KASTURBA MEDICAL COLLEGE
MANIPAL
(A constituent unit of MAHE, Manipal)

THE DRUG TIMES

Newsletter from Department of Pharmacology, Kasturba Medical College, Manipal
Issue 4, December 2021

This issue of DRUG TIMES provides information about Omicron variant of corona virus, current status of COVID-19 vaccines and newly authorized drugs, their approval status in children and adolescents, medical device and drug safety alerts, FDA new drug approvals and history of chloroquine.

Omicron

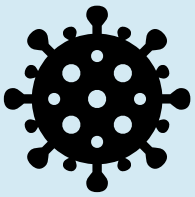
SARS-CoV-2 **V**irus **E**volution is being studied by a group of experts who form the **T**echnical **A**dvisory **G**roup (TAG-VE). They intermittently monitor and evaluate progression of SARS-CoV-2 to see if specific mutations/combinations of mutations alter the behaviour of the virus. A SARS-CoV-2 variant of interest (**VOI)** is one with genetic changes that affect characteristics of virus and is identified as causing significant community transmission in multiple countries signifying a developing risk to global public health. A SARS-CoV-2 variant of concern (**VOC)** is one that meets the description of a VOI and is found to be associated with one or more of the following changes:

- Increase in transmissibility or detrimental change in COVID-19 epidemiology; OR
- Increase in virulence or change in clinical disease presentation; OR
- Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics

TAG-VE assembled on 26th November 2021 to evaluate the SARS-CoV-2 variant: B.1.1.529. The first established B.1.1.529 infection was from a specimen collected on 9th November 2021 and was first reported to WHO on 24th November 2021. WHO has voted B.1.1.529 as a VOC and named it Omicron.

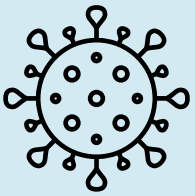
What do we know about Omicron?

Transmissibility: Omicron appears more transmissible based on worldwide data. The number of people testing positive with this variant initially increased in areas of South Africa and is now seen globally.



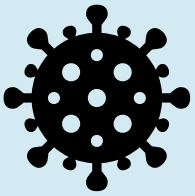
Severity of disease: Various data suggest an increasing rate of hospitalization. This can be due to large number of infected people, rather than a specific infection with Omicron. Till date, sufficient data which suggests that symptoms associated with Omicron are different from other variants, are lacking.

Effectiveness of prior SARS-CoV-2 infection: As per the current information, increased risk of reinfection with Omicron has been suggested by earlier studies as compared to other variants of concern.



Effectiveness of vaccines: Current vaccines remain effective against severe disease and death.

Effectiveness of current tests: PCR tests continue to detect infection with Omicron. S gene target failure (SGTF) or S gene dropout due to loss at Spike position 69-70 has been reported. Diagnostic tests using the SGTF approach may lead to faster detection rates.



Effectiveness of current treatments: The patients with severe COVID-19 can still be managed with Corticosteroids and IL6 Receptor Blockers.

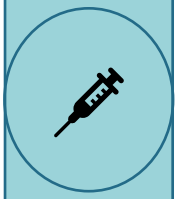
Studies underway: Currently WHO is coordinating with researchers worldwide to comprehend transmissibility, severity, role of vaccines and diagnostic tests, and effective treatments for Omicron.

https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern

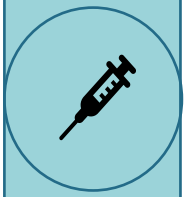
https://www.who.int/news/item/28-11-2021-update-on-omicron

COVID-19 vaccines till date

16th January 2021 marked the beginning of COVID 19 vaccination in our country. On 21st October 2021, by crossing the 100-crore mark cumulative vaccination, our country has achieved a significant landmark in its battle against Covid-19. Below is a list of all the vaccines approved till date for emergency use by WHO and India in both adult, children and adolescent category.



Vaccine	WHO-EUA	India-EUA	Adult(>18yrs)	Children & Adolescents*
#Comirnaty	✓		✓	✓ (5-17yrs)
Covishield	✓	✓	✓	
Janssen	✓	✓	✓	
#Moderna	✓	✓	✓	✓(12-17yrs)
Sinopharm	✓		✓	
Sinovac-CoronaVac	✓		✓	✓(3-17yrs)
Covaxin	✓	✓	✓	✓(12-17yrs)
Sputnik V		✓		
$ZycovD		✓		✓ (12-17yrs)
$Covovax	✓	✓	✓	
$Corbevax		✓	✓	
Nuvaxovid	✓		✓	



Emergency use authorization by different countries for children and adolescents.

