Drug Information Bulletin

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Content

Editorial

Essential Medicines List (EML) is one of the tools for implementing Rational Use of Medicines (RUM).World Health Organization (WHO) is publishing Model List of Essential Drug since 1977 and has already published 18th Edition of the same. India did not have any such list till mid nineties and the First National Essential Drug List for India has been published in the year of 1996. The second and third version has been renamed as "National List of Essential Medicines) and has published in 2003 and 2011 respectively. Till 2002 the list did not have much relevance in the health care system in India. It became more relevant by insertion of a statement in the objective of the National Pharmaceutical Policy 2002 which is that "Ensuring abundant availability at reasonable prices within the country of good quality essential pharmaceuticals of mass consumption".

A recent study by the Public Health Foundation of India and the Institute for Studies in Industrial Development as published in the BMJ, found that this price regulation was limited to 17% of the drugs prescribed in India. This left most of the market untouched and provided only marginal financial relief to patients. The report showed that price controls covered just 1% of drugs in the market for anemia, 5% of respiratory drugs, 7% of antidepressants, 15% of drugs for diabetes, 18% of drugs for tuberculosis, 13% of anti-malarial drugs, 23% of cardiac drugs, and 35% of antibiotics. It also highlighted a risk that drug companies may introduce new formulations to avoid price controls—for example, changing paracetamol from a 500 mg tablet to a 650 mg tablet—something that the authors said might be irrational and even unsafe.

Experts opined that the current NLEM does not cover most of the drugs of current use and the provisions of the DPCO 2013 is not sufficient to control the prices adequately. Experts suggested that more drugs require to be added in the current NLEM, and DPCO 2013 require to be revised to prevent price control evasion in most cases.

Dr. Subhash C. Mandal
\Editor

New Drug: Mirabegron

Approved indication: overactive bladder
Betmiga (Astellas)
25 mg and 50 mg film-coated tablets
Australian Medicines Handbook section 13.1

People with overactive bladder have urgency with or without frequency and nocturia. Antimuscarinics such as oxybutynin, tolterodine, solifenacin (Aust Prescr 2006;29:138-43) and darifenacin are the mainstay of drug treatment (Aust Prescr 2014;37:10-3). They are often used in conjunction with bladder training.

Mirabegron is an agonist of beta3 adrenergic receptors. It works by activating these receptors in the detrusor muscle of the bladder. This relaxes the muscle and increases bladder capacity.

The safety and efficacy of mirabegron has been evaluated in three placebo-controlled, 12-week studies.1-3 A pooled analysis of the trials found that once-daily 50 mg and 100 mg doses statistically improved incontinence and micturition frequency 4 However, there was no dose–response effect. The mean number of incontinence episodes per day fell by 1.48 with mirabegron 50 mg and by 1.54 with the 100 mg dose. Incontinence episodes fell by 1.09 a day with placebo. Although an active control was included in one of the trials (extended-release tolterodine), a statistical comparison with mirabegron was not reported.2

The most common adverse effects with mirabegron and placebo included hypertension (7.3% vs 7.6% of participants), nasopharyngitis (3.4% vs 2.5%), urinary tract infection (3% vs 1.8%), headache (2.9% vs 3.1%), dry mouth (2% vs 2.1%) and constipation (1.6% vs 1.4%).4 Tachycardia was common, occurring in 1.2% of people taking mirabegron 50 mg. Palpitations and atrial fibrillation have also been reported. Blood pressure monitoring is recommended, especially in patients with hypertension, and mirabegron is not recommended in uncontrolled hypertension. Caution is urged in those who may have a prolonged QT interval.

In a long-term extension study of safety (52 weeks), 11 of 820 people who received mirabegron 100 mg had a neoplasm (benign or malignant). Only 1 of 812 people reported a neoplasm with mirabegron 50 mg and 4 of 812 people who received tolterodine.

Following an oral dose, mirabegron reaches peak plasma concentrations after 3−4 hours. Steady-state concentrations are achieved after seven days. The terminal half-life is approximately 50 hours and the drug is eliminated in the urine (55%) and faeces (34%). This drug is not recommended in patients with end-stage renal disease or severe hepatic impairment.

In animal studies, mirabegron has shown reproductive toxicity and is excreted in milk. It is therefore not recommended in pregnancy or lactation.

Mirabegron is transported and metabolised by multiple pathways so there is potential for drug interactions. Monitoring and dose adjustment may be needed with concomitant drugs that are extensively metabolised by CYP2D6 and have a narrow therapeutic index, such as flecainide and imipramine. Mirabegron also increases exposure to concomitant digoxin so digoxin should be started at a low dose and titrated based on serum concentrations.

Mirabegron is indicated for urgency, increased micturition frequency and urgency incontinence in adults with overactive bladder. It showed only modest efficacy in the trials with the average number of incontinence episodes being reduced by around 1.5 a day. This was compared to people given placebo who had approximately 1.1 fewer incontinence episodes a day. Currently, there are limited comparative and long-term efficacy data with this drug. In the UK5, mirabegron is only recommended when antimuscarinic drugs are contraindicated, ineffective or not tolerated.

