Drug Information Bulletin

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Content

Editorial

Greetings from Drug Information Bulletin!

It is my proud penning down the editorial at a historical moment – the completion of 17 years of publication of this Drug Information Bulletin. The weekly bulletin started its journey in April 2007, brought out by the Drug Information Centre (DIC), IPA, Bengal Branch and is now a bi weekly bulletin jointly published by Drug Information Centre, IPA- Bengal Branch & Regulatory Affairs Division (RAD), IPA. As far as my knowledge, this is the first of its kind of bulletin serving its readers from all spheres of the society like-Pharmacists, Doctors, Nurses, health workers, NGOs, and general public worldwide. It has received reach accolades and great appreciation from most of the readers due to its content and its regular publication. Initially it was started to serve IPA members then receiving request from other professional stake holders, as well as request from other countries the bulletin marched ahead. Presently we have readers from different countries all over the world and different strata of the society.

Some hospitals and educational institutes are forwarding this bulletin among their faculty members and keeping hard copies in their libraries with our prior permission so that students can read this. A number of Drug Information Centers are reproducing this with our permission both in Govt. and private sector.

This is a free service to anybody and everybody, and any person / institute interested in drug information, and we have never accepted any donation or advertisement from anybody for this publication to keep our voice unbiased.

This has been possible due to help and cooperation from all of our readers and mentors. Hope this bulletin will continue its service to the society with help from all of you in future too! Greetings to all.

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New Drug: Plazomicin injection for intravenous use

Initial U.S. Approval: 2018

WARNING: NEPHROTOXICITY, OTOTOXICITY, NEUROMUSCULAR BLOCKADE and FETAL HARM See full prescribing information for complete boxed warning. • Nephrotoxicity has been reported with ZEMDRI. The risk of nephrotoxicity is greater in patients with impaired renal function, the elderly, and in those receiving concomitant nephrotoxic medications. • Ototoxicity, manifested as hearing loss, tinnitus, and/or vertigo, has been reported with ZEMDRI. Symptoms of aminoglycoside associated ototoxicity may be irreversible and may not become evident until after completion of therapy. • Aminoglycosides have been associated with neuromuscular blockade. During therapy with ZEMDRI, monitor for adverse reactions associated with neuromuscular blockade particularly in high-risk patients. • Aminoglycosides, including ZEMDRI can cause fetal harm when administered to a pregnant woman. INDICATIONS AND USAGE: ZEMDRI is an aminoglycoside antibacterial indicated for the treatment of patients 18 years of age or older with Complicated Urinary Tract Infections (cUTI) including Pyelonephritis. As only limited clinical safety and efficacy data are available, reserve ZEMDRI for use in patients who have limited or no alternative treatment options.To reduce the development of drug-resistant bacteria and maintain effectiveness of ZEMDRI and other antibacterial drugs, ZEMDRI should be used only to treat infections that are proven or strongly suspected to be caused by susceptible microorganisms.

DOSAGE AND ADMINISTRATION: • Administer ZEMDRI 15 mg/kg every 24 hours by intravenous (IV) infusion over 30 minutes to patients 18 years of age or older with creatinine clearance greater than or equal to 90 mL/min. • Recommended duration of treatment is 4 to 7 days for cUTI, including pyelonephritis. • Assess creatinine clearance in all patients prior to initiating therapy and daily during therapy. • Recommended initial dosage regimen for patients with renal impairment is shown in the table below. Estimated CLcr a (mL/min) Recommended Dosage for ZEMDRI b Dosing Interval Greater than or equal to 60 to less than 90 15 mg/kg Every 24 hours Greater than or equal to 30 to less than 60 10 mg/kg Every 24 hours Greater than or equal to 15 to less than 30 10 mg/kg Every 48 hours a CLcr estimated by the Cockcroft-Gault formula. (2.3) b Calculate dosage using Total Body Weight (TBW). For patients with TBW greater than IBW by 25% or more, use adjusted body weight. • See Full Prescribing Information for subsequent dosage adjustment based on changes in renal function or Therapeutic Drug Monitoring (TDM). • See Full Prescribing Information for instructions on preparation of the solution, stability in intravenous fluids and drug compatibilities.

