FDA approves Fluzone® High-Dose influenza vaccine for the over 65s

Sanofi Pasteur's Fluzone® High-Dose, an inactivated influenza virus vaccine, has been approved by the FDA following the company's supplemental biologics license application. It was approved via the FDA's accelerated approval pathway, which helps effective and safe medical products for life-threatening diseases become available to the public sooner. As part of its accelerated approval, Sanofi Pasteur is now required to conduct further studies to confirm that the vaccine decreases the risk of contracting the seasonal influenza disease.

The new vaccine will be available to hospitals and clinics for immunizations in time for the 2010–2011 influenza season and is intended to prevent disease caused by the subtypes A and B of the influenza virus.

Fluzone High-Dose was designed with those aged over 65 years specifically in mind and the vaccine generates a more robust immune response than the original Fluzone vaccine, in an attempt to help protect those most at risk from the virus. The high-dose vaccine contains 60 mcg of hemagglutinin per strain of the virus, compared with 15 mcg per strain in the standard-dose, and is administered as a single injection.

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The Phase III clinical trials forming the basis of its accelerated approval compared the immune response triggered by Fluzone High-Dose and the standard dose Fluzone in 3876 adults over the age of 65 years and demonstrated that the High-Dose vaccine triggered a significantly greater immune response. Serum hemagglutinin inhibition titers were carried out 28 days after immunization to measure the immune response to the two vaccines, with higher hemagglutinin inhibition titers observed in those who received the High-Dose vaccine, indicating a greater immune response. However, the study did not investigate whether the new vaccine causes a decrease in influenza disease after vaccination and controlled studies investigating this in accordance with its accelerated approval will need to be carried out.

> *"While research still needs to be carried out to demonstrate it is effective in preventing influenza, researchers anticipate positive results based on the Phase III trials, with the High-Dose vaccine evoking a statistically greater immune response to the virus than the standard dose Fluzone vaccine, already approved for all ages above 6 months."*

The rate of serious adverse effects of the new vaccine was shown to be comparable to the standard dose vaccine, but nonserious adverse effects, as expected, were more frequent owing to the higher hemagglutinin content.

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Source: Falsey AR, Treanor JJ, Tornieporth N, Capellan J, Gorse GJ: Randomized, double-blind controlled Phase III trial comparing the immunogenicity of high-dose and standard-dose influenza vaccine in adults 65 years of age and older. J. Infect. Dis. *200(2) 172–180 (2009).*

in the news...

- Artificial heart approved for long-term use offers hope to end-stage heart failure patients **pg 166**
- Intravenous immunoglobulin shows potential as treatment for pain syndrome **pg 166**
- Emergency contraceptive pill ellaOne® may be effective for up to 5 days after sexual intercourse **pg 167**
- Rotavirus vaccines could save millions of lives **pg 167**
- Recent drug approvals **pg 168**

future medicine part of fsg

Artificial heart approved for long-term use offers hope to end-stage heart failure patients

A new option for patients with end-stage heart failure struggling on conventional therapy has been recently granted premarket approval by the FDA. HeartMate II left ventricular assist system is now available for use as destination therapy and comes from circulatory device manufacturer, Thoratec Corporation.

The HeartMate II was originally approved as a temporary measure for those awaiting transplantation ('bridge-to-transplantation') in 2008, but this recent approval provides a fresh wave of hope for those not eligible for transplant. The target patient group for this device is those with New York Heart Association (NYHA) Class IIIB or IV end-stage left ventricular failure who have received optimal medical therapy for at least 45 of the last 60 days, and who are not candidates for cardiac transplantation.

FDA approval comes on the back of the recent safety trials carried out by the company. The HeartMate II Destination Therapy trial lasted for two years and incorporated 200 randomized, controlled patients at 38 centers. The HeartMate II compared favorably to the HeartMate XVE, and this was further supported by data illustrating that 409 patients opted for the HeartMate II over the HeartMate XVE when replacement was required.

Thoratec plan to carry out postapproval surveillance of the device, to report adverse events and other safety and tolerability markers.

Source: http://phx.corporate-ir.net/phoenix.zhtml?c=95989&p=irol-newsArticle&ID=1377221-&highlight

Intravenous immunoglobulin shows potential as treatment for pain syndrome

Research at the University of Liverpool (UK) has provided evidence for the efficacy of immunotherapeutic treatment of complex regional pain syndrome.

