UPFRONT

Boehringer—Lilly alliance to launch first diabetes drug in India

Boehringer Ingelheim India and Eli Lilly and Company India (Lilly), which represents the Boehringer Ingelheim–Lilly global alliance in India, announced the launch and commercial availability of Linagliptin (brand name Trajenta) 5 mg film-coated tablets.

Trajenta (Linagliptin 5 mg tablets) is the alliance's first new product introduction, globally. In India, the Boehringer Ingelheim- Lilly alliance already co-promotes Humalog (injection Lispro).

Linagliptin (Trajenta) is an original research product of Boehringer Ingelheim.

The Boehringer Ingelheim—Lilly alliance in India now offers oral anti-diabetics as well as contemporary injectable insulins. These offer a choice to the doctor in deciding the optimum therapy, depending on the patient's needs. "This alliance combines the strengths of two of the world's leading pharmaceutical companies. While the combined field force provides the spread to touch doctors treating diabetes across the country, the new launch provides more choice to the clinician," said Sharad Tyagi, Managing Director, Boehringer Ingelheim India.

Melt van der Spuy, Managing Director, Lilly India said, "This launch of Linagliptin (Trajenta) marks an important milestone for the alliance, demonstrating our ongoing commitment to providing pioneering healthcare solutions. The alliance will continue to focus on bringing to India innovative products and services to address the unmet patients needs amidst the growing Indian diabetes epidemic."

The product will leverage the alliance's distribution network and will be available on prescription in pharmacy outlets across the country.

Company Watch

Sanofi ties up with Joslin Diabetes Center

Sanofi and the Joslin Diabetes Center, a teaching and research affiliate of Harvard Medical School, announced a new collaboration to promote the development of new medicines for the treatment of diabetes and related disorders. The collaboration was unveiled at the 2012 Bio International Convention in Boston, Mass

Page 17

BEYOND THE BAN

The Government of India recently banned the use of serology-based test kits for diagnosis of tuberculosis. But this will translate into better diagnosis rates only if the GoI is willing to go beyond the ban and physicians decide to think beyond these kits, analyses **VIVEKA ROYCHOWDHURY**

Almost a year after the World Health Organization (WHO) issued a rare 'negative' policy recommendation urging countries to ban the use of antibody-based test kits for active tuberculosis (TB) detection, India's Ministry of Health & Family Welfare became the first – and so far the only - country to issue a notification banning the manufacture, sale, distribution, use and import of such serodiagnostic kits.

WHO's recommendation in July last year came after a year of rigorous analysis of evidence by WHO and global experts. 94 studies were evaluated - 67 for pulmonary TB (TB in the lungs) and 27 for extra-pulmonary TB (TB elsewhere in other organs). Overwhelming evidence showed that the blood tests produced an unacceptable level of wrong results - false-positives or false-negatives - relative to tests endorsed by WHO.

For a country saddled with an estimated one fifth of the global burden of TB cases, with some estimates putting a total of 9.2 million new cases and 1.7 million deaths every year, proper TB diagnosis could go a long way to controlling the spread of this highly communicable disease.

Thus it is no wonder that TB detection/diagnosis and treatment is top priority of India's Ministry of Health & Family Welfare. In fact, 'universal access to quality TB care for all TB patients' is the objective of the Revised National Tuberculosis Control Programme (RNTCP) which aims at detecting and successfully treating 90 per cent of all TB cases by 2015. This Programme has seen substantial infusion of funds over the past 13 years since its implementation, and there have been success stories as well. A total of ₹ 1447 crore has been allocated for the 11th Five year plan by the Planning Commission. (*See BOX: Vital stats of India's TB control programme*)

Dr Karin Weyer, Coordinator, Diagnostics, Laboratories and Drug Resistance, Stop TB Department, World Health Organization, hopes that this ban will greatly improve patient diagnosis and reduce costs for both patients and health services in India.

