



Drug Information Bulletin

Drug Information Centre (DIC)

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Editorial

In the recent past a few Pharmacy Councils have taken some steps against violations like- dispensing by a person other than a pharmacist, engaging a Pharmacist more than one place at a time is a silver line, when profession is crying for stringent implementation of the Pharmacy Act and Pharmacy Practice Regulation -2015 (PPR-2015).

Engagement of Pharmacist in serving the prescription of a registered practitioner has been made mandatory by an amendment of sec 42 of Pharmacy Act 1940, in the year of 1984 and it was further bolstered by the amendment of Rule 65 of Drugs and Cosmetics Rules 1945 in the same year. Dispensing by pharmacists is mandatory worldwide for better health care services.

Promulgation and notification of Pharmacy Practice Regulation 2015 in the month of January 2015 by Pharmacy Council of India (PCI) is a landmark event in the history of Pharmaceutical Profession in India, which will certainly help in giving proper shape to the unorganized state of Pharmacy Practice in India. In the present regulation the Pharmacy Practice is well defined and the same has set up certain regulation to regulate the same.

Indian Pharmaceutical Association has requested all State Health Secretaries and all state Drugs Controllers time and again for proper implementation of PPR-2015, but there is no positive result. Hope all other professional organizations will also take up the matter for its implementation for the sake of improving public health.



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New Drug: Carfilzomib for multiple myeloma

Approved indication: multiple myeloma
vials containing 30 mg and 60 mg powder
Australian Medicines Handbook section 14.1.8

Carfilzomib is a new intravenous drug for multiple myeloma. It is indicated for people with relapsed or refractory disease after at least one previous therapy. It should be given in combination with dexamethasone or with lenalidomide and dexamethasone.

Like bortezomib, carfilzomib is a proteasome inhibitor. It works by interfering with the system for breaking down proteins within cells. As cancer cells are rapidly multiplying, inhibiting proteasomes causes proteins to accumulate. In vitro and animal studies, this slows cell growth and eventually causes cell death.

The approval of carfilzomib is based on two randomised open-label trials – ASPIRE¹ and ENDEAVOR.² The trials enrolled people who had been treated with 1–3 previous therapies.

In the ASPIRE study, carfilzomib with lenalidomide and dexamethasone was compared to lenalidomide and dexamethasone alone for 18 treatment cycles. Patients who had previously progressed on bortezomib or lenalidomide with dexamethasone, or had previously discontinued lenalidomide and dexamethasone because of an adverse effect, were not allowed in the trial.¹

The progression-free survival of patients was longer when carfilzomib was added to lenalidomide and dexamethasone compared with those given lenalidomide and dexamethasone alone (26.3 vs 17.6 months, $p=0.0001$). Also more patients in the carfilzomib arm had at least a partial response to treatment (87.1 vs 66.7%, $p<0.001$).

Diarrhoea (42.3% vs 33.7%), thrombocytopenia (29.3% vs 22.9%), cough (28.8% vs 17.7%), fever (28.6% vs 20.8%), upper respiratory tract infection (28.6% vs 19.5%), hypokalaemia (27.6% vs 13.4%), hypertension (14.5% vs 7.5%), and headache (13.5% vs 8%) were more common with carfilzomib than with the comparator.¹

In the ENDEAVOR study, carfilzomib plus dexamethasone was compared to bortezomib plus dexamethasone. Although patients who had

previously been treated with carfilzomib or bortezomib were allowed in the trial, they must have had at least a partial response to the treatment before relapse and not discontinued because of an adverse effect.²

As in the ASPIRE trial, progression-free survival was significantly longer in the carfilzomib arm compared with the comparator (18.7 vs 9.4 months, $p<0.0001$). Overall response rates were also higher (76.9 vs 62.6%, $p<0.0001$).²

Anaemia (40.8% vs 27.6% of patients), fever (31.3% vs 14.7%), dyspnoea (30.5% vs 13.2%), hypertension (29.8% vs 9.6%), cough (26.1% vs 14.9%), muscle spasms (19.7% vs 6.1%), and bronchitis (21.4% vs 10.1%) were more frequent with carfilzomib than with bortezomib.²

Cardiac failure (7%) was reported with carfilzomib in the trials, as was myocardial infarction (2%) and myocardial ischaemia (1%). Some of these cases were fatal. Other serious and potentially life-threatening adverse events with carfilzomib include pulmonary and hepatic toxicities, pulmonary hypertension, dyspnoea, hypertension, acute renal failure, tumour lysis syndrome, infusion reactions, thrombocytopenia, posterior reversible encephalopathy syndrome and thrombotic microangiopathy. Patients need to be closely monitored during treatment and the dose of carfilzomib may need to be reduced or stopped until symptoms have resolved. Checking hydration, fluid requirements and electrolytes is important.

This drug is not recommended during pregnancy and contraception should be used during treatment. There are no data in humans but carfilzomib caused embryo-fetal toxicity in pregnant rabbits. It is not known if the drug is excreted in breast milk.

