# Drug Information Bulletin

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## Content



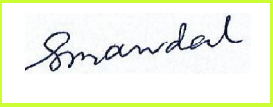
## Editorial

Notification by Govt. of India directing all Pharmacy, Chemist and Druggist dispensing anti-tubercular medicines, shall notify respective tuberculosis patients along with details of medicines to local Public Health Authority, namely, District Health Officer or Chief Medical Officer of a District and Municipal Health Officer of urban local bodies in whatever way they are known; or their designated District Tuberculosis Officers.

Pharmacy, Chemist and Druggist, failing to notify may attract the provisions of sections 269 and 270 of the Indian Penal Code (45 of 1860), as the case may be, which are reproduced below: "269. Negligent act likely to spread infection of disease dangerous to life. - Whoever unlawfully or negligently does any act which is, and which he knows or has reason to believe to be, likely to spread the infection of any disease dangerous to life, shall be punished with imprisonment of either description for a term which may extend to six months, or with fine, or with both. 270. Malignant act likely to spread infection of disease dangerous to life. - Whoever malignantly does any act which is, and which he knows or has reason to believe to be, likely to spread the infection of any disease dangerous to life, shall be punished with imprisonment of either description for a term which may extend to two years, or with fine, or with both." This is an appropriate step to ensure proper tuberculosis diagnosis and its management in patients and their contacts and to reduce tuberculosis transmission and further to address the problems of emergence and spread of Drug Resistant-Tuberculosis, it is essential to collect complete information of all tuberculosis patients.

This direction is also applicable for Medical Practitioners and Medical Laboratories as notified vide F.No. Z-28015/2/2012-TB dtd. 16th March 2018 (available at: http://www.cdsco.nic.in/writereaddata/management%20in%20patients.pdf ).

This is a golden opportunity for the pharmacists engaged in community pharmacy to establish them as one of the important health care provider.

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## China approves antiviral Favilavir to treat coronavirus

Regulatory officials in China announced recently that they have approved the antiviral Favilavir for use in the treatment of the novel coronavirus COVID-19.

The approval by the National Medical Products Administration was based on the drug's efficacy against the virus in clinical trials started in response to the ongoing outbreak, which has sickened more than 70,000 people globally. The vast majority of the cases have been identified in Hubei province, China.

Specific results of the clinical trial involving favilavir, formerly known as fapilavir, have not been released. The drug was tested in 70 patients with confirmed COVID-19 infection in the city of Shenzhen.

The drug, developed in China by Zhejiang Hisun Pharmaceutical Company originally to treat catarrhal, or inflammation of the nose and throat, is one of three currently being investigated for possible use in the treatment of COVID-19.

The company has begun producing the drug in large quantities to meet the demand created by the outbreak, though it is not the only one being investigated for use against COVID-19.

Another drug option, remdesivir, is being developed by U.S. drugmaker Gilead. Originally intended to treat Ebola virus, remdesivir has reportedly been used to treat one American sickened with COVID-19, and the patient in question has recovered fully.

However, the drug is still undergoing clinical trials and has not yet been approved to treat either COVID-19 or Ebola.

Meanwhile, doctors in South Korea have reported that they have used the HIV combination drug lopinavir plus ritonavir -- marketed as Kaletra -- to successfully treat COVID-19 in a 54-year-old patient.

Researchers in China have also asked patients who have fully recovered from COVID-19 to donate their blood plasma for possible use as the basis of a new treatment for the virus. Mike Ryan, executive director of the World Health Organization's Emergencies Program, said Monday the approach, known as hyperimmune globulin therapy, has been used for decades to in the treatment of viral diseases, including diphtheria.

The theory is that those who have recovered from viral infections have antibodies against the disease in their blood, and that those antibodies can be passed on to others who have been infected via transfusion, providing their immune system with a needed "boost," he explained. However, the key to its effectiveness is timing -- transfusions need to be performed early enough in the course of the disease for the antibodies to work. Chinese researchers started clinical trials of the approach in COVID-19 patients last week."It's an important area to pursue, but it's not always successful," Ryan added.