There are signs that the advisory from WHO was having the desired impact, even before the Government of India (GoI) ban. According to data provided by the Foundation for Innovative New Diagnostics (FIND), orders from India for GeneXpert test modules, one of the WHO recommended tests provided at concessional prices to countries like India with a high TB burden, showed a steady pick up from six modules through Q3 2010 to 96 in Q1 2012. The country clocked a total of 114 test modules for the entire period from Q3 2010 to Q1 2012.

The cost of such TB testing kits is expected to drop even further with the executive board of UNITAID recently approving funding of $30 million to scale up access to Xpert MTB/RIF which will further reduce the cost of its use. This test, an automated, cartridge-based nucleic amplification assay for the simultaneous detection of TB and rifampicin resistance directly from sputum in under two hours, is based on the GeneXpert platform. which was developed as a partnership between FIND, Cepheid Inc. and the University of Medicine and Dentistry of New Jersey, with support from the US National Institutes of Health. WHO endorsed the technology in December 2010 and is monitoring the global roll-out of the Xpert MTB/RIF test modules.

A task half done?

But will the GoI ban really make a difference? Experts in the field like Dr Madhukar Pai, Professor, Dept of Epidemiology & Biostatistics, McGill University, Montreal, Canada; and Co-chair, Stop TB Partnership's New Diagnostics Working Group feel that the WHO endorsed tests, such as molecular tests and liquid cultures are quite expensive for India, especially in the private sector. He feels efforts are needed to extend special, reduced prices to the private sector, not just the public sector.

Ameera Shah, Managing Director and Chief Executive Officer, Metropolis Healthcare, takes the argument a step ahead. She says that though the GoI has gone ahead and banned the antibody test, it should have also provided an alternative. Of the tests giving more specificity, the sputum-based tests, the culture-based test takes up to six weeks to give results while the alternative test, the molecular biology test, costs around ₹ 1,500—₹ 2,000, thanks to a 27 per cent customs duty. This is obviously too expensive for most patients in India.

Shah makes the point that if this import duty on the TB molecular biology test is waived, as also the duties on other imported TB test kits, this ban will serve its purpose of patients having a

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President- Research & Innovation
Super Religare Laboratories

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And a viable alternative is definitely the need of the hour. Jayant Singh, Industry Manager, Healthcare Practice, South Asia and Middle East, Frost & Sullivan says that the number of tests being done to diagnose TB is about 20 to 22 lakh per year but the fact that most of these tests are not accurate in terms of sensitivity and specificity, pose even greater problems.

Expanding on the problem, Singh says that the microscopy test tends to detect not more than 35 per cent of the cases, a chest X-ray is only useful for pulmonary TB and serological tests tend to give a lot of false positive results.

With microscopy and chest X-ray, a lot of positive cases are left out (false negatives) and with serological tests, a lot of negative cases are reported as positive (false positives). Both situations are dangerous as in the first case, the infection is not controlled because of undiagnosed and untreated cases while false positives leads to misuse of Anti TB Therapy (ATT) due to which antibiotic resistance sets in leading to the more dangerous form of TB: MDR (Multi Drug Resistant) TB. MDR TB cannot be treated by standard TB drugs and the cost of treatment also goes up, says Singh spelling out a scenario which is already playing out in India. Another factor leading to MDR TB is incomplete course of therapy as patients tend to stop taking the drug after the first three-four months once they get partial relief from the symptoms.

"The only and best option is to open as many culture centres as possible and detect TB using the microbiology techniques," advocates Singh.

As Dr BR Das, President—Research & Innovation, Super Religare Laboratories (SRL) points out, various clinical studies have convincingly demonstrated limited clinical utility of all available TB serology kits but unless more effective diagnostic tools are available, serological assays for difficult-to-diagnose infectious diseases like TB will continue to be used.

