Drug Information Bulletin

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Content

Editorial

Access to essential medicines is a problem throughout the globe especially in the developing and under developed countries. India is not an exception, where only 35-50 percent of its population has access to essential medicines, though India is the third largest producer of medicines and is exporting to about 200 countries. Experts believe there are several complex reasons behind it. One of them is irrational use of medicines. Prescribing in generic name is considered as one of the important tools for improving rational use of medicines.

In India Central Government, several State Governments and some agencies have instructed the doctors under Govt. sector to prescribe in generic name but unfortunately it has not been strictly implemented.

Though a small fraction of our population is covered by govt. sector health facilities and mostly depends on private health care facilities, it was noticed that recently a few state Governments have taken stringent measures for its implementation. It is expected that it may bring tangible changes in improving the health care system in India.

Recently the Govt. of India proposed to amend the sec. 1.5 of "Indian Medical Council (Professional conduct, Etiquette and Ethics) Regulations 2002" as "Every Physician should prescribe drugs with generic names legibly and preferably in capital letters and he/she shall ensure that there is a rational prescription and use of drugs" and sought opinion from the general public. It is believed that this amendment will ensure that all doctors both Govt. and private sectors will be forced to prescribe in Prescribe name and in capital letters only. The suggestion should be sent at ali.rizvi@nic.in by 17.08.15. Hope all stake holders will send their opinion in favour of the amendment for improving access to medicine further.

Dr. Subhash C. Mandal
Editor

New Drug: Ofatumumab

Approved indication: B cell chronic lymphocytic leukaemia
Arzerra

100 mg/5 mL and 1000 mg/50 mL concentrate for infusion
Australian Medicines Handbook section 14.2.1

Chronic lymphocytic leukaemia is the most common adult leukaemia and is characterised by an accumulation of abnormal B lymphocytes. Ofatumumab adds to the growing number of treatments for this disease, including bendamustine (Aust Prescr 2014;37:214-21), chlorambucil, fludarabine (Aust Prescr 1995;18:86-7), rituximab (Aust Prescr 1999;22:20-3) and alemtuzumab (Aust Prescr 2006;29:167-71).

Ofatumumab is a human monoclonal antibody. Like rituximab, it binds to an epitope of CD20, which is expressed on B lymphocytes and B cell tumours. Binding to CD20 is thought to cause cell death mainly through complement-dependent cytotoxicity and antibody-dependent cell-mediated cytotoxicity.

Ofatumumab is approved for two indications in chronic lymphocytic leukaemia:

- first line in combination with chlorambucil or bendamustine for people who cannot have fludarabine
- as monotherapy for refractory disease.

First-line treatment when fludarabine cannot be given

In an open-label trial, ofatumumab added to chlorambucil was compared with chlorambucil alone in 447 previously untreated patients in whom fludarabine was contraindicated (e.g. due to age or comorbidities). They received treatment for a maximum of twelve 28-day cycles or for a minimum of three months. Ofatumumab was given intravenously (300 mg on day 1 and 1000 mg on day 8 for the first cycle, followed by 1000 mg on day 1 of subsequent cycles) and chlorambucil was given orally (10 mg/m^2 on days 1–7 of each cycle). Progression-free survival was statistically longer with ofatumumab and chlorambucil compared to chlorambucil alone (22.4 months vs 13.1 months). The overall response rate was also higher with combination treatment than with chlorambucil alone (82% vs 69%). This trial is currently unpublished.

In a single-arm trial, the same dose of ofatumumab was combined with bendamustine (90 mg/m^2 intravenously on days 1–2 of each 28-day cycle) in 44 previously untreated people who could not have fludarabine. After a median of six cycles, almost all patients had responded with 43% of them having a complete response. This trial has also not yet been published.

Refractory disease: Ofatumumab monotherapy is also approved for patients whose disease is refractory to fludarabine and alemtuzumab. Survival of these patients is often less than a year. In an open-label dose-escalation study, 33 patients were given weekly intravenous infusions for four weeks. There were three different ofatumumab regimens – one 100 mg dose followed by three 500 mg doses (3 patients), one 300 mg dose followed by three 1000 mg doses (3 patients), or one 500 mg dose followed by three 2000 mg doses (27 patients).1 After 19 weeks, one patient in the lowest dose group and 13 patients in the highest dose group had a partial remission. Although two patients maintained their response until week 27, the others had progressive disease. Overall, the median progression-free survival was approximately 3.5 months.