References:

1. Nitti VW, Auerbach S, Martin N, Calhoun A, Lee M, Herschorn S. Results of a randomized phase III trial of mirabegron in patients with overactive bladder. J Urol 2013;189:1388-95.
2. Khullar V, Amarenco G, Angulo JC, Cambronero J, Hoye K, Milson I, et al. Efficacy and tolerability of mirabegron, a β(3)-adrenoceptor agonist, in patients with overactive bladder: results from a randomised European-Australian phase 3 trial. Eur Urol 2013;63:283-95.
3. Herschorn S, Barkin J, Castro-Diaz D, Frankel JM, Espuna-Pons M, Gousse AE, et al. A phase III, randomized, double-blind, parallel-group, placebo-controlled, multicentre study to assess the efficacy and safety of the β 3 adrenoceptor agonist, mirabegron, in patients with symptoms of overactive bladder. Urology 2013;82:313-20.
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5. Mirabegron for treating symptoms of overactive bladder. National Institute for Health and Care Excellence. 2013.

Source: Australian Prescriber

Regulatory Pain for GSK's Crocin Advance

GlaxoSmithKline's fast-relief analgesic, Crocin Advance, might cause pain to the company. Rejecting its plea to exempt the medicine from price control, the National Pharmaceutical Pricing Authority (NPPA) is instead set to penalise GSK Consumer Healthcare for overcharging consumers by selling the drug at over double its MRP (maximum retail price) as fixed by the regulator, official sources said.

NPPA has told GSK to immediately reduce the market price of Crocin Advance and give a compliance report. Currently, Crocin Advance paracetamol fast release 500 mg is priced at Rs 30 for a strip of 15 tablets, whereas the price of paracetamol 500 mg is capped at 94p for a tablet or around Rs 14 for a strip of 15.

The NPPA letter was issued to GSK on Wednesday. The letter, reviewed by Business Standard, was also sent to Remidex Pharma, which manufactures Crocin Advance for GSK Consumer Healthcare in India.

The regulator plans to issue an overcharging notice to GSK Consumer Healthcare within the next few days and is likely to impose a hefty penalty on the company.

According to sources, NPPA had constituted an experts' panel headed by K K Bhutani, director of the National Institute of Pharmaceutical Education and Research. The committee also had doctors from Ram Manohar Lohia Hospital and the All India Institute of Medical Sciences in Delhi. The panel examined the application and rejected it.

GSK said it had yet to get official word from NPPA. "We have been and will continue to be compliant with the law of the land," the company said. GSK had launched Crocin Advance in India in 2011. It had claimed the product was a 'new drug', with optizorb technology which releases its medicine up to five times faster than ordinary paracetamol

tablets, providing fast relief. On this basis, the company sought exemption from price control, while also contending Crocin Advance was developed through indigenous research and development (R&D). Under para 32 (iii) of the Drug Price Control Order (DPCO), 2013, a 'new drug' developed through indigenous R&D can be kept out of price control for five years.

According to NPPA's letter, the product does not qualify for the exemption because "the formula and process technology were transferred from R&D Parsippany (in New Jersey, USA) to R&D India in May 2006" and the R&D centre in India is also not approved by the department of scientific and industrial research, as is required under the DPCO.

GSK Consumer Healthcare sells paracetamol under several over-the-counter brands such as Crocin, Crocin Advance, Crocin Pain Relief, Crocin Cold and Flu. It also has a baby and kids range of Crocin.

According to an official source, the company is planning to gradually stop selling the conventional Crocin brand while promoting the other brands, including Crocin Advance.

According to IMS Health data, Crocin Advance is currently the fifth largest brand among top paracetamol-based products.

Annual sales were Rs 10.3 crore during the 12 months ended February 2014. Calpol, another paracetamol-based product marketed by GSK Pharma, tops the list with annual sales of Rs 84.3 crore.

India's IP regime has support of legal experts, nonprofits in U.S.

Law professors and nonprofit groups in the U.S. say India's patent laws and intellectual property regime comply with international law despite trade sanctions that could be imposed by the U.S. "India's adoption and one-time use of compulsory licensing and Section 3(d) of the Indian Patents Act are TRIPS-compliant and do not justify elevation of India on the U.S.'s 2014 Special 301 Watchlist," said Matthew Kavanagh of the Health Global Access Project. The Pharmaceutical Research and Manufacturers of America and other U.S. groups have objected to actions such as India's use of a compulsory license for one drug and the denial of a patent for another.

Source: The Financial Express (India)

India urged to standardize TB treatment regimen to avoid drug-resistant strains

Earlier and faster diagnosis of tuberculosis is critical to treating patients and to reducing the numbers with drug-resistant forms of the disease, according to Margaret Chan, director general of the World Health Organization. In India, which has the world's highest number of TB patients, Medecins Sans Frontieres said that poor prescribing practices and availability of a wide range of dosages and combinations put many TB patients at risk for drug-resistant strains of the disease. MSF is calling for a "standardized first-line daily tuberculosis treatment regimen" in India to fight the problem.

Source: MedicalXpress.com, McClatchy Washington Bureau

Forthcoming Event:

World Health Day Celebration

7th April 2014

Theme:

Vector-Borne Diseases

Venue:

IPA Auditorium, 22 B Panchanontola Road, Kolkata-700029

Time: 6.00 pm