

## Review Article

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# Drugs used against COVID-19

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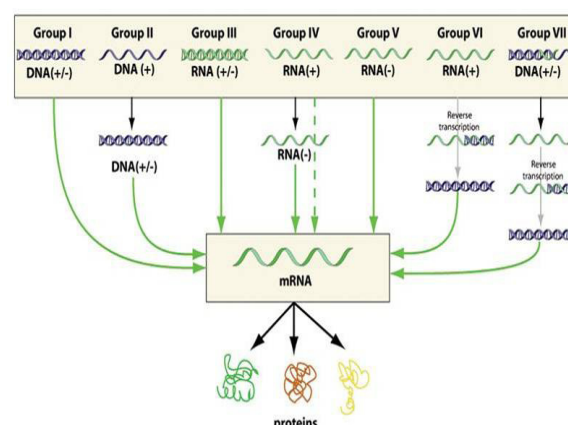
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**Keywords:** drugs; COVID-19; viruses.

## Introduction

- Viruses are small obligate intracellular parasites, which by definition contain either a RNA or DNA genome surrounded by a protective, virus-coded protein coat.
- Viruses range from the structurally simple and small parvoviruses and picornaviruses to the large and complex poxviruses and herpesviruses.
- Viruses are classified on the basis of morphology, chemical composition, and mode of replication.
- The viruses that infect humans are currently grouped into 21 families, reflecting only a small part of the spectrum of the multitude of different viruses whose host ranges extend from vertebrates to protozoa and from plants and fungi to bacteria.



**Figure 1:** Virus Structure.

The following properties have been used as a basis for the classification of viruses.

Virion morphology, including size, shape, type of symmetry, presence or absence of peplomers, and presence or absence of membranes.

Virus genome properties, including type of nucleic acid (DNA or RNA), size of genome in kilobases (kb) or kilobase pairs (kbp), strandedness (single or double), whether linear or circular, sense (positive, negative, ambisense), segments (number, size), nucleotide sequence, G+C content, and presence of special features (repetitive elements, isomerization, 5'-terminal cap, 5'-terminal covalently linked protein, 3'-terminal poly(A) tract).

Genome organization and replication, including gene order, number and position of open reading frames, a strategy of replication (patterns of transcription, translation), and cellular sites (accumulation of proteins, virion assembly, virion release).

Virus protein properties, including number, size, and functional activities of structural and nonstructural proteins, amino acid sequence, modifications (glycosylation, phosphorylation, myristylation), and special functional activities (transcriptase, reverse transcriptase, neuraminidase, fusion activities).

Antigenic properties.

Physicochemical properties of the virion, including molecular mass, buoyant density, pH stability, thermal stability, and susceptibility to physical and chemical agents, especially ether and detergents.

Biologic properties, including natural host range, mode of transmission, vector relationships, pathogenicity, tissue tropisms, and pathology.

### Classification of virus on the basis on presence of virus

The envelope is a lipid-containing membrane that surrounds some virus particles. It is acquired during viral maturation by a budding process through a cellular membrane

Virus encoded glycoproteins are exposed on the surface of the envelope. These projections are called peplomers.

#### Enveloped virus

- **DNA viruses:** Herpesviruses, Poxviruses, Hepadnaviruses
- **RNA viruses:** Flavivirus, Toga virus, Coronavirus, Hepatitis D, Orthomyxovirus, Paramyxovirus, Rhabdovirus, Bunyavirus, Filovirus
- **Retroviruses**
- **Non-enveloped virus**
- **viruses-** parvovirus, adenovirus and papovavirus.
- **RNA viruses-** Picornavirus, Hepatitis DNA A virus and Hepatitis E virus.