#Maybe discontinued in India due to domestic output of more affordable and easier-to-store vaccines.

$Has obtained EUA but yet to be deployed for mass immunization in India.

The latest to join the list are vaccines Covovax, Corbevax and Nuvaxovid. The Serum Institute of India under licence from Novavax have produced NVX-CoV2373/Covovax which got its WHO approval on 17th December 2021 and DCGI approval on 28th December 2021. Nuvaxovid, the originator product for Covovax received WHO approval on 21st December 2021. Corbevax is a protein subunit vaccine developed by Indian Biopharmaceutical firm Biological E Ltd and got approved by DCGI on 28th December 2021.

Health, frontline workers and elderly with comorbidities or other health problems will start receiving booster shots provided they have completed 9 months or 39 weeks from the date of second dose. Vaccination will also be started for children between 15 and 18yrs from January 2022 as per the guidelines to date.

A sero-survey in India during June-July 2021 found that all age group children could become infected as well as spread the virus. Some countries have reported rare incidence of myocarditis/pericarditis with mRNA COVID-19 vaccines. The Global Advisory Committee on Vaccine Safety in October 2021 found that the benefits of mRNA COVID-19 vaccines outweigh the risks with regard to hospitalization and deaths in all age groups.

It is not vaccines that will stop the pandemic, but vaccination. With this in mind a worldwide initiative called COVAX (Covid 19 Vaccines global access) was launched under the joint directive of GAVI (Global Alliance for Vaccines and Immunization), CEPI and WHO to ensure equitable access to vaccines, and make sure that all nations can protect their people initiating with the vulnerable population.

https://cdsco.gov.in/opencms/opencms/en/biologicals/Vaccines/

https://www.who.int/news/item/17-12-2021-who-lists-9th-covid-19-vaccine-for-emergency-use-with-aim-to-increase-access-to-vaccination-in-lower-income-countries

New pills on the block

As the battle against Covid 19 continues, it is welcome to have more drugs to combat the same. USFDA has paved a new way by authorizing the first oral antiviral drugs in the treatment of Covid 19. Here are the details of these drugs.

	Paxlovid (Nirmatrelvir & Ritonavir)	**Molnupiravir**
Indication	Mild to moderate coronavirus disease in adults and children above 12yrs and weighing ≥ 40Kg	Mild to moderate coronavirus disease in adults only
Mechanism of action	"Nirmatrelvir inhibits a SARS-CoV-2 protein and stops the virus replication and ritonavir slows down metabolism of nirmatrelvir causing high concentration and thus prolonging its action"	"Introduces errors into the SARS-CoV-2 virus genetic code and prevents further virus replication"
Dosage	3 tablets (2 tablets of nirmatrelvir 150mg each and 1 capsule of ritonavir 100mg) taken together orally every 12th hourly for 5 days	4 capsules 200mg each taken orally every 12th hourly for 5 days
Adverse effects	Impaired sense of taste, diarrhoea, high blood pressure, muscle aches	Diarrhoea, nausea, dizziness
Clinical trial	EPIC-HR	MOVe-OUT
Outcome of the trial	"0.8% of the 1039 patients who received Paxlovid were hospitalized or died during 28 days of follow-up compared to 6% of the 1046 patients who received placebo"	"6.8% of the 709 people who received molnupiravir were hospitalized or died during 29 days of follow-up compared to 9.7% of the 699 people who received a placebo"

Following points have to be kept in mind regarding these drugs.

1. Safety and effectiveness continue to be evaluated for the treatment of COVID-19.
2. For pre-exposure/post-exposure prevention of COVID-19 or beginning of treatment due to severe COVID-19, they are not authorized.
3. In individuals for whom COVID-19 vaccination and a booster dose are recommended, they are not a substitute.

https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-oral-antiviral-treatment-covid-19

https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-oral-antiviral-treatment-covid-19-certain

Medical device alert

Monitoring of events associated with below mentioned medical devices by health care professionals and if found, reporting to NCC - MVPI is solicited.