Complex regional pain syndrome (CRPS) is a chronic pain condition that causes burning pains in a limb and usually develops after an injury but then continues after the injury has healed.

The discomfort caused by CRPS can be severe and there are instances of patients requesting amputations in an attempt to alleviate the pain. It is estimated that long-term CRPS affects approximately 1 in 5000 in the UK.

The study was a randomized double-blind placebo-controlled trial that enrolled individuals that had suffered from CRPS for between 6 and 30 months, had not benefited from previous treatment, and had pain intensity greater than four out of ten on a numerical rating scale. The researchers treated the patients with 0.5 g/kg IVIG, and then normal saline, in different treatment sessions that were separated by at least 28 days.

The results of the intervention demonstrated that, in the 12 patients that completed the trial, average pain intensity was reduced by 1.55 units after IVIG treatment compared with placebo (95% CI: 1.29–21.82; $p < 0.001$) and that in 25% of the patients, pain intensity after IVIG treatment was reduced by more than 50%.

The authors recognize that, the small size of the study is a major limitation but suggest that this finding has the potential to prompt further research into novel pain relief for CRPS. Andreas Goebel who headed the Liverpool CRPS treatment research explains: "in CRPS, the real effect of this treatment in [the] clinic may turn out to be even greater than what we have already seen, because IVIG can be given in higher doses, and repeated treatment may have additional effects. IVIG is normally repeated every 4 weeks and we are working to develop ways which would allow patients to administer the treatment in their own home".

Source: Goebel A, Baranowski A, Maurer K et al.*: Intravenous immunoglobulin treatment of the complex regional pain syndrome. A randomized trial.* Ann. Int. Med. *152 (3), 152–158 (2010); National Health Service – Complex regional pain syndrome: www.nhs.uk/Conditions/Complex-Regional-Pain-Syndrome/Pages/Introduction.aspx*

Emergency contraceptive pill ellaOne® may be effective for up to 5 days after sexual intercourse

A study that set out to compare the efficacy and safety of a newer form of emergency contraceptive, ulipristal acetate, with the most commonly administered form, levonorgestrel (Plan B®), found that ulipristal acetate appears to be more effective for a longer period of time, and may prevent unwanted pregnancy for up to 5 days after unprotected sexual intercourse, compared with a window of 3 days with Plan B. Available by prescription in Europe under the brand name ellaOne®, it could, therefore, provide healthcare workers and women with an effective, alternative form of emergency contraceptive (EC).

Anna Glasier and colleagues from the Family Planning and Well Woman Services at Dean Terrace Centre (Edinburgh, UK), enrolled women with regular menstrual cycles who attended a family planning clinic to obtain EC within 5 days of unprotected sexual intercourse. A total of 2221 women were randomly assigned to receive a single, supervised dose of 30 mg ulipristal acetate (n = 1104) or 1.5 mg Plan B (n = 1117) orally in a randomized, multicenter, noninferiority trial. Of these women, 1696 received the EC within 72 h of sexual intercourse (ulipristal acetate, n = 844; levonorgestrel, n = 852). Participants were followed-up 5–7 days after the expected onset of subsequent menses and the primary end point measured was pregnancy rate in women who received EC within 72 h. The study found that there were 22 pregnancies in the group that received levonorgestrel, compared with 15 in the group that received ulipristal acetate. In the 203 women who received EC between 72 h and 120 h after sexual intercourse, there were three pregnancies, all of which were in the levonorgestrel group. Ulipristal acetate appeared to work consistently for up to 5 days, whereas levonorgestrel decreases in effectiveness over time.

Glasier explained that the discrepancy may be due to the different modes of action between the two pills; Plan B contains synthetic progesterone and mimics the effects of the natural hormone by interfering with ovulation as the egg develops, whereas ellaOne delays ovulation. Glasier also cautioned that more safety data are needed before the new drug can be recommended for over-the-counter use, and estimated that the drug costs about three times more than Plan B. The study was designed and funded by HRA Pharma, which produced ellaOne, and the study was published in *The Lancet*.

Sources: www.medicalnewstoday.com; Glasier AF, Cameron ST, Fine PM et al.*: Ulipristal acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis.* Lancet *doi: 10.1016/S0140–6736(10) 60101–60108 (2010) (Epub ahead of print).*

Rotavirus vaccines could save millions of lives

Two recent studies in Mexico and Africa have demonstrated the lifesaving impact of the two rotavirus vaccines RotaTeq (Merck & Co.) and Rotarix (GlaxoSmithKline), potentially saving 2 million children over the next decade. The two studies demonstrated that deaths from diarrhea were significantly reduced in babies receiving the vaccine, with the death rate reduced by 61% in Africa and 35% in Mexico.