By the end of treatment, malignant B cells in peripheral blood had decreased by a median of 97% (15–100%) in patients given the highest ofatumumab dose. Normal B cells were also depleted and this was sustained until week 24, after which cell numbers started to increase.1

In another trial, the efficacy of ofatumumab was assessed in a subset of 59 patients with

disease refractory to fludarabine and alemtuzumab. Participants were given eight weekly infusions then monthly infusions for four months (first dose of 300 mg followed by 2000 mg doses). After 24 weeks, 58% of these patients had responded to treatment – all were partial responses. Median progression-free survival was 5.7 months (4.5–8 months) and median overall survival was 13.7 months.2

Safety and precautions: In 138 people who received monotherapy for refractory disease, almost two-thirds had an infusion-related reaction to ofatumumab. These were mostly mild to moderate and occurred during the first and second infusion. Other common adverse events included infection (67% of patients), cough (18%), diarrhoea (16%), anaemia (16%), fatigue (15%), fever (15%), neutropenia (15%), dyspnoea (13%), nausea (11%) and rash (10%). Overall, 37 of the infections were serious and 13 that started during treatment led to death. Six deaths were due to sepsis, five to pneumonia, one to *Fusarium* infection and one to progressive multifocal leukoencephalopathy.2

In 261 people who received ofatumumab with chlorambucil or bendamustine, neutropenia was the most common event (31%) and was serious in most cases. Nausea (25%), rash (25%), fever (22%), diarrhoea (17%), fatigue (16%), cough (15%), pruritus (13%), vomiting (12%), dyspnoea (11%), headache (10%) and urticaria (10%) were also frequently reported.

As with monotherapy, infusion-related reactions were very common during the first cycle of combination therapy and were the reason for stopping treatment in 3% of patients. Because of this risk, which can include serious effects such as respiratory and cardiac problems, premedication with an analgesic, an antihistamine and a corticosteroid is recommended, particularly at the beginning of therapy. The first and second infusions should be given more slowly, starting at 12 mL/hour. The rate can be increased later if reactions do not occur.

As cytopenias are common, blood counts (including platelets) should be monitored regularly. Because ofatumumab reduces the number of B lymphocytes, there is an increased risk of infection. Neurological symptoms such as confusion, dizziness, loss of balance, difficulty with walking or talking could be a sign of progressive multifocal leukoencephalopathy and should be investigated further. There is also a risk of hepatitis B reactivation, so people with evidence of previous infection should be monitored during and for 6–12 months after treatment. Live vaccines are not recommended.

Conclusion: Ofatumumab as monotherapy for refractory disease, or in combination with chlorambucil or bendamustine when fludarabine cannot be given, seems to prolong progression-free survival in people with chronic lymphocytic leukaemia. Premedication is recommended to reduce infusion-related reactions, particularly at the beginning of treatment. Prescribers should be aware that progressive multifocal leukoencephalopathy can occur with this drug.

References:

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2. Wierda WG, Kipps TJ, Mayer J, Stilgenbauer S, Williams CD, Hellmann A, et al. Ofatumumab as single-agent CD20 immunotherapy in fludarabine-refractory chronic lymphocytic leukemia. J Clin Oncol 2010;28:1749-55.

Ref. Aust Prescr 2015;38:Aust Prescr 2015;38:138-42

FDA extends prescription drug track, trace deadline

The deadline for complying with the Drug Supply Chain Security Act was extended

by the FDA from July 1 to Nov. 1 because more time is needed to adopt electronic platforms that are capable of collecting and managing prescription drug tracking data. To comply with the law, tracing files should be maintained by dispensers or portal vendors to monitor the distribution of prescription treatments across the country. The law also requires drugmakers, dispensers, repackagers and wholesale distributors to collaborate with the FDA to design an interoperable track-and-trace system within the next decade.
For Details: Healthcare IT News

Biosimilar of blood cancer and arthritis drug is introduced in India

Hyderabad based Hetero pharma has launched biosimilar drug Rituximab under the brand name of MABALL, used in the treatment of blood cancer. Hetero will be competing with Intas, Dr Reddys who have biosimilar brand of this product. Rituximab was originally developed by Swiss drug maker Roche and is also used in treatment of rheumatoid arthritis.

Hetero will launch a single dose vial of

Government mulls providing over 50 essential drugs at cheaper rates

The Indian Government is mulling providing more than 50 essential drugs, including those used in treatment of cancer and AIDS, at cheaper rates to a large section of the population, Union Minister Ananth Kumar said on Wednesday.

As of now, the government keeps a tab on the prices of essential medicines which are included in the National List of Essential Medicines (NLEM).

"..there are about 100 crore people in the country who are either below poverty line, or in low income group or in middle income group. So there is need to ensure health security for such people," Minister of Chemicals and Fertilisers Ananth Kumar said at an event on Wednesday .

"Therefore we would like to provide them drug security and for that we need to provide 50-55 such medicines which are used to cure cough, viral, flu, typhoid, diabetes, hypertension, HIV AIDS and cancer.

"These 50-55 medicines are very essential and we need a bracket of such 50-55 medicines which should be provided at cheaper rates and are of good quality. Therefore the government is looking into this and exploring this," Kumar stated.

The minister also emphasized that for the sake of health security there is need to re-energise and revive the sick pharma PSUs and said that the government is working on it. Besides this, there is also need to bring medical devices under the list of NLEM to keep a check on their prices, he added.

Meanwhile, as per Drug Price Control Order (DPCO), 2013, NPPA fixes ceiling prices of the medicines under NLEM and no person is authorised to sell them at a price exceeding the price notified by NPPA

Forthcoming Event

75th FIP World Congress of Pharmacy and Pharmaceutical Sciences 2015

Düsseldorf, Germany • 29 September - 3 October 2015

Better practice – Science based, evidence driven

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