### Classification of virus on the basis of mode of transmission

**Virus transmitted through respiratory route:** Swine flu, Rhino virus, Corona virus.

**Virus transmitted through faeco-oral route:** Hepatitis A virus, Polio virus, Rota virus.

**Virus transmitted through sexual contacts:** Retro virus.

**Virus transmitted through blood transfusion:** Hepatitis B virus, HIV.

**Zoonotic virus:** Virus transmitted through biting of infected animals. Eg. Rabies virus, Alpha virus, Flavi virus

#### Antiviral drugs

An agent that kills a virus or that suppresses its ability to replicate and, hence, inhibits its capability to multiply and reproduce.

**Figure 2:** Different viruses.

Virus	Antiviral drug	Target
Herpes viruses	Vidarabine	Virus polymerase
Herpes simplex	Acyclovir	Virus polymerase
Cytomegalovirus	Gancyclovir	Virus polymerase
Retroviruses (HIV)	Zidovudine, Didanosine, Zalcitabine, Lamivudine	Reverse transcriptase
Retroviruses (HIV)	Saquinavir, Ritonavir, Indinavir, Nelfinavir	HIV protease
HCV, HSV	Ribavirin	RNA mutagen
Influenza A	Amantadine, Rimantadine	Haemagglutinin protein
Influenza B	Relenza and Tamiflu	Neuraminidase Inhibitor
Picorna viruses	Pleconaril	Blocks attachment
Hepatitis B & C	Interferons	Cell defence proteins

### COVID VIRUS

#### Introduction

- Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus.
- Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness.
- The best way to prevent and slow down transmission is to be well informed about the COVID-19 virus, the disease it causes and how it spreads. Protect yourself and others from infection by washing your hands or using an alcohol based rub frequently and not touching your face.
- The COVID-19 virus spreads primarily through droplets of

saliva or discharge from the nose when an infected person coughs or sneezes, so it's important that you also practice respiratory etiquette (for example, by coughing into a flexed elbow).

## Symptoms

COVID-19 affects different people in different ways. Most infected people will develop mild to moderate illness and recover without hospitalization.

**Most common symptoms:** Fever, dry cough, tiredness.

**Less common symptoms:** Aches and pains, sore throat, diarrhoea, conjunctivitis, headache, loss of taste or smell, a rash on skin, or discolouration of fingers or toes.

**Serious symptoms:** Difficulty breathing or shortness of breath, chest pain or pressure, loss of speech or movement.

## Prevention

To prevent infection and to slow transmission of COVID-19, do the following:

- Wash your hands regularly with soap and water, or clean them with alcohol-based hand rub.
- Maintain at least 1 metre distance between you and people coughing or sneezing.
- Avoid touching your face.
- Cover your mouth and nose when coughing or sneezing.
- Stay home if you feel unwell.
- Refrain from smoking and other activities that weaken the lungs.
- Practice physical distancing by avoiding unnecessary travel and staying away from large groups of people.

## Drugs used to treat corona virus

### 1. Remdesivir

#### A. IUPAC name:

2-ethylbutyl (2S)-2-[[[S]-{[(2R,3S,4R,5R)-5-{4-aminopyrrolo [2,1-f][1,2,4]triazin-7-yl]-5-cyano-3,4-dihydroxyoxolan-2-yl] methoxy}(phenoxy)phosphoryl]amino]propanoate

#### B. Trade name:

Veklury

#### Dosage forms:

Intravenous powder for injection (100 mg); intravenous solution (5 mg/mL)

#### C. Structure:

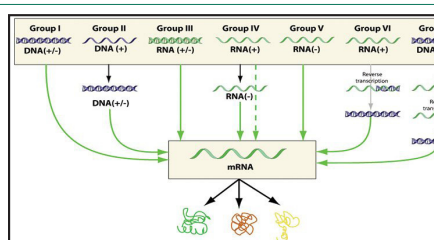


Figure 3: Remdesivir.