Rotavirus is the leading factor responsible for severe diarrhea, which claims the lives of over half a million children 5 years and under every year, with nearly half occurring in Africa. Rotavirus vaccines are part of the standard immunization process in developed countries, such as the USA, but developing countries, where the issue is most rife, do not have sufficient access to the vaccines and are suffering as a result.

Mathuram Santosham, John Hopkins University, Baltimore, commented that "Widespread use of these vaccines has the potential to prevent about 2 million deaths over the next decade. The vaccines should be introduced immediately in areas with high mortality from rotavirus infection."

Mexico was one of the first countries to introduce the rotavirus vaccine in 2006 and deaths due to diarrheal diseases decreased during the 2009 season by over 65% in children under 2 years of age. Similar results were seen in studies in South Africa and Malawi, where the incidence of severe rotavirus disease fell by 61.2% in vaccinated children during the first year of life. A joint statement released by the nonprofit organization PATH and the GAVI Alliance, who both promote vaccination in the developing world, said "This demonstrates real-world impact that is crucial as other countries consider rotavirus vaccine introduction."

The results of the two studies offer great hope to the millions of people at risk of rotavirus disease and health organizations are keen to ensure the vaccines reach those in most need. Tachi Yamada, president of the Global Health Program concluded "Diarrhea is rarely a life-threatening problem in rich countries, but in the developing world it is a leading cause of death in children. The world now has an effective vaccine against rotavirus, with the potential to save hundreds of thousands of lives every year. The next challenge is to ensure that rotavirus vaccines reach all those in need."

Sources: Madhi SA, Cunliffe NA, Steele D et al. *Effect of human rotavirus vaccine on severe diarrhea in African infants.* N. Engl. J. Med. *362(4) 289–298 (2010); Richardson V, Hernandez-Pichardo J, Quintanar-Solares M* et al. *Effect of rotavirus vaccination on death from childhood diarrhea in Mexico.* N. Engl. J. Med. *362(4) 299–305 (2010).*

Drug Approvals November 2009 to January 2010.

Trade name	*Generic name*	*Indication*	*Region*	*Manufacturer*	*Date approved*
Endocrinology & metabolism					
Victoza®	Liraglutide	To be used as an adjunct to diet and exercise to improve glycemic control in adults with Type 2 diabetes mellitus	USA	Novo Nordisk	January 2010
Gastroenterology & hepatology					
Resolor®	Prucalopride	The symptomatic treatment of chronic constipation in women in whom laxatives fail to provide adequate relief	Germany	Movetis	January 2010
Hematology					
Wilate®	Coagulation factor VIII complex	For the treatment of spontaneous and trauma-induced bleeding episodes in patients with all types of von Willebrand disease	USA	Octapharma USA	December 2009
Infectious disease					
Prevenar 13	Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)	For active immunization for the prevention of invasive disease, pneumonia, and acute otitis media caused by 13 *Streptococcus pneumoniae* serotypes in infants and children from 6 weeks to 5 years of age	EU	Pfizer	December 2009
Neurology					
Ampyra™	Dalfampridine	To improve walking in patients with multiple sclerosis	USA	Acorda	January 2010
	Morphine sulfate oral solution, 20 mg/ml	For the relief of moderate to severe, acute and chronic pain in opioid-tolerant patients	USA	Roxane Laboratories	January 2010
Zyprexa™ Relprevv™	Olanzapine pamoate	Schizophrenia in adults	USA	Eli Lilly	December 2009
Respiratory					
Onbrez® Breezhaler®	Indacaterol	Chronic obstructive pulmonary disease	EU	Novartis	December 2009
Other					
Elonva®	Corifollitropin alfa	For controlled ovarian stimulation in combination with a GnRH antagonist for the development of multiple follicles in women participating in an assisted reproductive technology program	EU	Organon BioSciences	January 2010
Kalbitor®	Ecallantide	To treat sudden and potentially life-threatening fluid buildup that can occur in people with a rare genetic condition known as hereditary angioedema	USA	Dyax Corp	December 2009
Vagifem®	Estradiol vaginal tablets	For the treatment of atrophic vaginitis due to menopause	USA	Novo Nordisk	December 2009