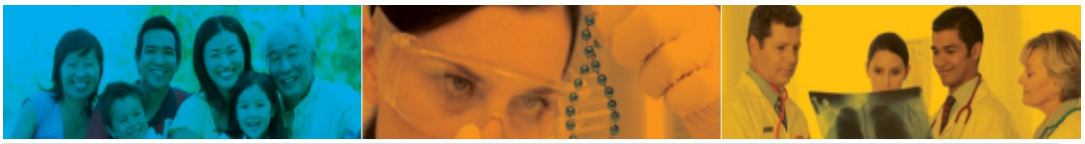

Clinical Research Newsletter Volume - 7, July 2016

LAMBDA

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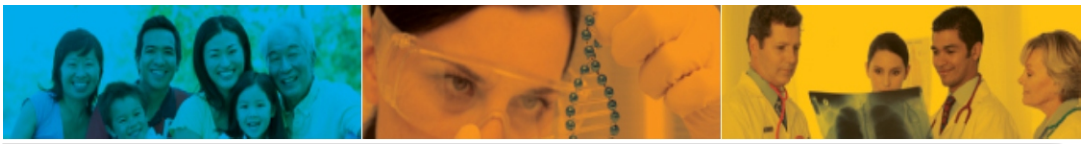


LAMBDA

GLOBAL NEWS

1.1. Folic acid intake during pregnancy could protect children from possible side-effect of antiepileptic drugs

June 01, 2016

- If pregnant women take antiepileptic drugs, the child can develop autistic traits. The administration of folic acid preparations appears to be a suitable means of preventing this serious side-effect.
- This finding is suggested by a Norwegian study presented at the Congress of the European Academy of Neurology in Copenhagen.

1.2. IOF urges clinicians in Asia to prepare for escalating crisis of osteoporosis among elderly people

June 20, 2016

- The International Osteoporosis Foundation (IOF) is calling on doctors in the Asia-Pacific region to prepare for an immense rise in the number of elderly people suffering broken bones as a result of osteoporosis.
- It is estimated that, in mainland China, Hong Kong, Chinese Taipei, Japan, and Korea, from 12.5 to 38.7% of older women and from 3.2 to 12.4% of older men have osteoporosis.

1.3. Obama signs chemical safety bill into law

June 22, 2016

- President Barack Obama signed into law a bill that will overhaul, for the first time in 40 years, the way chemical substances are regulated in the US.
- Although the new law, which updates the Toxic Substances Control Act of 1976, deals with regulations governed by the Environmental Protection Agency (EPA) rather than the US Food and Drug Administration (FDA), it integrates principles to replace and reduce animal-based tests with human-relevant methods to assess the toxicity of chemicals.

1.4. EMA and FDA begin collaborations on patient engagement

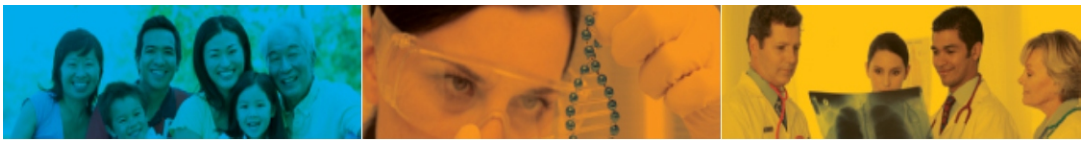
June 22, 2016

- The European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) began exchanging more information on the best practices of involving patients in the development, evaluation and post-authorization tracking of medicines.
- The new cluster is expected to meet three to four times per year via hour-and-a-half long teleconferences, and will involve officials from FDA's Office of International Programs, Office of Health and Constituent Affairs, as well as from the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research.

1.5. Brexit creating a period of uncertainty for EU, UK drug and device regulators

June 28, 2016

- The fallout from the UK referendum is continuing to create strife among the ranks of the European Medicines Agency (EMA), though a top EMA official told the DIA (Develop Innovate Advance) annual conference in Philadelphia that business at the agency will carry on as usual as negotiations continue.
- Emer Cooke, head of international affairs at the EMA, said that the Brexit decision, which may cause the agency to leave London, “is a decision that affects a lot of the staff of the agency, personally and professionally.”.