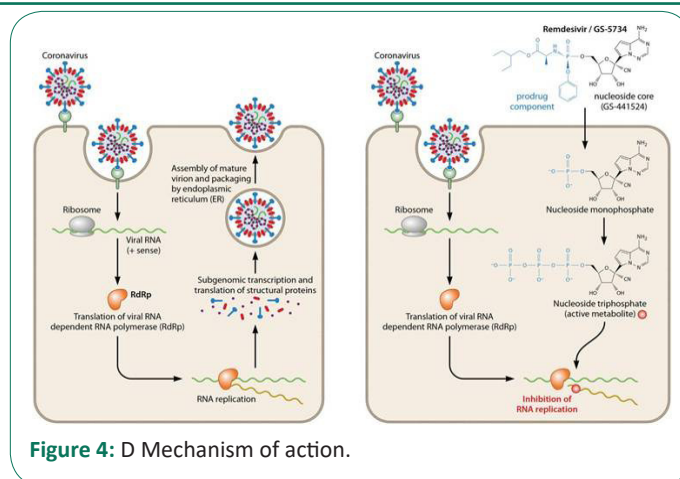


Figure 4: D Mechanism of action.

#### D. Uses:

- Remdesivir is used to treat people with coronavirus disease 2019 (COVID-19) who are in a hospital.
- Remdesivir is for use in adults and children at least 12 years old and weighing at least 88 pounds (40 kilograms).
- Remdesivir may also be used for purposes not listed in this medication guidelines

#### E. Side effects:

- An infusion reaction may occur with remdesivir with symptoms such as low blood pressure, nausea, vomiting, sweating, and shivering. The healthcare professional should monitor for side effects during remdesivir treatment.
- Information is limited and it is unknown at this time if remdesivir causes serious side effects.
- In the case of a serious allergic reaction, symptoms may include: rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing.
- This is not necessarily a complete list of possible side effects.
- The doctor should be contacted for medical advice about side effects.

### 2. Hydroxychloroquine and chloroquine

#### A. IUPAC name:

**Hydroxychloroquine:** 2-[[[4-[(7-chloroquinolin-4-yl) amino] pentyl](ethyl)amino]ethan-1-ol.

**Chloroquine:** 7-chloro-N-[5-(diethyl amino) pentan-2-yl] quinolin-4-amine.

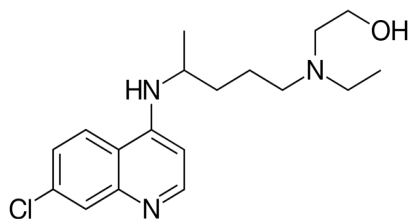
#### B. Trade name:

**Hydroxychloroquine:** Plaquenil.

**Chloroquine:** Aralen

#### C. Structure:

**Hydroxychloroquine:**



#### Chloroquine:

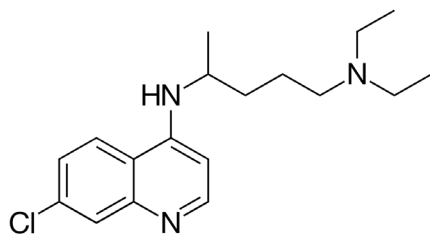


Figure 5: Structures of hydroxychloroquine and hloroquine

#### D. Mechanism of action

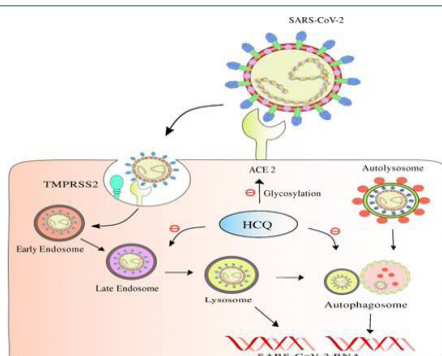


Figure 6: Mechanism of hydroxychloroquine:

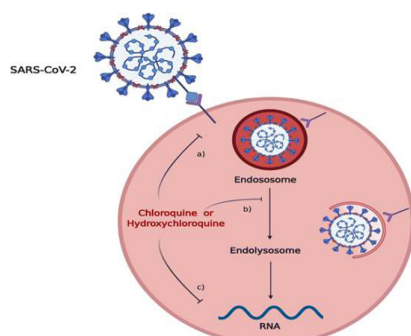


Figure 7: Mechanism of chloroquine.