DOSAGE FORMS AND STRENGTHS: ZEMDRI injection 500 mg/10 mL (50 mg/mL) is a single-dose vial containing Plazomicin sulfate equivalent to 500 mg Plazomicin free base.

CONTRAINDICATIONS: ZEMDRI is contraindicated in patients with known hypersensitivity to any aminoglycoside.

WARNINGS AND PRECAUTIONS: • Hypersensitivity Reactions, including anaphylaxis: Reported for aminoglycosides. If an allergic reaction occurs, discontinue ZEMDRI. • Clostridium difficile-Associated Diarrhea: Reported for nearly all systemic antibacterial drugs. Evaluate if diarrhea occurs.

ADVERSE REACTIONS: Most common adverse reactions (≥ 1% of patients treated with ZEMDRI) are decreased renal function, diarrhea, hypertension, headache, nausea, vomiting and hypotension.

Source: USFDA

Status in India: Plazomicin injection 500mg/10ml (50mg/ml) Indicated in patients 18 years of age or older for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis caused by the following susceptible microorganism(s) • Escherichia coli, • Klebsiella pneumoniae, • Proteus mirabilis, and • Enterobacter cloacae approved by CDSCO on 02-02-2024

Many cancer drugs remain unproven 5 years after accelerated approval-USFDA study

The U.S. Food and Drug Administration's accelerated approval program is meant to give patients early access to promising drugs. But how often do these drugs actually improve or extend patients' lives?

In a new study, researchers found that most cancer drugs granted accelerated approval do not demonstrate such benefits within five years.

It is expected that a drug got accelerated approval required to show definite prof within 5 years.

The program was created in 1992 to speed access to HIV drugs. Today, 85% of accelerated approvals go to cancer drugs.

It allows the FDA to grant early approval to drugs that show promising initial results for treating debilitating or fatal diseases. In exchange, drug companies are expected to do rigorous testing and produce better evidence before gaining full approval.

Patients get access to drugs earlier, but the trade-off means some of the medications don't pan out. It's up to the FDA or the drug maker to withdraw disappointing drugs, and sometimes the FDA has decided that less definitive evidence is good enough for a full approval.

The new study found that between 2013 and 2017, there were 46 cancer drugs granted accelerated approval. Of those, 63% were converted to regular approval even though only 43% demonstrated a clinical benefit in confirmatory trials.

The research was published in the Journal of the American Medical Association and discussed at the American Association for Cancer Research annual meeting in San Diego on Sunday.

Ref. The Associated Press

Resumption of penicillin production in India –a welcoming step

Three decades after the India's last penicillin manufacturing unit was shut down, the country will start producing this active pharmaceutical ingredient (API or bulk drug) used in several antibiotics. According to the Union Ministry of Health and Family Welfare (MoHFW), production of penicillin-G will resume in 2024.

Production of penicillin-G was phased out in the 1990s, when the country's markets were flooded with cheaper alternatives, largely from China. The decline in API production was noticed only in a few circles until late 2019, when supply chains were disrupted following China's stringent regulations on its industry. The Covid pandemic made the problem grave and API shortages threatened to have serious ramifications outside India's borders, given the country's status as the largest manufacturer of generic medicines. The resumption of penicillin manufacturing owes in great measure to the government's production-linked investment (PLI) scheme.

Pen-G manufacture is cost-intensive and involves a complex fermentation and extraction process. That's why drug manufacturers find it prudent to outsource their production. The situation has compounded in the last few years because Chinese penicillin makers have been producing well below their capacity. In 2019, the public sector Hindustan Antibiotics Ltd was reportedly the government's first choice to restart its production under the Make in India scheme. However, the PSU expressed its inability to participate in the venture, citing resource constraints. About the same time, the Department of Health Research informed the MoHFW that India needs more than 13,000 million doses of penicillin in the next three years to deal with bacterial infections that cause rheumatic fever – India has amongst the highest death rates from such illnesses. The government also received requests from doctors to procure this drug. Broad-spectrum antibiotics, such as azithromycin, that have been used as penicillin substitutes are known to harm essential bacteria naturally present in the human body, leaving a patient vulnerable to harmful germs.

