King Saud University
College of Pharmacy
Drug and Poison
Information Center

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AHA: e-cigarettes should be subject to strict federal regulation

Due to concerns that e-cigarette use among youths could lead to nicotine addiction and encourage use of conventional tobacco products, the American Heart Association have issued new recommendations stating that e-cigarettes should be subject to a federal ban for minors.

Source Written by *Honor Whiteman*

In this issue .. ..

Medical News

NIH to Launch Human Safety Study of Ebola Vaccine Candidate

Initial human testing of an investigational vaccine to prevent Ebola virus disease will begin next week by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

The early-stage trial will begin initial human testing of a vaccine co-developed by NIAID and GlaxoSmithKline (GSK) and will evaluate the experimental vaccine's safety and ability to generate an immune system response in healthy adults. Testing will take place at the NIH Clinical Center in Bethesda, Maryland.

The study is the first of several Phase 1 clinical trials that will examine the investigational NIAID/GSK Ebola vaccine and an experimental Ebola vaccine developed by the Public Health Agency of Canada and licensed to New Link Genetics Corp. The others are to launch in the fall. These trials are conducted in healthy adults who are not infected with Ebola virus to determine if the vaccine is safe and induces an adequate immune response.

In parallel, NIH has partnered with a British-based international consortium that includes the Wellcome Trust and Britain's Medical Research Council and Department for International Development to test the NIAID/GSK vaccine candidate among healthy volunteers in the United Kingdom and in the West African countries of Gambia (after approval from the relevant authorities) and Mali. Additionally, the U.S. Centers for Disease Control and Prevention has initiated discussions with Ministry of Health officials in Nigeria about the prospects for conducting a Phase 1 safety study of the vaccine among healthy adults in that country. The pace of human safety testing for experimental Ebola vaccines has been expedited in response to the ongoing Ebola virus outbreak in West Africa. According to the World Health Organization (WHO), more than 1,400 suspected and confirmed deaths from Ebola infection have been reported in Guinea, Liberia, Nigeria, and Sierra Leone since the outbreak was first reported in March 2014.

Medical News (cont..)

"There is an urgent need for a protective Ebola vaccine, and it is important to establish that a vaccine is safe and spurs the immune system to react in a way necessary to protect against infection," said NIAID Director Anthony S. Fauci, M.D. "The NIH is playing a key role in accelerating the development and testing of investigational Ebola vaccines." "Today we know the best way to prevent the spread of Ebola infection is through public health measures, including good infection control practices, isolation, contact tracing, quarantine, and provision of personal protective equipment," added Dr. Fauci. "However, a vaccine will ultimately be an important tool in the prevention effort. The launch of Phase 1 Ebola vaccine studies is the first step in a long process."

"Tried and true public health interventions, strong supportive medical care and the rapid testing of Ebola vaccines and antiviral treatments can help to reduce suffering now and in the future," said CDC Director Thomas R. Frieden, M.D., M.P.H. The investigational vaccine now entering Phase 1 trials was designed by Nancy J. Sullivan, Ph.D., chief of the Biodefense Research Section in NIAID's Vaccine Research Center (VRC). She worked in collaboration with researchers at the VRC, the U.S. Army Medical Research Institute of Infectious Diseases, and Okairos, a Swiss-Italian biotechnology company acquired by GSK in 2013. Phase 1 clinical trials are the first step in what is typically a multi-stage clinical trials process. During Phase 1 studies, researchers test an investigational vaccine in a small group of people to evaluate its safety and the immune response it provokes. Phase 2 clinical trials of investigational vaccines are designed to further assess safety and immune response in larger numbers of volunteers. Under certain circumstances, the vaccine's ability to prevent infection or disease (called efficacy) can be determined in a Phase 2 trial. Phase 3 clinical trials are directed predominantly at determining efficacy.

The NIAID/GSK Ebola vaccine candidate is based on a type of chimpanzee cold virus, called chimp adenovirus type 3 (ChAd3). The adenovirus is used as a carrier, or vector, to deliver segments of genetic material derived from two Ebola virus species: Zaire Ebola and Sudan Ebola. Hence, this vaccine is referred to as a bivalent vaccine. The Zaire species of the virus is responsible for the current Ebola outbreak in West Africa. The vaccine candidate delivers one part of Ebola's genetic material to human cells, but the adenovirus vector does not replicate. Rather, the Ebola gene that it carries allows the cells of the vaccine recipient to express a single Ebola protein, and that protein prompts an immune response in the individual. It is important to know that the Ebola genetic material contained in the investigational vaccine cannot cause a vaccinated individual to become infected with Ebola.