#### E. Uses

Hydroxychloroquine is used to treat: rheumatoid arthritis, discoid and systemic lupus erythematosus (SLE), juvenile idiopathic arthritis (JIA).

Chloroquine is used to treat or prevent malaria, a disease caused by parasites that enter the body through the bite of a mosquito. Chloroquine is not effective against all strains of malaria, or against malaria in areas where the infection has been resistant to a similar drug called hydroxychloroquine.

Chloroquine is also used to treat amoebiasis (infection caused by amoebae).

Chloroquine may also be used for purposes not listed in this

medication guide.

#### F. Side effects:

**Hydroxychloroquine:** headache, dizziness, loss of appetite, nausea, diarrhoea, stomach pain, vomiting, rash.

#### Chloroquine:

- A seizure.
- Ringing in your ears, trouble hearing.
- Severe muscle weakness, loss of coordination, under-active reflexes.
- *Low blood cell counts*--fever, chills, tiredness, mouth sores, skin sores, easy bruising, unusual bleeding, pale skin, cold hands and feet, feeling light-headed or short of breath.
- *Low blood sugar*--headache, hunger, sweating, irritability, dizziness, fast heart rate, and feeling anxious or shaky. or
- *A serious drug reaction that can affect many parts of your body*--skin rash, fever, swollen glands, muscle aches, severe weakness, unusual bruising, or yellowing of your skin or eyes.

Taking chloroquine long-term or at high doses may cause irreversible damage to the retina of your eye.

Stop taking chloroquine and tell your doctor if you have: blurred vision, trouble focusing, trouble reading; distorted vision, poor night vision; changes in your colour vision; hazy or cloudy vision; seeing light flashes or streaks, seeing halos around lights; or increased sensitivity to light.

Common side effects may include: nausea, vomiting, diarrhoea, stomach cramps; headache; unusual changes in mood or behaviour; hair loss; or change in hair or skin colour.

#### 3. Azithromycin

##### A. IUPAC Nname:

(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-11-[[[(2S,3R,4S,6R)-4-(dimethylamino)-3-hydroxy-6-methyloxan-2-yl]oxy]-2-ethyl-3,4,10-trihydroxy-13-[[[(2R,4R,5S,6S)-5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yl]oxy]-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-azacyclopentadecan-15-one

##### B. Trade name:

1. Act Azithromycin
2. AzaSITE
3. Ag-azithromycin

##### C. Structure:

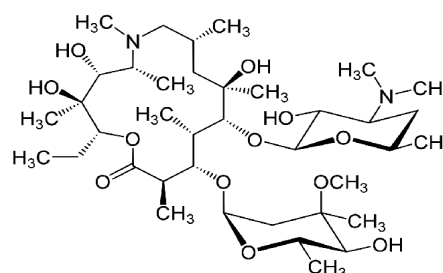


Figure 8: Structure of azithromycin.



## D. Mechanism of action:

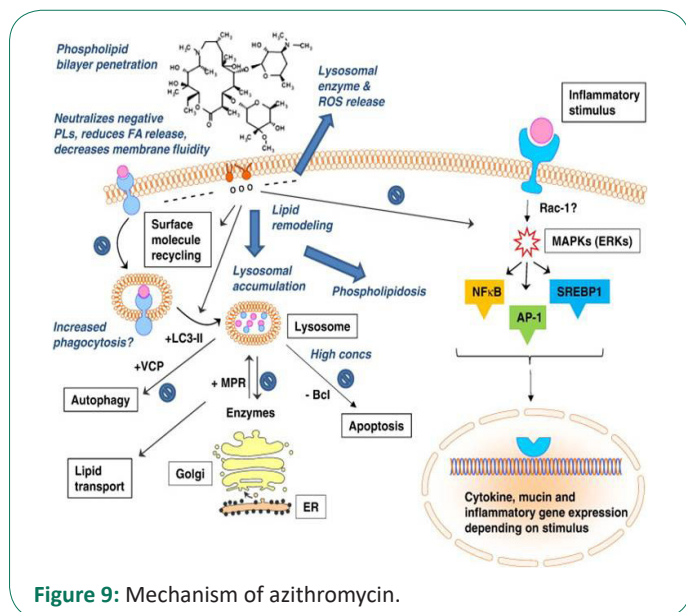


Figure 9: Mechanism of azithromycin.