DOMESTIC NEWS

2.1. National reference standards for vaccines released in India June 07, 2016

- The Indian Pharmacopeia Commission (IPC) has released the national reference standards, specifically referred as the Indian Pharmacopoeia Reference Substances (IPRS Vaccines), the first such initiative to be undertaken of its kind.
- The standards would include IP monographs which act as the national reference standards for vaccines.
- The standards were released on the occasion of the 5th Expert Committee Meeting held in Kasauli, Himachal Pradesh, jointly organised by IPC and Central Drugs Laboratory (CDL).

2.2 Indian drug advisory board backs proposed API import license fee hike June16, 2016

- A plan to charge drug firms more to import APIs into India has won the support of the Government's Drugs Technical Advisory Board (DTAB).
- The ministry of Health and Family welfare proposed revising the Drugs and Cosmetic Act, 1940 to increase the importation fee from “One thousand US dollars” to “five thousand US dollar” per API imported.

2.3. Indian pharma segment may not be impacted by Brexit June 26, 2016

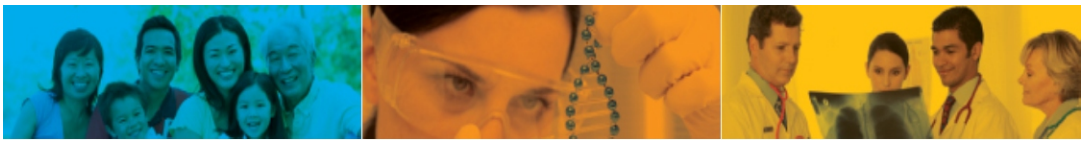
- The Indian pharmaceutical segment is unlikely to be impacted adversely due to Britain's decision to move out of the European Union (EU) as the entire EU market accounts for around 12 per cent of India's total exports of pharmaceuticals.
- According to a CRISIL report, the share of the UK is only 3.5 per cent. However, few companies like Aurobindo and Wockhardt, with higher exposure to Europe, will see some impact.
- The pharmaceutical scrips like Sun Pharmaceutical, Dr Reddy's Laboratories, Lupin, Cipla, Cadila Healthcare, Glenmark Pharmaceutical, Wockhardt, Torrent Pharma and Biocon opened higher as compared to Friday’s close.

2.4. Govt withdraws Drugs and Cosmetics (Amendment) Bill, 2013 June 27, 2016

- The Union Cabinet, chaired by the Prime Minister Narendra Modi, has decided to withdraw the Drugs and Cosmetics (Amendment) Bill, 2013, which had been introduced in the Rajya Sabha on 29.08.2013.
- The Bill had been examined by the Standing Committee of Parliament which had made a number of recommendations for changing the provisions of the Bill.

2.5. CDSCO renews WC certificate to API units to ease export to EU countries June 27, 2016

- The Central Drugs Standard Control Organisation (CDSCO) has started renewing the written confirmation (WC) certificate to active pharmaceutical ingredients (API) manufacturers for exporting APIs to European Union (EU).
- The certificate was made mandatory by EU in 2013 which confirms the compliance of good manufacturing practice (GMP) as per EU standards with the validity period of 3 years



REGULATORY NEWS

3.1. Aspirin-containing heartburn drugs: FDA warns of serious bleeding risk June 06, 2016

- The US FDA warned consumers about the risk of serious bleeding when using over-the-counter (OTC) aspirin-containing antacid drugs to treat heartburn, sour stomach, acid indigestion or upset stomach.
- The new warning comes as FDA added a warning in 2009 about the risk of serious bleeding the labels of all OTC products that contain NSAIDs, including aspirin-containing antacid products.

3.2. FDA issues new guidance on osteoporosis drug development June 13, 2016

- The US FDA issued new draft guidance calling for drugmakers to conduct long-term nonclinical bone quality studies for osteoporosis treatments.
- According to FDA, such studies are necessary for osteoporosis drugs to determine whether the drugs result in poorer bone quality when taken for long periods of time. Additionally, FDA says these studies should be nonclinical, as "there are no validated and reliable methods for the noninvasive assessment of bone quality in humans."

