Drug Information Bulletin

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Content

Editorial

Use of generic medicines is gradually getting popularity. Several countries have already passed suitable legislation to reduce Govt. health expenditure and the cost to individuals of their medicines. Use of generic medicines is also considered as one of the tools of propagating concept of Rational Use of Medicines

It may be noted that several state Governments and the Govt. of India has directed the doctors working under the Government health care system to prescribe in generic name. The Medical Council of India has also directed all prescriber to prescribe in generic name as far as possible. Inspite of such instructions prescribing in generic name could not be ensured in several cases especially in private settings. Experts believe that awareness needs to be created amongst the prescriber in addition to issuing orders.

Dr. Subhash C. Mandal
Editor

New Drug: Glycopyrronium bromide

Approved indication: chronic obstructive pulmonary disease
Seebri breezhaler (Novartis)
capsules containing 50 microgram powder for inhalation
Australian Medicines Handbook section 19.1.2

Long-acting bronchodilators have a role in the maintenance treatment of patients with symptomatic chronic obstructive pulmonary disease (COPD). One option is a long-acting anticholinergic drug and prescribers can now choose between tiotropium and glycopyrronium bromide.
Glycopyrronium is not a new drug. Also known as glycopyrrolate, an injectable form has been used by anaesthetists to

dry up secretions. It blocks acetylcholine at muscarinic receptors. In the lung, acetylcholine acts on smooth muscle to cause bronchoconstriction, so antagonising this with inhaled glycopyrronium will result in bronchodilation. This begins within five minutes and is sustained for 24 hours.

After the dry powder is inhaled, using a specific device, about 40% is absorbed, mainly through the lungs. Most of the absorbed dose is excreted in the urine. After inhalation the elimination half-life is 33–57 hours. Clearance will be reduced by renal disease, but no dose reduction is recommended for patients with a glomerular filtration rate above 30mL/min/1.73 m^2.

The approval of glycopyrronium is based on two main trials, GLOW 1[1] and GLOW 2[2] . Both trials assessed lung function in patients over 40 years old with a smoking history of at least 10 pack-years. These patients had moderate-to-severe COPD with a forced expiratory volume in one second (FEV_1) that was under 80%, but more than 30%, of the predicted value after bronchodilation. Approximately 50% of the patients were using inhaled corticosteroids.

In GLOW 1, 552 patients were randomised to inhale 50 microgram glycopyrronium once daily while 270 were randomised to take a placebo. Although the trial was for 26 weeks, the primary outcome was a measurement of mean trough FEV_1 at 12 weeks. At the start of the trial the mean post-bronchodilator FEV_1 was 1.49 L in the glycopyrronium group and 1.45 L in the placebo group. The FEV_1 improved from the first day of active treatment. After 12weeks the trough FEV_1 (measured just before the next dose) was 1.408 L with glycopyrronium and 1.301 L with placebo. The 108 mL difference in FEV_1 is statistically significant and the advantage over placebo was still present at 26 weeks.[1]

GLOW 2 was also placebo controlled, but also included an open-label tiotropium arm. There were 529 patients randomised to take glycopyrronium, 269 to take placebo and 268 to take tiotropium (18 microgram once daily). All the patients had a mean post-bronchodilator FEV_1 of 1.5 L at the start of the 52-week study. The primary outcome measure was the mean trough FEV_1 at 12 weeks. These values were 1.469 L for glycopyrronium, 1.455 L for tiotropium and 1.372 L for placebo. The advantage over placebo, 97 mL for glycopyrronium and 83 mL for tiotropium, was statistically significant.[2]

The GLOW trials studied several secondary outcomes. Compared to placebo glycopyrronium reduced dyspnoea and the risk of exacerbations.[1, 2] The smaller GLOW 3 trial showed improved exercise tolerance after three weeks in 55 patients who took glycopyrronium compared with the 53 who took placebo.[3]

As glycopyrronium is a muscarinic receptor antagonist it has predictable anticholinergic adverse effects. Dry mouth is the most common and there is a possibility of precipitating urinary retention and narrow-angle glaucoma in susceptible patients. Although it is uncommon, some patients develop atrial fibrillation. Inhaling a dry powder can cause coughing and throat irritation. There are no studies of pregnant or lactating women.

Inhaled glycopyrronium has a greater effect than placebo, but more experience is needed to see if improvements in lung function lead to improved clinical outcomes. Many patients will not respond. In a pooled analysis of GLOW 1 and GLOW 2 the proportion of patients with a clinically meaningful improvement (≥100 mL) in trough FEV_1 was 52% at week 12 and 49.7% at week 26. After a

year only 42.5% of patients had a clinically meaningful improvement. Similarly, many patients' symptoms did not improve significantly. After 26 weeks, 57.8% of patients had a clinically relevant improvement in their quality of life compared with 61% of the tiotropium group and 47.6% of the placebo group.4 GLOW 3 showed a significant benefit, but the absolute improvement in exercise endurance compared to placebo was under 90 seconds.3

Although glycopyrronium has an early onset of effect, it is not approved for acute bronchospasm. On current evidence, glycopyrronium does not seem to have any advantages over tiotropium.

