Drug Information Bulletin

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Content

Editorial

Greetings from Drug Information Bulletin!

Recently Govt. of India has released 5th version of National List of Essential Medicines (NLEM) 2022, which includes 384 drugs, 8 drugs more than the earlier version. This time 26 drugs were deleted from the NLEM 2015 and added 34 items. The primary purpose of NLEM is to promote rational use of medicines considering the three important aspects i.e., Safety, efficacy and cost. It also helps in optimum utilization of healthcare resources and budget; drug procurement policies, health insurance; improving prescribing habits; medical education and training for health care professionals; and drafting pharmaceutical policies.

The concept is based on the premise that a limited list of carefully selected medicines will improve quality of health care; provide cost-effective health care and better management of medicines. The NLEM is a dynamic document and is revised on a regular basis considering the changing public health priorities as well as advancement in pharmaceutical knowledge. The National List of Essential Medicines was first formulated in 1996 and it was revised thrice earlier in 2003, 2011, and 2015.

WHO is publishing Essential Medicines List since 1977, and the first Essential Medicines List for Children was published in 2007. Though the WHO Model Lists of Essential Medicines are updated every two years by the Expert Committee on Selection and Use of Essential Medicines, it is not updated in India regularly.

Since 2013 the price of all medicines under NELM is controlled by Drugs Price Control order, though there is some fallacy in implementing DPCO. Because of this fact manufacturers are more concerned about the NLEM. A sector of healthcare professionals feels that some more costly medicines widely used in India should have been included in this list.

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New Drug: Denosumab

Prolia (Amgen)
vials containing 60 mg/mL solution for injection
Approved indication: osteoporosis
Australian Medicines Handbook section 10.3.3

Denosumab is a humanised monoclonal antibody approved for the treatment of osteoporosis in postmenopausal women. This antibody works by binding RANKL (receptor activator of nuclear factor-κβ ligand) and blocking the interaction with its receptor on the surface of osteoclasts. This inhibits the development and activity of osteoclasts and leads to decreased bone resorption and increased bone density.

Following a subcutaneous dose of denosumab 60 mg, maximum serum concentrations are typically reached one to four weeks later. Denosumab has a half-life of 25–30 days. It is not eliminated via hepatic metabolism and dose adjustment is not needed in patients with renal impairment.

The approval of denosumab for osteoporosis is mainly based on a large phase III randomised trial which enrolled 7868 women aged 60–90 years. These women had to have a bone mineral density T score of less than –2.5 at the lumbar spine or total hip before being randomised to receive subcutaneous denosumab 60 mg or placebo every six months. After three years of treatment, the incidence of new vertebral fractures (measured radiolographically) was significantly lower for denosumab than for placebo (2.3% vs 7.2%). Denosumab also significantly reduced the cumulative incidence of hip fractures (0.7% with denosumab vs 1.2% with placebo) and nonvertebral fractures (6.5% with denosumab vs 8% with placebo). Over the same time period, denosumab was associated with a relative increase in bone mineral density at the lumbar spine (9.2%) and hip (6%) in a subset of 441 women. Markers of bone turnover (serum C-telopeptide) and bone formation (serum procollagen type I N-terminal propeptide) were also decreased in women receiving denosumab.[1] Although the efficacy data from this trial looks promising, a meta-analysis of three randomised controlled trials found that denosumab was not associated with a significant reduction in fracture risk in postmenopausal women.[2]

The efficacy of denosumab in reducing fractures has not been compared to other treatments for osteoporosis. However, a phase III trial looking at bone mineral density compared denosumab (six-month dose) to alendronate (70 mg orally each week) in women with low bone mass (T score ≤ –2.0). After 12 months, bone mineral density of the hip had increased more with denosumab than with alendronate (3.5% vs 2.6%). Although this was statistically significant, the clinical significance of this change is unclear. This increase was associated with a more pronounced decrease in markers for bone turnover in the denosumab group.[3]

In the placebo-controlled trial, eczema and flatulence were more common with denosumab than placebo (3% vs 1.7% and 2.2% vs 1.4%). Cellulitis, a serious adverse event, was also more frequent in women receiving denosumab (12/3886) compared to those receiving placebo (1/3876).[1] This may not be so surprising as RANKL is expressed on immune cells and its inhibition could make people more susceptible to infections. When a larger safety cohort (over 8000 people) was analysed, serious infections were more common with denosumab than placebo (3.4% vs 2.8%) and included abdominal, ear and urinary tract infections as well as cellulitis. Endocarditis, infected arthritis and skin ulcers were also more frequently reported. Malignancies are also a concern with denosumab and cancers were slightly more common with denosumab than with placebo (7.8% vs 7.1%). These risks should be considered when prescribing denosumab and patients should be informed of them.

In the safety cohort, serious pancreatitis occurred more commonly with denosumab than with placebo (9 cases vs 1 case). This proved fatal in two people.

Low osteoclast and osteoblast counts have been observed with denosumab. This could potentially delay healing of fractures. Transient hypocalcaemia can occur with denosumab and is a contraindication to treatment. Calcium and vitamin D supplementation is recommended for all patients. Neutralising antibodies were not found in women who received denosumab.

Denosumab seemed to reduce fractures in postmenopausal women with low bone density in a large placebo-controlled trial. However, because of lack of head-to-head trials it is not known how this efficacy compares with current treatments for osteoporosis. Women may prefer the six-monthly dosing of denosumab but will need to consider its increased risks of infections and malignancies. Postmarketing surveillance for these adverse effects is needed.