## E. Uses:

Azithromycin can fight a wide range of bacteria, including many in the *Streptococcus* family. It can stop harmful bacteria from growing.

Healthcare providers tend to use this drug to treat mild-to-moderate infections of the lungs, sinuses, skin, and other body parts.

A doctor may prescribe azithromycin to treat the following bacterial infections:

- Sinus infections related to *Moraxella catarrhalis* or *Streptococcus pneumoniae*
- Community-acquired pneumonia related to *Chlamydia pneumoniae*, *Haemophilus influenzae*, or *S. pneumoniae*
- Chronic obstructive pulmonary disease (COPD) complications related to *M. catarrhalis* or *S. pneumoniae*
- Some skin infections related to *Staphylococcus aureus*, *Streptococcus pyogenes*, or *Streptococcus agalactiae*
- Tonsillitis related to *S. pyogenes*
- Urethritis and cervicitis related to *Chlamydia trachomatis*
- Cervicitis genital ulcers (in males) related to *Haemophilus ducreyi*
- Certain ear infections in children aged 6 months and over, such as those related to *M. catarrhalis*

**F. Side effects:** Diarrhoea or loose stools, Nausea, Abdominal pain, Stomach upset, Vomiting, Constipation, Dizziness, Tiredness, Headache, Vaginal itching or discharge, Nervousness, Sleep problems (insomnia), Skin rash or itching, Ringing in the ears, Hearing problems, Or decreased sense of taste or smell.

## 4. Kaletre

Kaletre is a combination of a protease inhibitor lopinavir (200 mg) plus a booster dose (50 mg) of ritonavir in the same pill. The trade name is Kaletra in Western countries and Aluvia in low income countries. In resource-limited countries this is a brown tablet with the same design (trade name Aluvia).

## A. IUPAC name:

Lopinavir: (2S)-N-[(2S,4S,5S)-5-[2-(2,6-dimethylphenoxy)acetamido]-4-hydroxy-1,6-diphenylhexan-2-yl]-3-methyl-2-(2-oxo-1,3-diazinan-1-yl)butanamide

Ritonavir: (1,3-thiazol-5-yl)methyl N-[(2S,3S,5S)-3-hydroxy-5-[(2S)-3-methyl-2-[[methyl]([2-(propan-2-yl)-1,3-thiazol-4-yl)methyl])carbamoyl]amino}butanamido]-1,6-diphenylhexan-2-yl]carbamate

## B. Trade name: Aluvia

## C. Structure: Lopinavir:

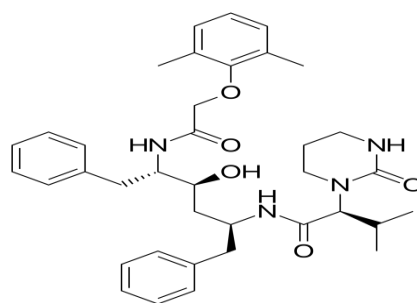


Figure 10: Structure of lopinavir.

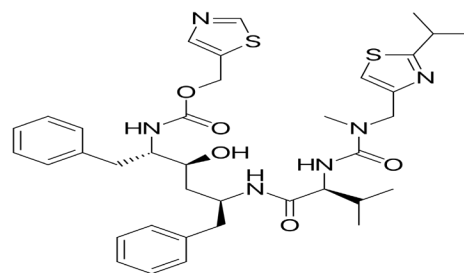


Figure 10: Structure of ritonavir.