Carfilzomib is administered in 28-day cycles. An intravenous infusion is given on two consecutive days each week for three weeks followed by a 12-day rest period. After administration, carfilzomib is rapidly metabolised by peptidase cleavage and epoxide hydrolysis and the inactive metabolites are excreted in the urine. On the basis of preliminary data, interactions with other medicines are not expected.

Consider giving patients antiviral prophylaxis to prevent herpes zoster infection.

Thromboprophylaxis is recommended in patients also receiving lenalidomide and dexamethasone depending on their risk.

More than 75% of pre-treated patients appeared to respond to carfilzomib when given as combination therapy. However, it is not yet known if it will extend survival. Toxicity may limit treatment and fatal reactions can occasionally occur so monitoring is paramount.

References:

1. Stewart AK, Rajkumar SV, Dimopoulos MA, Masszi T, Špička I, Oriol A, et al; ASPIRE Investigators. Carfilzomib, lenalidomide and dexamethasone for relapsed multiple myeloma. *N Engl J Med* 2015;372:142-52.
2. Dimopoulos MA, Moreau P, Palumbo A, Joshua D, Pour L, Hájek R, et al; ENDEAVOR Investigators. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOUR): a randomised, phase 3, open-label, multicentre study. *Lancet Oncol* 2016;17:27-38.

Source: Australian Prescriber, Vol. 41, issue 2.

Status in India: Carfilzomib Sterile Lyophilized Powder for Injection 60mg/vial (50ml vial) was approved by the CDSCO for marketing and manufacturing in India on 17.01.2017. For relapsed or refractory multiple myeloma-

- Carfilzomib for injection is indicated in combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.
- Carfilzomib for injection is indicated as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

IPC discusses strategy with research institutions for using ADR info for health research

The Indian Pharmacopoeia Commission (IPC) is in talks with health research institutions like Indian Council of Medical Research (ICMR), Department

of Biotechnology (DBT) and Council of Scientific and Industrial Research (CSIR) for devising strategies for effective use of adverse drug reactions (ADRs) information for health research in Indian population for patient safety.

The ADR data is currently collected through 250 ADR monitoring centres (AMCs) across the country as part of pharmacovigilance programme of India (PvPI) launched by Central Drugs Standard Control organisation (CDSCO) in July 2010 with Ghaziabad-based IPC as the national co-ordinating centre (NCC).

Simultaneously, as part of the strategy, the union health ministry is also planning to strengthen the existing AMCs to increase ADR monitoring and get pan India ADR information effectively.

Explains IPC Scientific Director Dr G N Singh, "The emphasis is on how ADR data can be used for research through data mining and also developing information technology tools and apps for better monitoring and reporting through adverse drug reaction monitoring centres in the country as part of the PvPI."

IPC will further take PvPI forward in hospitals across the country so that it could also be implemented at PHC and taluka-level health centres to get pan India qualitative and substantive ADR information. As of today, there are in total 250 AMCs in the country. Around 40 AMCs were established last year at district hospitals based in the North Eastern part of India, Uttar Pradesh and Himachal Pradesh. Union health ministry is aggressively planning to explore possibilities of identifying district hospitals across the country to be developed as AMCs.

Medical colleges, hospitals and institutes approved by the Medical Council of India (MCI) can act as AMCs. Once enrolled, they are required to efficiently collect the ADR information from the patients, do follow up with them to check the completeness of the ADR reports.

IPC serves as a nodal agency for the AMCs. The registered AMCs across the country play an important role in timely reporting of ADRs to IPC. Once enrolled, IPC also provides logistical and technical support to AMCs for their smooth functioning.

Source: Pharmabiz

Maharashtra FDA proposes registration of Ayurvedic Medicine Shops

The Maharashtra Food and Drug Administration (FDA) has proposed to make registration of shops selling Ayurvedic drugs mandatory, an official said today.

"We have sent a proposal to the government. The move is aimed at bringing standardisation and put a check on adulteration of Ayurvedic medicines," said Nitin Deore, Assistant Commissioner (Drugs), FDA.

"There are an estimated five lakh shops in the state which sell Ayurvedic medicines. But these are not registered with the FDA. They only obtain a license under the Shop Act from local governing bodies, which doesn't ensure quality of the products sold," Deore told PTI.

"Most of the time, Ayurvedic drug consumption is a kind of self-medication. Many people take Ayurvedic drugs without prescriptions," he said, adding that hence registration of shops selling

them with the FDA is necessary.

The FDA has recommended charging a fee of Rs 2,500 for registration, which will have to be renewed every five years, official said.

Source: Business Standard

Recommendations on stent use for unruptured aneurysms issued by FDA

A series of recommendations on the safe and effective use of neurovascular stents for stent-assisted coiling of unruptured aneurysms was released by the FDA to health care providers after reports of periprocedural events associated with the devices. The recommendations include cautious selection of patients and stents and careful observation of microguide wires and microcatheters during procedures, as well as discussing risks and alternate treatments with patients, among other recommendations.

Ref.: [Medscape \(free registration\)](#)



Padmashri Mr. Dilip Shanghvi is being greeted by Indian Pharmaceutical Congress Association (IPCA) members on his assuming the post of IPCA President. 70th Indian Pharmaceutical Congress will be held at Amity University, Noida during 21-23 December 2018

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