For details: https://www.upi.com/Health_News/2020/02/17/China-approves-antiviral-favilavir-to-treat-coronavirus/5291581953892/?sl=2

## WHO: Coronavirus vaccine could be ready in 18 months

The World Health Organization said the first vaccine for the emerging coronavirus, now called COVID-19, could be available in 18 months. WHO Director-General Dr. Tedros Adhanom Ghebreyesus said the outbreak holds "a very grave threat for the rest of the world" though 99% of the cases are in China.

**For details:** Fox News

## New Drug: Tisagenlecleucel for B-cell cancers

Approved indication: B-cell cancers

Kymriah (Novartis)

infusion bag containing modified autologous T cells

Tisagenlecleucel is a genetically modified cell therapy developed for relapsed and refractory B-cell cancers. It is specifically approved for children and young adults (≤25 years old) with B-cell precursor acute lymphoblastic leukaemia, and for adults with diffuse large B-cell lymphoma (the most common form of non-Hodgkin lymphoma).

This product is prepared using the patient's own T cells. These are harvested from blood, then, in the laboratory, a transgene is introduced which encodes a protein called chimeric antigen receptor (CAR). This receptor is expressed on the surface of the T cells and allows them to bind to the CD19 antigen on B cells and precursor B cells.

This binding activates inflammatory cytokines and destroys the CD19-positive cells.

Before the modified T cells are administered, the patient is given a short course of chemotherapy (2–4 days) to deplete their lymphocytes. To reduce the risk of an infusion reaction to tisagenlecleucel, patients are given paracetamol and an antihistamine 30–60 minutes beforehand.

Following lymphodepleting chemotherapy, participants were given a single infusion of tisagenlecleucel (median dose of 3.1 x $10^6$ T cells/kg). The primary end point of the trial was an overall remission rate of more than 20%. This was defined as complete remission or complete remission with incomplete blood count recovery that lasted for at least 28 days.

In patients with at least three months follow-up, the remission rate was 81%. The event-free survival rate was 73% at six months and 50% at 12 months. The overall survival rate was 90% at six months and 76% at 12 months.[1]

In the other trial, tisagenlecleucel was assessed in 93 adults with relapsed or refractory diffuse large B-cell lymphoma.[2] The participants had previously received at least two lines of therapy.

After lymphodepleting therapy, patients were given a median of 3.0 x $10^8$ cells by infusion. The best overall response was 52% (40% had a complete response and 12% had a partial response). The estimated probability of overall survival at 12 months was 49%. In those who had a complete response, this was 90%.[2]

Tisagenlecleucel has several serious and sometimes fatal adverse effects. Patients need to be closely monitored in the first week after infusion and need to stay within two hours of the facility where they received the infusion for the first month.

Cytokine release syndrome is very common with tisagenlecleucel. This is an inflammatory reaction that can cause hypotension, pulmonary oedema and coagulopathy and result in multiorgan failure. In the leukaemia trial, 81% of patients in the safety cohort developed cytokine release syndrome – 44% of these cases were severe. In the lymphoma trial, 58% of patients were affected including 22% who were severely affected. The median onset of these reactions was three days and their duration was 7–8 days. The anti-interleukin-6 antibody, tocilizumab, can be used to treat moderate to severe cases. A minimum of four doses of the drug should be kept on hand before the infusion is started. Corticosteroids may be used in life-threatening cases. Emergency equipment should also be available. Risk factors for severe cytokine release syndrome in leukaemia patients include high tumour burden, progressive disease following lymphodepleting therapy, infection and fever.

Encephalopathy and confusion or delirium were frequently reported – 38% in the leukaemia trial and 21% in the lymphoma trial. Headache was also very common in both trials (35% and 23%), as were nausea, diarrhoea, hypotension, tachycardia, acute kidney injury and hypokalaemia. A third of children and young adults with leukaemia had elevated liver enzymes.