"The experimental NIAID/GSK vaccine performed extremely well in protecting nonhuman primates from Ebola infection," Dr. Fauci noted. The candidate vaccine builds upon three earlier NIAID-developed investigational Ebola vaccines that began Phase 1 clinical trial testing in 2003. "The knowledge gained from each of those trials has contributed to the development of the candidate vaccine we are now studying, as well as our improved understanding of human immune responses to investigational Ebola vaccines," said John R. Mascola, M.D., director of NIAID's Vaccine Research Center. The Phase 1 clinical trial, called VRC 207, will be led by principal investigator Julie E. Ledgerwood, D.O., chief of the VRC's clinical trials program, and will be conducted among 20 healthy adults ages 18 to 50 years. Participants will be divided into two groups of 10 participants each. One group will receive an intramuscular injection of the NIAID/GSK experimental vaccine. The second group will receive a single injection of the same vaccine but at a higher dose. A number of safety features are built into the study's design, including daily and weekly reviews of patient data by clinical staff and the study protocol team. Additionally, the trial features a staged enrollment plan that requires interim safety reviews after three participants have been vaccinated and have undergone three days of follow up before enrolling additional study participants into the group. Participants in both groups will be seen and evaluated by clinical staff nine times over a 48-week period.

SOURCE: www.niaid.nih.gov.

European Commission grants EYLEA licence for the treatment of visual impairment due to diabetic macular oedema

Bayer HealthCare today announces that EYLEA® (aflibercept solution for injection) has been approved by the European Commission for the treatment of visual impairment due to diabetic macular oedema (DMO).EYLEA is an established treatment for other eye conditions that could now offer patients with DMO significant visual benefits, from start of treatment, without the need for strict monthly hospital visits (after an initial five monthly loading doses); potentially reducing the burden of treatment for patients already having to manage theirdiabetes. Bayer plans to launch EYLEA in the UK for this indication in the coming months; with guidance from the Scottish Medicines Consortium (SMC) and the National Institute for Health and Care Excellence (NICE) expected in November 2014 and June 2015, respectively.

Dr.SobhaSiva Prasad, Consultant Ophthalmologist, Moorfields Eye Hospital and King's College Hospital London said, "It is good news for patients and ophthalmologists that we now have a further treatment option available for visual impairment due to DMO. Eylea has shown impressive results in clinical trials, with significant visual gains, meaning it has the potential to save people's sight."The recommended dose of EYLEA for the treatment of DMO is 2 milligrams (mg). Treatment is initiated with one injection per month for five consecutive doses, followed by one injection every two months without any requirement for monitoring between injections. After the first 12 months of treatment, the treatment interval may be extended based on visual and anatomic outcomes.

The submission to the European Commission for the EYLEA DMO indication was based on data from the positive Phase III VIVID-DME and VISTA-DME studies which showed that EYLEA is capable of delivering sustained visual acuity gains compared to laser photocoagulation.

In the VIVID-DME study, after Week 52, patients receiving EYLEA 2 mg every other month (after 5 initial monthly injections) had a mean gain from baseline in best corrected visual acuity (BCVA) of +10.7 letters ($p<0.0001$). This is equivalent to a gain of more than two lines on the Early Treatment Diabetic Retinopathy Scale (ETDRS) (eye chart to assess visual acuity). Patients receiving laser photocoagulation had a mean change from baseline in BCVA of +1.2 letters.[3]In the VISTA-DME study, after Week 52, patients receiving EYLEA 2 mg every other month (after 5 initial monthly injections) had a mean gain from baseline in BCVA of +10.7 letters ($p<0.0001$), compared to patients receiving laser photocoagulation who had a mean change from baseline in BCVA of +0.2 letters. Further secondary endpoints in the VIVD-DME and VISTA-DME studies included the change from baseline in central retinal thickness, diabetic retinopathy severity score and vision related quality of life.

In both studies, EYLEA was well tolerated with a similar overall incidence of adverse events (AEs), serious ocular AEs, and serious non-ocular AEs across the treatment groups and the laser control group.EYLEA has been licensed in the UK for the treatment of wet age related macular degeneration (wAMD) since November 2012.[2] EYLEA was accepted by the SMC for use within NHS Scotland for the treatment of wAMD in April 2013. It was recommended by NICE for this use on the NHS in England and Wales in July 2013 and availability to eligible wAMD patients is now mandated across England and Wales.[5]EYLEA was licensed in the UK for the treatment of visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO) in August 2013. NICE recommended EYLEA for this indication in February 2014 for use in England and Wales, with the SMC accepting EYLEA for use within NHS Scotland for this indication in April 2014.