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Physician power

The role of the physician in controlling TB infection cannot be ignored. "The role of physicians is primordial", says Rajeev Kumria, Head Business Development, Transasia Biomedicals, "as it is the physician who makes the decision for choosing diagnostics and therapeutics. The physician guides and counsels patients depending upon the clinical conditions to recommend the right type of diagnostic test subsequently leading to correct therapy." His observation is that physicians sometimes recommend wrong tests, either due to lack of information on the latest tests or lack of availability of other better alternatives. Therefore he feels there is a need for doctors to be educated on these factors so that they can steer the patient towards the right diagnostic and therapeutic solutions.

Similarly, Das says physicians can counsel patients to provide site specific specimens such as sputum for pulmonary cases instead of blood which invariably is expected to provide incorrect results.

So it seems that the GoI ban will not really have the desired results unless physicians stop prescribing the banned tests. Singh warns that we need to see the "bigger" picture — a wrong treatment leading to drug resistance TB and spreading it further is more disastrous for society than patients not diagnosed and not treated. Though either of the scenarios are acceptable, he opines that if forced to make a choice, then not using serological tests is a better choice than using it.

What the GoI can do is make the

WHO-prescribed tests cheaper and thus more accessible by reducing or scrapping custom duties on imported tests. As Pai says, a good TB test should be considered "life-saving" for duty exemption. It thus goes without saying that import duty exemption on such TB test kits will help prevent thousands of TB related deaths every year.

But besides government action, industry too can and must chip in. As Pai points out, diagnostics manufacturers must also realise that most TB patients in India, even those in the private sector, are poor, and unless prices are reduced, good TB tests will remain unaffordable to them. The fact that the advanced test need to be imported also indicates the lack of innovative disease diagnosis kits made in India. Kumria states that the Indian industry is primarily involved in design and manufacturing of cost mass base screening test devices and instruments. Listing the underlying reasons for this sad state of affairs, he says, "The Indian university culture is also not entirely in sync with the global practices which boost innovation and entrepreneurship among qualified students."

Kumria notes that a part of the pharma, biotech, healthcare industry are pure R&D companies which get easy funding to innovate and then get either sold to larger companies or sell/license the technologies. Within this realm are individual innovations from young scientists who are encouraged to innovate and start their own companies straight out of university after Ph.D's. Most of the successful scientists in developed world are also successful entrepreneurs. This is not so in India and it needs to change, urges Kumria.

Hopefully this dismal situation could change soon. Last year, Pai had helped organise the first ever conference on TB diagnostics in India, which focused on the need to develop innovative TB diagnostics. He indicates that since the meeting in Bangalore in 2011, Indian companies have begun developing more affordable molecular TB tests, although none are on the market as yet. Pai hopes these tests will be shown to be valid and accurate and can be scaled up within India as a replacement for serological tests.

Thus it seems logical that both the government, the diagnostics industry as well as the physician fraternity will need to walk that extra mile if they are really committed to curb the TB epidemic in India.

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Vital stats of India's TB control programme

India's Revised National Tuberculosis Control Programme (RNTCP) has completed 13 years of its implementation with four years of full nation-wide coverage. Since its inception the programme has initiated over 12.6 million patients on treatment thus saving more than 2.2 million lives. RNTCP has definitely made strong strides towards achieving the Millennium Development Goals of relating to the prevalence and mortality due to TB by 2015 as compared to the 1990 levels. A total of Rs 1,447 crore has been allocated for the 11th Five year plan by the Planning Commission.

In 1997, when the programme was initiated, an estimated five lakh deaths occurred due to TB each year in the country, which has reduced to 2.8 lakh in 2010. Population surveys conducted by Tuberculosis Research Centre, Chennai, in a sub-district population in Tamil Nadu, show a 12 per cent annual decline in prevalence of TB disease after implementation of RNTCP services. Since 2007 the programme is achieving the global targets of 70 per cent case detection and 85 per cent cure rates in new smear positive patients. These are encouraging trends for RNTCP as it steadily works towards achieving the Millennium Development Goals (MDGs) by 2015. The ultimate goal of the programme remains a "TB-free India", and clearly it is a long journey towards this goal. (*Source: TB INDIA 2011: Revised National TB Control Programme: Annual Status Report*)