The PLI scheme envisages a support of 20 per cent for the first four years, 15 per cent for the fifth year, and 5 per cent for the sixth year on eligible sales of fermentation-based bulk drugs and hormones such as insulin. It's early years for the scheme and India still imports close to 90 per cent of all APIs for antibiotics.

It is a challenge for the authorities to promote Make in India and ensure affordability.

Source: The Indian Express

Methotrexate Risk of photosensitivity reactions

The MHRA has advised patients to take precautions when exposed to the sun to avoid photosensitivity reactions when taking methotrexate treatment. Photosensitivity reactions (which include phototoxicity, where a drug is activated by exposure to UV light and causes damage to the skin that can look and feel like a sunburn or a rash) can occur with both low-dose and high-dose treatment.

Methotrexate is an immunosuppressant medicine that is used to treat inflammatory conditions such as rheumatoid arthritis, psoriasis, and Crohn's disease. It is also used as a cancer treatment. Photosensitivity reactions are established side effects of methotrexate treatment and are currently listed in the product information, including the Patient Information Leaflet. However, the Pharmacovigilance Expert Advisory Group (PEAG) of the MHRA was concerned that it is not a well-known side effect and many patients may not be aware of the additional risks of sun exposure during methotrexate treatment. Prescribers and pharmacists are reminded to inform patients of the risk of photosensitivity reactions and to advise them to use a product with a high sun protection factor and clothing that covers the skin when in the sun. The MHRA is working with Marketing Authorisation Holders of methotrexate medicines to provide updates to the product information as appropriate.

Reference: Drug Safety Update, MHRA, 30 August 2023 (link to the source within www.gov.uk/mhra)

Ketamine Risk of prolonged use leads to severe liver and uro-nephrological damage

The ANSM is reminding health-care professionals by issuing a Direct Health-care Professional Communication (DHPC) that there is an increase in the number of hepatobiliary (cholestasis or cholangitis) and uro-nephrological (non-infectious cystitis, interstitial cystitis, acute renal failure, hydronephrosis), most often serious, after prolonged or repeated use of ketamine. Ketamine is a narcotic whose prescription is limited to 28 days. The ANSM reminded health-care professional to respect the recommended dosages of ketamine and to limit exposure over time, and monitor liver function, renal function and urinary cytology closely if taken repeatedly or over prolonged time.

Reference: Security information, ANSM, 30 August 2023

Pembrolizumab and Atezolizumab Potential risk of aplastic anaemia

Health Canada has announced that the product information for pembrolizumab (Keytruda®) and atezolizumab (Tecentriq®) is to be updated to include the potential risk of aplastic anaemia, as well as for the other products in the immune checkpoint inhibitors (ICIs) drug class that are not currently labelled for this risk (Bavencio®, Imfinzi®, Jemperli® and Libtayo®), to include the risk of aplastic anaemia. Pembrolizumab (Keytruda®) and atezolizumab (Tecentriq®) are anti-cancer agents belonging to a class of drugs called ICIs. They are authorized for sale to treat different types of cancers. Triggered by safety information received from the manufacturers and published cases in the scientific literature, Health Canada reviewed information from the Canada Vigilance database and published literature. Health Canada reviewed 12 cases (1 Canadian and 11 international) of aplastic anaemia in patients receiving Keytruda. Of those 12 cases, 1 was found to be probably linked to the use of Keytruda, 9 (1 Canadian) were found to be possibly linked, 1 was unlikely to be linked and 1 could not be assessed. Health Canada reviewed 2 international cases of aplastic anaemia in patients receiving Tecentriq. Both cases were found to be possibly linked to the use of Tecentriq. Health Canada also reviewed 9 articles published in the scientific literature reporting cases of aplastic anaemia with the use of Keytruda or Tecentriq. The evidence reviewed further supports the link between the risk of aplastic anaemia and the use of Keytruda or Tecentriq.

Reference: Health Product InfoWatch, Health Canada, 17 August 2023 (link to the source within www.hc-sc.gc.ca)