Medical device name	**Event details**
TENDRIL STS (Pacing system analyzer)	Lead Impedance, threshold related issue, lead related issues and screw related issue during use
PROGLIDE	Oozing, hematomas, prolonged hospitalization
XIENCE XPEDITION Drug Eluting Stent	Balloon would not deflate during use, malfunctioning of the device
Antero medial distal femur locking plate	Device break
Panbio COVID-19 Ag rapid test device	False negative result

-As received from Materiovigilance Programme Of India

Drug Safety Alerts (PvPI)

Listed below are Suspected and Unexpected Serious Adverse Reactions (SUSARs) from the Pharmacovigilance Program of India (PvPI) database (Sep - Dec 2021) seen with drugs that are commonly prescribed. Health care professionals are advised to closely monitor the possibility of the below adverse drug reactions (ADRs) and if encountered, should be reported.

Suspected Drugs	**Indications**	**Adverse Drug Reactions**
Sofosbuvir	Chronic hepatitis C treatment along with other drugs	Stevens-Johnson Syndrome
Cefazolin	Respiratory tract infections, UTI, skin & soft tissues infection, septicaemia and other infections caused by susceptible organisms	Acute Generalised Exanthematous Pustulosis

Dimethyl Fumarate	Multiple sclerosis- relapse and remitting cases	Alopecia
Diclofenac	Chronic painful conditions like arthritis, ankylosing spondylitis, gout, dental pain post-operative pain, migraine attack	Skin hyperpigmentation

https://www.ipc.gov.in/mandates/pvpi/pvpi-updates/8-category-en/812-drug-alerts-2021.html

New Drug Approvals

The following drugs were approved by the US-FDA (30th July- 30th Nov, 2021):

DRUG NAME	APPROVAL DATE	INDICATION
Anifrolumab-fnia (type I interferon (IFN) receptor antagonist)	30/07/2021	Systemic lupus erythematosus cases along with standard therapy
Avalglucosidase alfa-ngpt (hydrolytic lysosomal glycogen-specific enzyme)	06/08/2021	Late-onset Pompe disease
Belzutifan (hypoxia-inducible factor inhibitor)	13/08/2021	Von Hippel-Lindau disease
Difelikefalin (kappa opioid receptor agonist)	23/08/2021	Moderate-to-severe pruritus associated with chronic kidney disease.
Lonapegsomatropin-tcgd (human growth hormone)	25/08/2021	Short stature due to deficiency of endogenous growth hormone
Mobocertinib (kinase inhibitor)	15/09/2021	Locally advanced or metastatic non-small cell lung cancer with EGFR exon 20 insertion mutations
Tisotumab vedotin-tftv (tissue factor-directed antibody and microtubule inhibitor)	20/09/2021	Cervical cancer cases- recurrent or metastatic
Atogepant (calcitonin gene-related peptide receptor antagonist)	28/09/2021	Prevent episodic migraines
Maralixibat (ileal bile acid transporter (IBAT) inhibitor)	29/09/2021	Cholestatic pruritus associated with Alagille syndrome
Avacopan (complement 5a receptor (C5aR) antagonist)	07/10/2021	Severe active anti-neutrophil cytoplasmic autoantibody-associated vasculitis in combination with standard therapy

Asciminib (kinase inhibitor)	29/10/2021	Philadelphia chromosome-positive chronic myeloid leukemia
Ropeginterferon alfa-2b-njft (interferon alfa-2b)	12/11/2021	Polycythemia vera
Vosoritide (C type natriuretic peptide (CNP) analog)	19/11/2021	Achondroplasia and open epiphyses in children above five years of age, to improve growth
Maribavir (cytomegalovirus (CMV) pUL97 kinase inhibitor)	23/11/2021	Post-transplant cytomegalovirus (CMV) infection
Pafolacianine (diagnostic agent binds to folate receptor)	29/11/2021	Identification of ovarian cancer lesions

https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2021

The rebirth of Chloroquine

Chloroquine (resochin) was discovered by Hans Andersag in 1934 while working for Bayer in Germany. On evaluation of the safety profile of this drug under the company's drug development program, it was considered too toxic for clinical advancement. Later Andersag developed a chloroquine derivative, sontochin, with a better safety profile. Clinical trials were conducted with this compound in collaboration with a French firm in North Africa in the early 1940s.

During the second World War, the French army found stocks of sontochin in Tunis which was later handed over to the Americans. The researchers in the US made minor modifications in the structure of the drug to increase its efficacy and named it chloroquine. Later, it was realized that chloroquine and resochin were identical. After the war, chloroquine became an important drug for malaria eradication program of the World Health Organization.

https://www.mmv.org/malaria-medicines/history-antimalarials

Hans Andersag

ImageCourtesy:https://link.springer.com/referenceworkentry/10.1007%2F978-3-662-43978-4_4043

Nothing in life is to be feared. It is only to be understood.

- Marie Curie

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