In the leukaemia study, there were seven deaths that were not related to disease progression. Two of them occurred within 30 days of the infusion. Causes included embolic stroke related to mycosis, cerebral haemorrhage (in the context of coagulopathy and resolving cytokine release syndrome), encephalitis after prolonged neutropenia and lymphopenia, and mycosis.

There were eight deaths in the lymphoma trial that were not related to disease progression. They all occurred at least 30 days after the infusion. Causes included multiple organ failure, cerebral haemorrhage, haemorrhage of a duodenal ulcer, pulmonary haemorrhage, chronic kidney disease, neuroendocrine carcinoma and sepsis.

Treatment with tisagenlecleucel should be delayed if someone has unresolved adverse effects from chemotherapy, uncontrolled infection, graft versus host disease, or rapidly progressing leukaemia or lymphoma. There is limited experience with this drug in patients who have active leukaemia or lymphoma in the CNS.

Treatment is not recommended in people with HIV or hepatitis B or C. Live vaccines should not be given for at least six weeks before tisagenlecleucel therapy and until the patient's

immune system has recovered following treatment.

After administration of tisagenlecleucel, the modified T cells undergo clonal expansion followed by a slow decline. The tisagenlecleucel transgene has been shown to persist in blood and bone marrow for up to two years after the infusion in some patients.

Tisagenlecleucel is the first chimeric antigen receptor therapy to be approved in Australia. Although response rates seemed high (81% in acute lymphoblastic leukaemia and 52% in lymphoma), it is hard to quantify efficacy as there were no comparators in the trials. Doctors and their patients also need to consider the serious and life-threatening toxicities that can occur with this therapy.

**References:**


1. Maude SL, Laetsch TW, Buechner J, Rives S, Boyer M, Bittencourt H, et al. Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia. N Engl J Med 2018;378:439-48.
2. Schuster SJ, Bishop MR, Tam CS, Waller EK, Borchmann P, McGuirk JP, et al. Tisagenlecleucel in adult relapsed or refractory diffuse large B-cell lymphoma. N Engl J Med 2019;380:45-56.


Ref. Australian Prescriber

## 8,700 Pharma Cos Claimed Tax Deductions for 'Gifts'

Pharma companies often refute allegations that doctors and chemists are sought to be "influenced" to push specific medicine brands, costly alternatives and even needless prescriptions but the evidence is out that this does not prevent them from claiming tax deductions on such expenses.

Around 8,667 pharmaceutical companies claimed income tax deduction under "sales promotion expenses" and "gifts" during 2019-20, the income tax department informed the Madras high court in response to a suo motu case taken up by the court against such unethical marketing practices.

"Though details have been given, it is evident from details furnished by the Income Tax department that about 1,410 companies during the assessment year 2019-20 (ITR-3), 1,915 companies during the assessment year 2019-20 (ITR-5) and 5,342 companies during assessment year 2019-20 (ITR-6) alone claimed deduction under "Sales Promotion Expenses" and 'Gift'," a two-judge bench comprising of N Kirubakaran and P Velmurugan said in a February 17 order.

Interestingly, the irregularities initially came to light in a tax dispute case between a pharmaceutical company and the I-T department. While the company wanted to pass the overcharged amounts as mere excess amount collected from consumers and dubbed them as refunds to the drug regulator, the tax authorities said overcharging is a violation of law and the amount paid to the National Pharmaceutical Pricing Authority (NPPA) was actually a penalty.

The judges said, "It is shocking and surprising to note that the company claimed deduction from Income Tax for the amount spent towards sale promotion expenses as well as for licences & taxes."

Information provided by the I-T department, prompted the court to take up the issue of unethical marketing practices by pharma companies. In an earlier order, the court said "promotional expenses including payment to the doctors" is "nothing but bribing".

"It is clear that even though it is prohibited under law, the pharmaceutical companies are still promoting their drugs by providing gifts, travel facilities, hospitality, cash or monetary grant to the doctors. It is also proved that drugs are overpriced illegally by the companies," one of the orders said pulling up companies for such practices.

The HC directed the I-T department to submit details about such claims made by companies, names of doctors as well as penalties paid by companies for drug overpricing.

Source: The Times of India