Source :***MNT(MEDICAL NEWS TODAY)***

FDA approves Avastin to treat patients with aggressive and late-stage cervical cancer

(August 14, 2014)

The U.S. Food and Drug Administration today approved a new use for Avastin (bevacizumab) to treat patients with persistent, recurrent or late-stage (metastatic) cervical cancer **.**Avastin works by interfering with the blood vessels that fuel the development of cancerous cells. The new indication for cervical cancer is approved for use in combination with chemotherapy drugs paclitaxel and cisplatin or in combination with paclitaxel and topotecan

The safety and effectiveness of Avastin for treatment of patients with cervical cancer was evaluated in a clinical study involving 452 participants with persistent, recurrent, or late-stage disease. Participants were randomly assigned to receive paclitaxel and cisplatin with or without Avastin or paclitaxel and topotecan with or without Avastin. Results showed an increase in overall survival to 16.8 months in participants who received chemotherapy in combination with Avastin as compared to 12.9 months for those receiving chemotherapy alone.

The most common side effects associated with use of Avastin in patients with cervical cancer include fatigue, decreased appetite, high blood pressure (hypertension), increased glucose in the blood (hyperglycemia), decreased magnesium in the blood (hypomagnesemia), urinary tract infection, headache and decreased weight. Perforations of the gastrointestinal tract and abnormal openings between the gastrointestinal tract and vagina (enterovaginal fistula) also were observed in Avastin-treated patients.

Source: Source: U.S.FDA

FDA Approves Belsomra (suvorexant) Tablets to treat difficulty in falling and staying asleep (insomnia)

August 13, 2014 -- The U.S. Food and Drug Administration today approved Belsomra (suvorexant) tablets for use as needed to treat difficulty in falling and staying asleep (insomnia). Belsomra is an orexin receptor antagonist and is the first approved drug of this type. Orexins are chemicals that are involved in regulating the sleep-wake cycle and play a role in keeping people awake. Belsomra alters the signaling (action) of orexin in the brain.

To assist health care professionals and patients in finding the best dose to treat each individual patient's sleeplessness, the FDA has approved Belsomra in four different strengths – 5, 10, 15, and 20 milligrams," said Ellis Unger, M.D., director of the Office of Drug Evaluation I in the FDA's Center for Drug Evaluation and Research. "Using the lowest effective dose can reduce the risk of side effects, such as next-morning drowsiness."

Belsomra should be taken no more than once per night, within 30 minutes of going to bed, with at least seven hours remaining before the planned time of waking. The total dose should not exceed 20 mg once daily. The most commonly reported adverse reaction reported by clinical trial participants taking Belsomra was drowsiness. Medications that treat insomnia can cause next-day drowsiness and impair driving and other activities that require alertness. People can be impaired even when they feel fully awake.

Source: U.S.FDA

PARADIGM-HF: New Drug Class Outclasses ACE-I in Chronic HF

Patients with chronic heart failure who take a newly developed drug that has effects both within and beyond the renin-angiotensin system, *instead* of the old-standby ACE inhibitor enalapril, will have fewer HF hospitalizations and die less often from cardiovascular causes, suggests a phase 3 trial that is huge both in size and its potential impact on clinical practice[1].

The risks of those two end points, as a composite as well as individually, fell by about 20% among the trial's patients with NYHA class 2–4 systolic heart failure who took the novel agentLCZ696 (Novartis) instead of the ACE inhibitor. All-cause mortality fell 16% on the novel agent. Follow-up averaged about 27 months.

The results in a general way have been known since April of this year, when Novartis announced that the Prospective Comparison of ARNI with ACE-I to Determine Impact on Global Mortality and Morbidity in Heart Failure(PARADIGM-HF) trial, with its >8000 patients, had been halted early after LCZ696 showed clinical superiority and at least comparable safety compared with the ACE inhibitor in an interim analysis. This was followed by an only slightly fuller announcement at a meeting in May, in which coprincipal investigator Dr Milton Packer (University of Texas Southwestern, Dallas) said that the agent "had demonstrated convincing superiority over high doses of enalapril," as reported then by heart wire .

The PARADIGM-HF results were scheduled to be announced today at a press conference here at theEuropean Society of Cardiology (ESC) 2014 Congress to coincide with its publication in the New England Journal of Medicine. The report's first author is the other co-principal investigator, Dr John JV McMurray (University of Glasgow, Scotland).