## D. Mechanism of action:

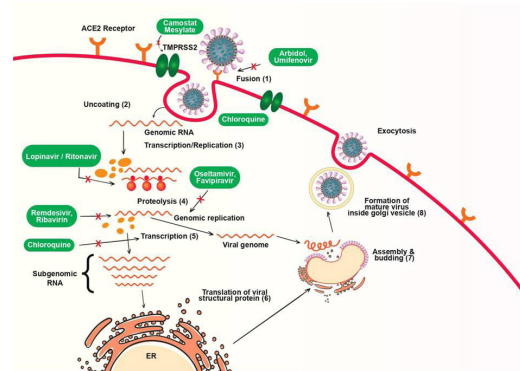


Figure 11: Mechanism of ritonavir

## E. Uses

This combination product contains two medications: Lopinavir and ritonavir. This product is used with other HIV medications to help control HIV infection. It helps to decrease the amount of HIV in your body so your immune system can work better. This lowers your chance of getting HIV complications (such as new infections, cancer) and improves your quality of life. Both lopinavir and ritonavir belong to a class of drugs known as HIV protease inhibitors. Ritonavir increases ("Boosts") the levels of

lopinavir. This helps lopinavir work better. Lopinavir/ritonavir is not a cure for HIV infection. To decrease your risk of spreading HIV disease to others, continue to take all HIV medications exactly as prescribed by your doctor. Use an effective barrier method (latex or polyurethane condoms/dental dams) during sexual activity as directed by your doctor. Do not share personal items (such as needles/syringes, toothbrushes, and razors) that may have contacted blood or other body fluids. Consult your doctor or pharmacist for more details.

#### F. Side effects:

Lopinavir and ritonavir may cause side effects: weakness, diarrhoea, gas, heartburn, weight loss, headache, difficulty falling asleep or staying asleep, muscle pain, numbness, burning, or tingling in the hands or feet, stomach pain, nausea, and vomiting,

Some side effects can be serious: nausea, vomiting, stomach pain, extreme tiredness, loss of appetite, pain in the upper right part of the stomach, yellowing of the skin or eyes, itchy skin, dizziness, lightheadedness, fainting, irregular heartbeat, blisters, rash

### 5. Dexamethasone:

#### A. IUPAC name:

(1R,2R,3aS,3bS,9aS,9bR,10S,11aS)-9b-fluoro-1,10-dihydroxy-1-(2-hydroxyacetyl)-2,9a,11a-trimethyl-1H,2H,3H,3aH,3bH,4H,5H,7H,9aH,9bH,10H,11H,11aH-cyclopenta[a]phenanthren-7-one.

#### B. Trade name:

1. Decadron
2. Accufix II

#### C. Structure:

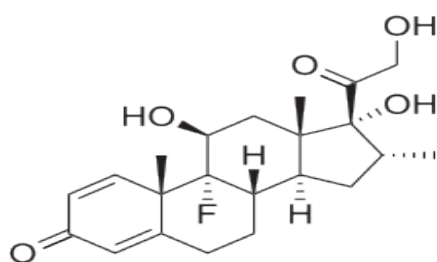


Figure 12: Structure of dexamethasone.

### D. Mechanism of action

#### E. Uses:

1. Dexamethasone is used to treat conditions such as arthritis, blood/hormone disorders, allergic reactions, skin diseases, eye problems, breathing problems, bowel disorders, cancer, and immune system disorders.

2. It is also used as a test for an adrenal gland disorder (Cushing's syndrome).

3. Dexamethasone belongs to a class of drugs known as corticosteroids. It decreases your immune system's response to various diseases to reduce symptoms such as swelling and allergic-type reactions.

#### F. Side effects:

- upset stomach, stomach irritation, vomiting, headache, dizziness, insomnia, restlessness, depression, anxiety, acne, increased hair growth, easy bruising, irregular or absent menstrual periods, upset stomach, stomach irritation, vomiting, headache, dizziness, insomnia, restlessness, depression, anxiety, acne, increased hair growth, easy bruising, irregular or absent menstrual periods.