3.3. FDA issues warning for fatal, heart-related imodium (loperamide) side effects June 14, 2016

- The FDA is warning health care professionals to be aware that use of higher than recommended doses of loperamide can result in serious cardiac adverse events. Specifically, it states that physicians should consider loperamide as a possible cause of unexplained cardiac events including QT interval prolongation, Torsades de Pointes or other ventricular arrhythmias, syncope, and cardiac arrest.
- According to the FDA statement, the agency has received 48 cases of serious heart problems associated with use of loperamide since it was first approved in 1976.

3.4. NIH finalizes single IRB policy to reduce redundancies June 21, 2016

- The National Institutes of Health (NIH) finalized a policy that will require NIH-funded clinical studies to be overseen by a single institutional review board (sIRB), beginning in May of next year.
- NIH made the announcement in a notice published to the Federal Register, saying its goal is to "enhance and streamline the IRB review process" for multi-site clinical trials.

3.5. DCGI Orders fixed-dose combination manufacturers to submit phase iv protocols

June 22, 2016

- Drug Controller General of India (DCGI) Dr. GN Singh has told producers of fixed-dose combinations (FDCs) to submit protocols for Phase IV clinical trials.
- The letter is the latest step in a long-running attempt by Singh and his colleagues to get manufacturers of certain FDCs to demonstrate the safety and efficacy of their products.
- Regulatory attempts to get FDC manufacturers to generate safety and efficacy data date back to at least the start of 2013.

DRUG APPROVALS AND LAUNCHES

4.1. EU approves second indication for subcutaneous form of Roche's rituximab June 01, 2016

- Roche's subcutaneous formulation of MabThera receives approval in Europe for people with chronic lymphocytic leukaemia which eases treatment burden compared with intravenous form
- The phase Ib SAWYER study demonstrated comparable safety and efficacy between MabThera SC and intravenous MabThera in combination with chemotherapy.

4.2. Eisai introduces new oral suspension formulation of antiepileptic drug, Fycompa in US June 01, 2016

- Eisai Co., Ltd. has launched Fycompa (perampanel) oral suspension, a new formulation of its in-house-discovered antiepileptic drug (AED) Fycompa, in the United States.
- Fycompa is a first-in-class AED discovered at Eisai's Tsukuba Research Laboratories.
- It is approved in the United States as an adjunctive therapy for the treatment of partial-onset seizures with or without secondarily generalized seizures, and primary generalized tonic-clonic (PGTC) seizures in patients with epilepsy 12 years of age and older.

4.3. Allergan announces FDA approval of BYVALSON June 06, 2016

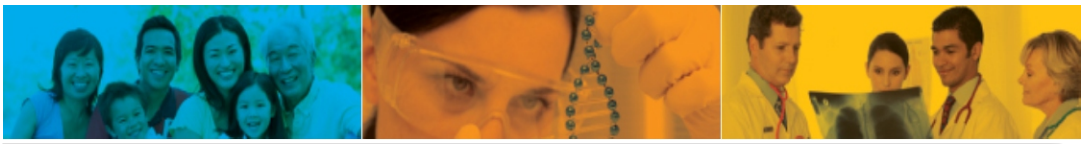
- Allergan plc, a leading global pharmaceutical company, announced the approval of BYVALSON™ (nebivolol and valsartan) 5 mg/ 80 mg tablets, by the U.S. FDA for the treatment of hypertension to lower blood pressure.
- BYVALSON is the first and only fixed-dose combination (FDC) of a beta blocker (BB) and angiotensin II receptor blocker (ARB) available in the U.S.

4.4. FDA Approved GONITRO™ (nitroglycerin) sublingual powder June 14, 2016

- Espero Pharmaceuticals, Inc., a privately held specialty pharmaceutical company, announced that the U.S. FDA has approved GONITRO™ (nitroglycerin) sublingual powder for acute relief of an attack or prophylaxis of angina pectoris due to coronary artery disease.
- With this approval, GONITRO™ is the first and only short-acting nitrate in a stabilized crystal granule form available in single dose packets.

4.5. FDA approves Epclusa for treatment of chronic hepatitis C virus infection June 28, 2016

- The U.S. FDA approved Epclusa to treat adult patients with chronic hepatitis C virus (HCV) both with and without cirrhosis (advanced liver disease).
- For patients with moderate to severe cirrhosis (decompensated cirrhosis), Epclusa is approved for use in combination with the drug ribavirin. Epclusa is a fixed-dose combination tablet containing sofosbuvir, a drug approved in 2013, and velpatasvir, a new drug, and is the first to treat all six major forms of HCV.
- The safety and efficacy of Epclusa for 12 weeks was evaluated in three Phase III clinical trials.