Hazard Ratio (95% CI) for Clinical Outcomes in PARADIGM-HF, LCZ696 vs Enalapril

End points	HR (95% CI)	p
CV death or HF hospitalization*	0.80 (0.73–0.87)	<0.001
Death from any cause	0.84 (0.76–0.93)	<0.001
CV death	0.80 (0.71–0.89)	<0.001
HF hospitalization	0.79 (0.71–0.89)	<0.001
End points	HR (95% CI)	p

LCZ696 is the first apparently successful drug in the angiotensin receptor-neprilysin inhibitor (ARNI) class, an inhibitor of angiotensin that can also potentiate endogenous natriuretic peptides, which are vasodilators. Chemically, it consists of the angiotensin-receptor blocker (ARB) **valsartan** affixed to the neprilysin inhibitor **sacubitril**, notes the paper.

Independent Views An editorial accompanying the PARADIGM-HF report proposed that LCZ696 "may prove to be the first disruptive agent to the heart-failure treatment algorithm, which has remained essentially unchanged for a decade"[2]. In her methodical comparison of the PARADIGM-HF patients with those in a half-dozen other major heart-failure studies, **Dr Mariell Jessup** (University of Pennsylvania, Philadelphia) concludes they are comparable to those in the other trials who had "mild to moderately severe" HF.

That could help allay concerns that an odd or unrepresentative patient cohort may have been responsible for the standout results of PARADIGM-HF. The trial "may well represent a new threshold of hope for patients with heart failure," she writes. "The beneficial results seen in PARADIGM-HF may apply to a wide spectrum of patients, even those who are currently receiving the best possible therapy."

Dr John GF Cleland was bullish on the new agent when commenting to heartwire . "LCZ696 is one of the great innovations in the management of heart failure in the past quarter century. The PARADIGM study shows that, for the management of stable outpatients with heart failure and a reduced left ventricular ejection fraction [HFREF] and, crucially, increased plasma concentrations of natriuretic peptides, LCZ696 is substantially superior to an ACE inhibitor (and by implication angiotensin-receptor blockers), in terms of reducing both morbidity and mortality. Patients also felt better on the newer agent; a small but highly significant effect." Cleland noted that the morbidity and mortality gains were more pronounced in patients with less severe symptoms, who may be at lower risk "but whose outcome may be more amenable to improvement with this therapy. This is crucially important, since it is the patient who appears stable on existing therapy, in whom a change in treatment may be considered unnecessary, who is most likely to benefit."

At first blush, PARADIGM-HF looks like a therapeutic home run for patients with heart failure and will likely lead to a change in our current practice guidelines in the future," Dr Douglas L Mann told heartwire . Patients who took the ARNI showed "dramatic effects" on the clinical end points, and the benefits were seen "in most of the subgroups that were examined, with the notable exceptions of black patients and patients with an ejection fraction >35%," he observed. "The drug LCZ696 also appeared to be safe and well tolerated." There were 428 blacks randomized in the trial; whites were the only listed ethnic group showing a significant LCZ696 effect for the primary end point or CV death. "One curious observation was that there was no apparent benefit for heart-failure patients who had not been treated previously with an ACE inhibitor," Mann also noted. Whether it stems from a statistical issue with the same size or whether it points to less benefit from starting ACE-inhibitor–naive patients on LCZ696 instead of an ACE inhibitor, he noted, should be studied further.

The trial randomized 8399 patients with NYHA class 2–4 heart failure with an LV ejection fraction <35% and elevated natriuretic peptides who completed at least four weeks of treatment with an ACE inhibitor or ARB equivalent to enalapril at 10 mg/day. They were maintained as possible on stable doses of beta-blockers, preferably with aldosterone inhibitors. They were assigned to either 200-mg LCZ696 or 10-mg enalapril, both twice daily, on top of the other guidelines-based therapy. Over a median of 27 months, the rate of CV death or HF hospitalization was 21.8% among LCZ696 patients and 26.5% for those taking enalapril; all-cause mortality was 13.3% and 16.5%, respectively. There were no significant differences between the LCZ696 and enalapril groups in prevalence of angioedema at any severity. Packer previously observed for heart*wire* that the new drug was designed specifically to avoid that complication. That was based primarily on experience with another agent with similar properties, omapatrilat, which was associated with a worrisome risk of angioedema partly responsible for the drug's withdrawal as a potential treatment for hypertension and heart failure drug a dozen years ago.