REFERENCES:

1. D'Urzo A, Ferguson GT, van Noord JA, Hirata K, Martin C, Horton R, et al. Efficacy and safety of once-daily NVA237 in patients with moderate-to-severe COPD: the GLOW1 trial. Respir Res 2011;12:156.
2. Kerwin E, Hébert J, Gallagher N, Martin C, Overend T, AlagappanVK, et al. Efficacy and safety of NVA237 versus placebo and tiotropium in patients with COPD: the GLOW2 study. Eur Respir J 2012;40:1106-14.
3. Beeh KM, Singh D, Di Scala L, Drollmann A. Once-daily NVA237 improves exercise tolerance from the first dose in patients with COPD: the GLOW3 trial. Int J Chron Obstruct Pulmon Dis 2012;7:503-13.
4. D'Urzo A, Kerwin E, Overend T, D'Andrea P, Chen H, Goyal P. Once daily glycopyrronium for the treatment of COPD: pooled analysis of the GLOW1 and GLOW2 studies. Curr Med Res Opin 2013 Nov 19. Epub ahead of print.

Source: Australian Prescriber

Dept of AIDS Control planning to extend third line ART at least through 10 centres of excellence

The Department of AIDS Control is planning to extend third line antiretroviral therapy (ART) for HIV/AIDS patients through 10 centres of excellence across the country under the recently-launched fourth phase of the National AIDS Control Programme.

This is being initiated as per the recommendation by the Technical Resource Group on ART some time back to provide third line ART for the patients.

At present, first line and second line antiretroviral therapy are given to HIV/AIDS patients free of cost in all ART Centres across the country, sources said.

As per the HIV/AIDS Bill which was recently introduced in the Parliament, the Central Government or the State Government should take measures for providing, as far as possible, antiretroviral therapy and Opportunistic Infection (OI) management to people living with HIV/AIDS.

Under NACP IV, it is proposed to have 600 ART Centres in the country by March 2017 to make available quality treatment to eligible people living with HIV/AIDS. The pre-ART follow up at ART centres is being strengthened. Emphasis is being given to pre-ART care.

Currently second line ART is being provided through centres of excellence and ART Plus centres. As on 31st March 2013, 27 ART Plus Centres are giving treatment in addition to the 17 centres of excellence, according to the Department.

It is planned to upgrade 7 more ART centres into ART Plus Centres in 2013-14 which will ensure that each state will have at least one ART centres to provide Second line ART . The process for same has already been initiated, sources said.

Source: Pharmabiz.com

Natco gets relief in Teva case

In a victory of sorts for Hyderabad-based drug company, Natco, the Delhi high court on Friday dismissed

a suit filed by Israel-based Teva Pharma against the domestic company seeking an injunction over marketing a blockbuster multiple sclerosis medicine, Copaxone, in the US.

The judgement is expected to pave the way for domestic company to launch the drug in the US market, subject to approval from the US Food & Drug Administration, sources told TOI. Copaxone, the largest branded drug sold by Teva, accounted for almost 20% of its revenue in 2012, with sales pegged at over $3 billion in the US alone.

More details of the judgement are yet to emerge, while it is learnt that the patent infringement case against Natco is still to be taken up.

The company will market the drug along with its partner, US-based Mylan Inc. Natco had signed an agreement with US-based Mylan to market its generic version of Teva's Copaxone in 2008. The agreement grants Mylan exclusive distribution rights in US and certain major markets. Subsequently, Teva sued the domestic company in the Delhi high court saying that it infringed its process patent, while seeking an injunction against selling the drug in the US. Natco has already commercialized successfully its glatiramer acetate product in the country.

Legal sources said that the case against Natco seeking the injunction was dismissed for lack of jurisdiction rights". It is understood that Teva may appeal against the order, though the company was not available for comments.

The patent on the Copaxone will expire in May 2015, so if the company launches the generic version in the US this year, it will boost sales significantly for over a year, adding to its profitability, experts say. Interestingly, in one of the rare instances, Teva's patent on the drug was invalidated in the US in July 2013, while the Indian courts are still debating the sanctity of the patent.

Last year, Natco received a favourable US ruling on the Copaxone patent case which invalidated Teva's monopoly rights on the drug.

Teva Pharma, which owns the rights for Copaxone, suffered a setback in July 2013 after a US court ruling gave the $4-billion drug less than a year of patent protection.

Natco is also embroiled in a court battle against German drug major Bayer which has challenged the Intellectual Property Appellate Board's order of compulsory licence issued to the company to protect its rights over patented cancer drug Nexavar.

Forthcoming Event:

1st Congress of Society for Ethnopharmacology

March 7-9, 2014
Sri Ramachandra University
Chennai, India

"Globalizing Traditional Medicines:
Present and Future Prospects"

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