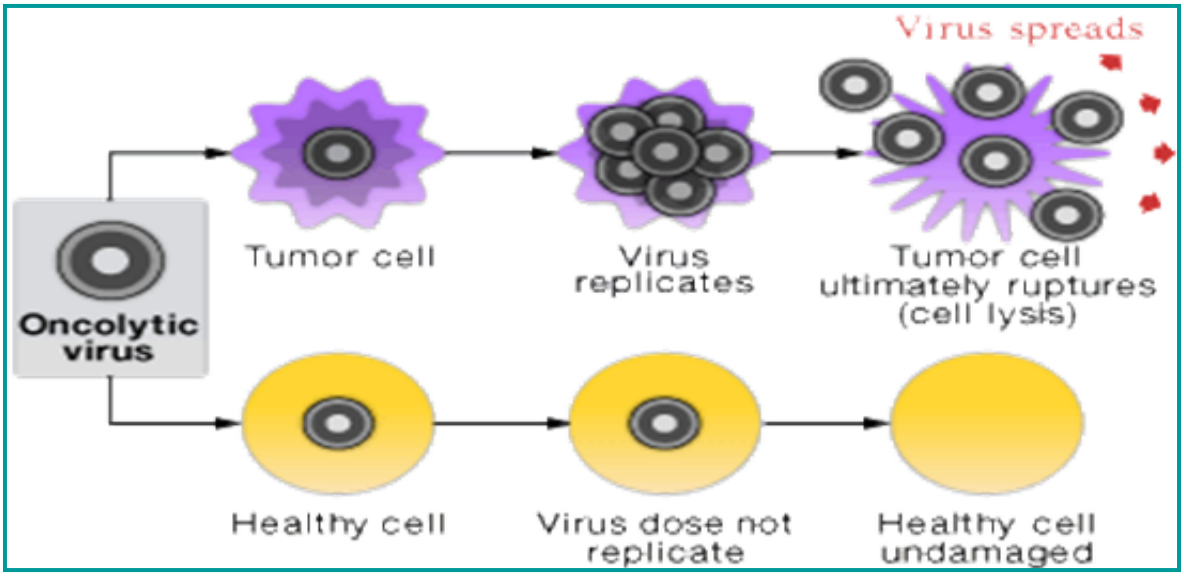
On Sept. 2, 2014 Amgen announced the submission of a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) via the centralized procedure for **Talimogene Laherparepvec** seeking approval for the treatment of adults with melanoma that is regionally or distantly metastatic.

Talimogene laherparepvec is an investigational oncolytic immunotherapy administered as an intralesional injection that is designed to initiate a systemic anti- tumor immune response.

Talimogene laherparepvec was designed to work in two important and complementary ways.

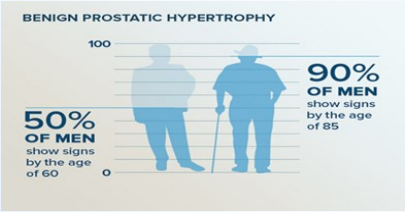
First, it is injected directly into tumors where it replicates inside the tumor's cells causing the cell to rupture and die in a process called lysis. The rupture of the cancer cells can release tumor-derived antigens, along with GM-CSF, that can stimulate a system-wide immune response where white blood cells are able to seek out and target cancer that has spread throughout the body.

If approved, **Talimogene laherparepvec** will represent the first in a class of novel agents known as oncolytic immunotherapies.



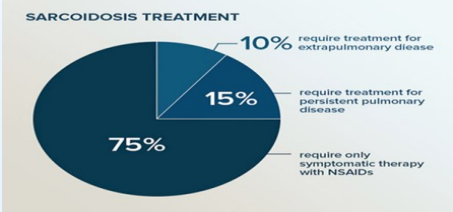
Did You Know

1. Benign prostatic hypertrophy (BPH) is considered part of the normal aging process in men. By 60 years of age, 50% of men demonstrate histopathologic BPH, and that rate increases to 90% by 85 years of age.



Source: www.medscape.com

2. Although more than **75%** of patients with sarcoidosis require only symptomatic treatment with NSAIDS, **10%** require treatment for extrapulmonary disease and **15%** for persistent pulmonary disease.



Source: www.medscape.com

3. Concerns that aspirin increases the risk for age-related macular degeneration (AMD) were first raised several years ago, but more recent studies confirm it.
The Australian Blue Mountains study analyzed data from a large, population-based eye study and found a statistically significant association between 15 years of regular aspirin use and development of neovascular AMD.

Source: www.medscape.com

4. Do Aspirin and Ibuprofen Interact?

In 2006, the U.S.FDA alerted healthcare professionals about the potential for ibuprofen to interfere with the antiplatelet effect of low-dose aspirin (81 mg daily). Ibuprofen (a reversible inhibitor) may interact with aspirin (an irreversible inhibitor) by competitive inhibition of the acetylation site of platelet cyclooxygenase (COX). As ibuprofen and aspirin occupy nearby sites on COX, ibuprofen may prevent access and binding of aspirin. Consequently, the antiplatelet action of aspirin may be reduced.

Recommendations:

- Avoid ibuprofen if possible or give it 2 hours after aspirin.
- Consider that the interaction may be unavoidable if ibuprofen is administered more than once daily.
- celecoxib, naproxen, and indomethacin may interact with aspirin.

Evidence suggests that acetaminophen, diclofenac, sulindac, and meloxicam may not interact.

Source: www.pharmacytimes.com, www.fda.gov

Upcoming Conferences

* 7th Breast & Gynecological International Cancer Conference 2015 (BGICC 2015), JANUARY 15, 2015 - JANUARY 16, 2015, Cairo, Egypt.

* Gulf Critical Care Forum 2015 (GCCF2015), 4th March 2015 to 4th March 2015 United Arab Emirates , Dubai.

* The 4th Global Congress for Consensus in Pediatrics and Child Health (CIP 2015)19 - 22 March • Ryad Mogador Agdal Zone Touristique Agdal Marrakesh, Morocco.

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