***Source**: McMurray JJV, Packer M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure.* N Engl J Med *2014; DOI:10.156/NEJMoa1409077*

الهيئة العامة للغذاء والدواء تحصر استخدام مستحضر "دومبيريدون"

في علاج الغثيان "بجرعات منخفضة ولفترة اقل"

29/09/1435

أطلقت الهيئة العامة للغذاء والدواء تنبيهاً للممارسين الصحيين و المرضى أوضحت فيه أنها قامت بدراسة مدى ارتباط استخدام مستحضر دومبيريدون Domperidone مع احتمالية حدوث أعراض جانبية خطيرة مثل الموت القلبي المفاجيء والرجفان البطيني

وقالت انها بعد مراجعة ملف السلامة الدوائية للمستحضر وعرض الموضوع على اللجان المختصة بالهيئة "تبين أن هناك احتمالية لحدوث هذه الأعراض الخطيرة خصوصاً عند استخدامه بجرعات كبيرة ولفترات طويلة" .

وبناء على هذه النتائج قامت الهيئة بحصر الاستخدام فقط على علاج الغثيان والقيء ولفترة قصيرة وبجرعات منخفضة على ألا تتجاوز الجرعة اليومية للمراهقين والبالغين الذين يبلغ وزنهم أكثر من 35 كيلوجراما على 10 ملجم ثلاث مرات يومياً عن طريق الفم أو 30 ملجم مرتان يومياً عن طريق الشرج لمدة أسبوع، كما يجب ألا تتجاوز الجرعة للأطفال الذين يبلغ وزنهم أقل من 35 كيلوجراما عن 0,25 ملجم لكل كيلوجرام ثلاث مرات يومياً ولمدة أسبوع .

وشددت الهيئة العامة للغذاء والدواء على منع استخدام مستحضر دومبيريدون للمرضى الذين لديهم فشل في القلب، نوبات قلبية سابقة، ذبحة صدرية ، عدم انتظام نبضات القلب .

يُذكر أن مستحضر دومبيريدون (Domperidone) مسجل في المملكة بالأسماء التجارية التالية :

موتيليوم(Motilium) , دومبى (Dompy) ,بروكينين (Prokinin) , اميستوب (Amistop) ,مودودوم (Mododom) .

الغاء تسجيل مستحضر بروتيلوس strontium ranelate (Protelos ®)

23/09/1435

أوضحت الهيئة العامة للغذاء والدواء أنه تم إلغاء تسجيل المستحضر الصيدلاني بروتيلوسو (Protelos ®) strontium ranelate الذي يستخدم لعلاج هشاشة العظام , وذلك بناءً على توصية لجنة تسجيل شركات ومصنع الأدوية ومنتجاتها المعتمدة , حيث اتضح أن المخاطر الناجمة عن استخدام المستحضر تفوق الفوائد العلاجية , ولوجود بدائل أكثر اماناً لعلاج هشاشة العظام .

وقد أوضحت الدراسات وقواعد رصد الأعراض الجانبية إلى أن استخدام المستحضربروتيلوس (Protelos ®) Strontiumranelate قد يؤدي لحدوث أعراض جانبية خطيرة مثل حالات احتشاء عضلة القلب (myocardial infarction) , وكذلك انسداد الأوعية الدموية (venous thrombotic and embolic events) وظهور اعراض جانبية على الجلد (DRESS).

Scientific Books: New Release

Davis's Drug Guide for Nurses by (byApril Hazard Vallerand PhD RN FAAN)

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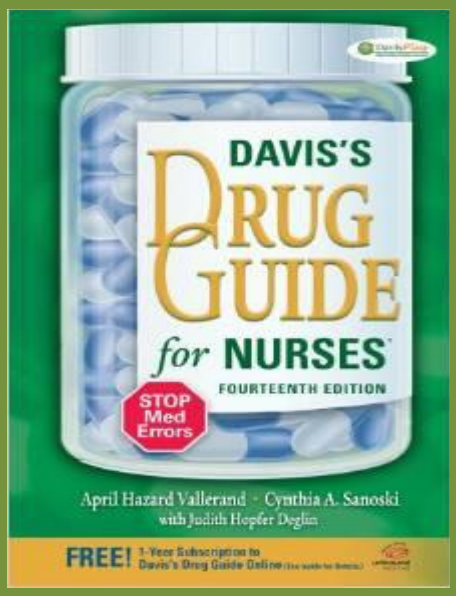

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Upcoming Conferences

- 6th - 7th October 2014 Pharmaceutical Dissolution Testing in London, United Kingdom
- 11th - 12th October 2014 Frontiers in Pharmaceutical Science & Research Columbia Institute of Pharmacy in Raipur (Chhattisgarh), India
- 20th - 21st October 2014 Orphan Drugs and Rare Diseases Holiday Inn Regents Park in London, UK
- 22nd - 23rd October 2014 GMP Auditor Training for Quality Systems Hotel Islington in London, United Kingdom

Editorial Board

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