DRUG DEVELOPMENT AND CLINICALTRIALS

5.1. Zydus gets FDA nod for phase II clinical trial of saroglitazar

June 04, 2016

- Zydus Cadila said it has received approval from the US health regulator to initiate a phase II clinical trial of Saroglitazar in patients with non-alcoholic steatohepatitis (NASH) of the liver.
- With a Phase III trial ongoing in India and a Phase II trial planned in US, the company is committed towards developing this drug for millions of patients with NASH, said CMD Pankaj Patel.
- The company has received nod from the US Food and Drug Administration (USFDA) to conduct randomised, double-blind phase II trial to evaluate Saroglitazar in strengths of 1mg, 2mg and 4mg versus placebo, Zydus Cadila said in a statement .

5.2. Lilly reports positive results from MONARCH 1 phase 2 study of abemaciclib monotherapy

June 06, 2016

- Eli Lilly and Company announced results from the MONARCH 1 phase 2 study of abemaciclib, a cyclin-dependent kinase (CDK) 4 and CDK 6 inhibitor, in patients with hormone-receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer.
- The safety and toxicity profile of twice daily, continuously dosed abemaciclib was consistent with previous phase 1 experience.

5.3. Sanofi, Regeneron's experimental drug dupilumab hits main goals of Phase III atopic dermatitis study

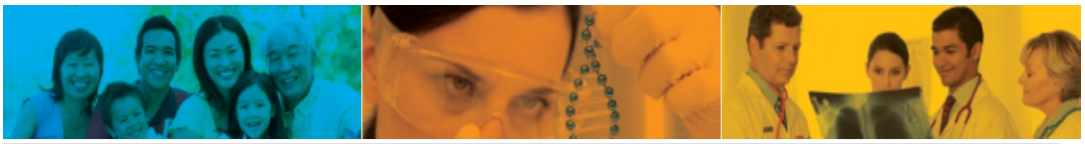
June 06 , 2016

- Sanofi and Regeneron Pharmaceuticals announced that a Phase III study of the experimental drug dupilumab in adults with moderate-to-severe atopic dermatitis (AD) met its primary and key secondary endpoints.
- Results showed that dupilumab significantly improved measures of overall disease severity at 16 and 52 weeks, when compared to placebo.
- The companies noted that the data, along with results from previous late-stage trials, will form part of a US regulatory submission for the therapy in the third quarter.

5.4. Diabetes drug holds promise for cancer treatment & prevention

June 07, 2016

- Use of metformin commonly used as the front-line treatment for type 2 diabetes improves survival for some breast cancer patients and shows promise as a treatment for patients diagnosed with endometrial hyperplasia, according to the results of two new studies presented by researchers from the Perelman School of Medicine, University of Pennsylvania at the American Society of Clinical Oncology (ASCO) Annual Meeting.
- Results show survival benefit for some breast cancer patients and potential treatment option for patients with endometrial hyperplasia.



MERGER/ACQUISITIONS/COLLABORATION

6.1. Cipla partner Stempeutics puts India on the world map of regenerative meds June 01, 2016

- Cipla New Ventures announced its plans to nurture innovative business ideas, the first product of that initiative has been approved under brand name Stempeucel, a drug that could possibly turn into a blockbuster.
- Biotechnology firm Stempeutics Research has received limited approval from the national drug regulator, Drug Controller General of India (DCGI), for its stem cell-based product Stempeucel for treatment of Buerger's Disease. Cipla has investments in Stempeutics.