References

1. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. N Engl J Med 2009;361:756-65.\r\n
2. Anastasilakis AD, Toulis KA, Goulis DG, Polyzos SA, Delaroudis S, Giomisi A, et al. Efficacy and safety of denosumab in postmenopausal women with osteopenia or osteoporosis: a systematic review and a meta-analysis. Horm Metab Res 2009;41:721-9.
3. Brown JP, Prince RL, Deal C, Recker RR, Kiel DP, de Gregorio LH, et al. Comparison of the effect of denosumab and alendronate on BMD and biochemical markers of bone turnover in postmenopausal women with low bone mass: a randomized, blinded, phase 3 trial. J Bone Miner Res 2009;24:153-61.

Status in India: Approved by CDSCO and available in several brands by several companies like-GSK, Dr. Reddys, Reliance, Alkem etc. Price of 60 mg injection varies from Rs. 8000 to Rs. 16000 as per market information.

WHO reveals surge in Tuberculosis cases for the first time in many years

The recent WHO reported an increase in the number of people suffering from tuberculosis (TB); this is the first time in many years.

The World Health Organization's 2022 Global TB report estimates that 10.6 million individuals developed Tuberculosis (TB) in 2021, an increase of 4.5% from 2020 and that 1.6 million people died from TB. Between 2020 and 2021, the burden of drug-resistant tuberculosis (DR-TB) grew by 3%, with 450 000 additional cases of Rifampicin-resistant TB (RR-TB) in 2021.

The COVID-19 pandemic and the ongoing conflicts in Eastern Europe, Africa, and the Middle East have adversely affected numerous services, including TB. Many TB patients were not diagnosed due to these ongoing issues accessing and providing necessary TB services.

WHO claims that decreases in the reported number of TB suggested an increase in the number of people with undiagnosed and untreated TB, which led to a rise in TB deaths and community transmission causing an increase in the number of people developing TB.

According to the report, there were 5.8 million new cases of TB reported in 2020, down from 7.1 million in 2019. Although there was a slight improvement to 6.4 million in 2021, still was well below pre-pandemic levels. It further showed that between 2019 and 2020, fewer individuals received RR-TB and multidrug-resistant TB (MDR-TB) treatments.

Dr Tereza Kasaeva, Director of WHO's Global TB Programme said, "the report provides important new evidence and makes a strong case for the need to join forces and urgently redouble efforts to get the TB response back on track to reach TB targets and save lives."

(Source:https://theprint.in/world/tuberculosis-cases-surged-for-the-first-time-in-many-years-who/1185037/)

Alcohol-based hand sanitizer Risk of eye injury

The US Food and Drug Administration (FDA) has issued a warning about exposure of hand sanitizer to the eyes (through splashing or touching the eyes after use). Exposure in the eye can result in serious injury, including severe irritation and damage to the surface of the eye. Hand sanitizers are over-thecounter (OTC) used to reduce virus and bacteria on hands. Eye exposure to hand sanitizer has been reported in all age groups; however, it has occurred most often in children. Such eye injuries have become much more

frequent, likely due to the marked increase in the use of alcohol-based hand sanitizer during the COVID-19 pandemic. Consumers and caregivers should avoid touching eyes after applying alcohol-based hand sanitizer to hands. Adults should always supervise young children using alcohol-based hand sanitizers, especially around some dispensers which often are at children's eye level and can splash. If alcoholbased hand sanitizer does accidentally splash or get in the eyes, the eyes should be thoroughly rinsed under gentle running water for 15 to 20 minutes.

Reference: MedWatch, US FDA, 11 February 2022 (link to the source within www.fda.gov)

Buprenorphine (buccal administration) Risk of dental problems

The US FDA has warned that dental problems have been reported with medicines containing buprenorphine that are dissolved in the mouth. Buprenorphine is an opioid used to treat opioid use disorder (OUD) and pain. The dental problems, including tooth decay, cavities, oral infections, and loss of teeth have been reported, including in patients with no prior history of dental issues. The buprenorphine medicines that are associated with dental problems are tablets and films that are dissolved under the tongue or placed against the inside of the cheek. Patients should continue taking buprenorphine medicine as prescribed. Steps to reduce risk of serious dental problems include: rinsing mouth with water, and waiting at least 1 hour before brushing teeth after buprenorphine medicines are dissolved. Health-care professionals should be aware that the benefits of buprenorphine medicines clearly outweigh the risks in treating OUD patients and should ask patients about oral health history prior to prescribing treatment with the medicines.

Reference: MedWatch, US FDA, 1 December 2021 (link to the source within www.fda.gov)

61st National Pharmacy Week Celebration

Indian Pharmaceutical Association, Bengal Branch

Programme:

20.11.2022: Inauguration Programme Indian Council for Cultural Relations, 9A Ho Chi Minh Sarani, Kolkata-700071

22.11.2022: Seminar at Brainware University, Barasat

23.11.2022: Students Day Celebration at JIS University, Agarpara.

24.11.2022: Scientific Day Celebration at Triguna Sen Auditorium, Jadavpur University, Kolkata-700032

26.11.2022: (a) Hospital Pharmacy Day Celebration at Barasat Zila Parisad Hall (b) Cultural Programme at IPA Auditorium

27.11.2022: Scientific Seminar at DSP Main Hospital, Durgapur