6.2. Lipidor and Cadila Pharmaceuticals partner on psoriasis product June 02, 2016

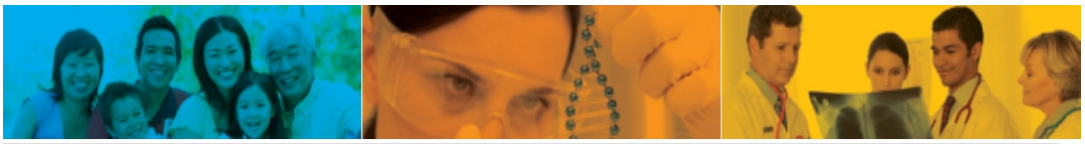
- Lipidor and Cadila Pharmaceuticals, one of the largest pharmaceutical manufacturing groups in India, have entered into a collaboration agreement for the commercialisation of a sprayable anti-psoriatic product.
- The sprayable product consists of the generic vitamin D analogue, Calcipotriol, formulated with Lipidor´s patented lipid-based drug delivery technology, Akvano and targets patients with mild to moderate psoriasis.
- Under the collaboration agreement, Cadila Pharmaceuticals will conduct a Phase III program in India starting in 2016.

6.3 Novartis joins Eisai to push Lenvima and Afinitor combo in US. June 03, 2016

- Japan's Eisai is counting on its cancer drug Lenvima to help it climb out of the financial malaise it has been in for several years. Now it has a partner in the US to help it reach its blockbuster goals, Novartis.
- The Swiss drugmaker, which faces its own challenges, will promote Lenvima in combination with its own Afinitor (everolimus). The partnership comes after the FDA last month approved the combo to treat certain patients with advanced kidney cancer.
- Both will not share any sales but they will each talk up the combo to healthcare providers and also appear together in some medical affairs events to get the word out.

6.4. Pfizer Completes Acquisition of Anacor June 24, 2016

- Pfizer Inc. announced that it has completed its acquisition of Anacor Pharmaceuticals, Inc. Under the terms of the transaction, each outstanding share of Anacor common stock has been converted into the right to receive $99.25 net in cash (without interest but subject to required withholding of taxes).
- The transaction is not expected to impact Pfizer's current 2016 adjusted financial guidance.
- Pfizer continues to expect the transaction to be slightly dilutive to Adjusted Diluted Earnings Per Share (EPS) (1) in 2017.



LAMBDA

PATENT (NEW APPROVAL/LITIGATION/SETTLEMENTS)

7.1. Supernus receives US patent covering Oxtellar XR June 24, 2016

- Supernus Pharmaceuticals, Inc., a specialty pharmaceutical company, announced the issuance on June 21, 2016 of a seventh patent (number 9,370,525) by the United States Patent and Trademark Office (USPTO) covering Oxtellar XR, its novel once-daily extended-release oxcarbazepine product for the treatment of epilepsy.
- The patent provides protection for the product with expiration that is no earlier than 2027.

7.2. Teva settles generic Byetta patent litigation with AstraZeneca June 25, 2016

- Teva Pharmaceuticals USA, Inc., a leading global pharmaceutical company, announced that the company has settled the patent litigation with AstraZeneca Pharmaceuticals LP, AstraZeneca AB and Amylin Pharmaceuticals.
- Teva entered into a settlement and license agreement with AstraZeneca, pursuant to which AstraZeneca granted a license to Teva to manufacture and commercialize the generic version of Byetta described in Teva's ANDA No. 205984 in the United States.

TECHNOLOGY/NDDS NEWS

8.1 Topical drug prevents sexual transmission of HIV June 14, 2016

- Findings published in the journal PLOS ONE confirm that researchers from the Oak Crest Institute of Science, located in Monrovia, CA, have demonstrated for the first time that two powerful antiretroviral (AVR) drugs can provide complete protection against HIV when delivered topically by a sustained release intravaginal ring (IVR) device.
- Results of the study confirmed that the combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) delivered at independently controlled rates via the pod-IVR were successful at preventing SHIV162p3 infection in a rigorous, repeat low-dose vaginal exposure model using normally cycling female pigtailed macaques.

8.2 Glide Technologies announces successful clinical proof-of-concept study with its novel octreotide June 28, 2016

- Glide Technologies announced results from a successful clinical proof-of-concept study that demonstrated its novel solid formulation of the most widely-used dose of octreotide (100 mcg) achieved bioequivalence to the currently marketed immediate release liquid injectable product (Sandostatin®).
- Glide's formulation was delivered using the company's proprietary needle-free Solid Dose Injector (SDI®), which provides the potential for room temperature stability and patient-friendly administration.
- Octreotide is approved for use in the treatment of acromegaly and certain neuroendocrine tumours, with the estimated market for immediate release liquid formulations exceeding $150 million.