### 6. Ivermectin

#### A. IUPAC name:

(1'R,2R,4'S,5S,6R,8'R,10'E,12'S,13'S,14'E-16'E,20'R,21'R,24'S)-21',24'-dihydroxy-12'-[[[(2R,4S,5S,6S)-5-[[[(2S,4S,5S,6S)-5-hydroxy-4-methoxy-6-methyloxan-2-yl]oxy]-4-methoxy-6-methyloxan-2-yl]oxy]-5,11',13',22'-tetramethyl-6-(propan-2-yl)-3',7',19'-trioxaspiro[oxane-2,6'-tetracyclo[15.6.1.1<sup>4,8</sup>.0<sup>20,24</sup>]pentacosane]-10',14',16',22'-tetraen-2'-one; (1'R,2R,4'S,5S,6R,8'R,10'E,12'S,13'S,14'E,16'E,20'R,21'R,24'S)-6-[(2R)-butan-2-yl]-21',24'-dihydroxy-12'-[[[(2R,4S,5S,6S)-5-[[[(2S,4S,5S,6S)-5-hydroxy-4-methoxy-6-methyloxan-2-yl]oxy]-4-methoxy-6-methyloxan-2-yl]oxy]-5,11',13',22'-tetramethyl-3',7',19'-trioxaspiro[oxane-2,6'-tetracyclo[15.6.1.1<sup>4,8</sup>.0<sup>20,24</sup>]pentacosane]-10',14',16',22'-tetraen-2'-one

#### B. Trade name:

1. Rosiver
2. Sklice
3. Soolantra
4. Stromectol

#### C. Structure:

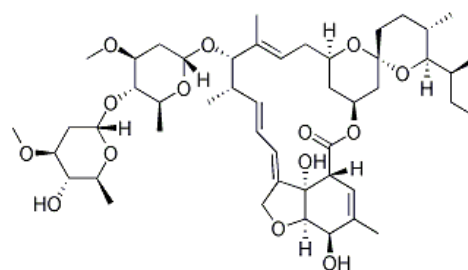


Figure 14: Structure of ivermectin.

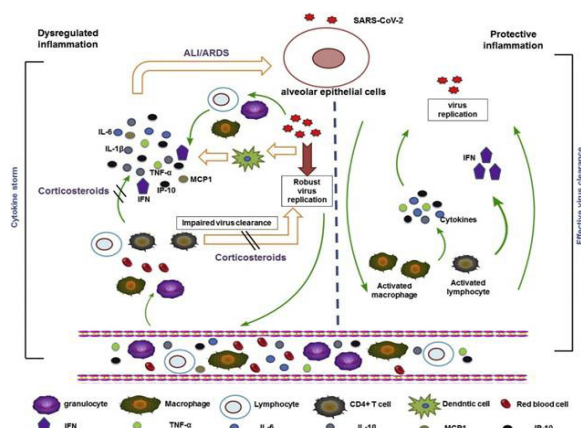
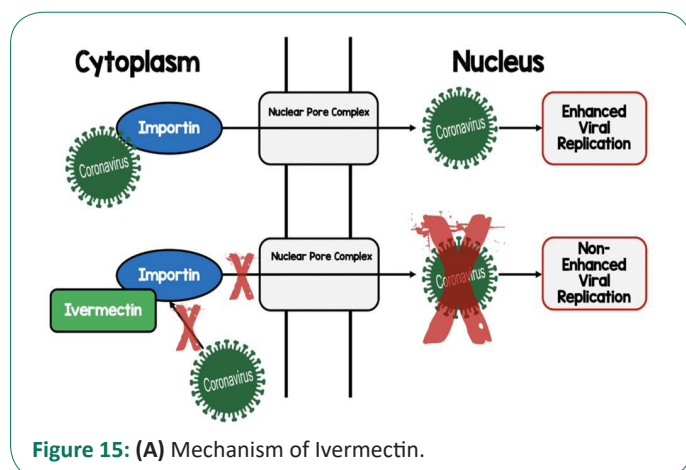
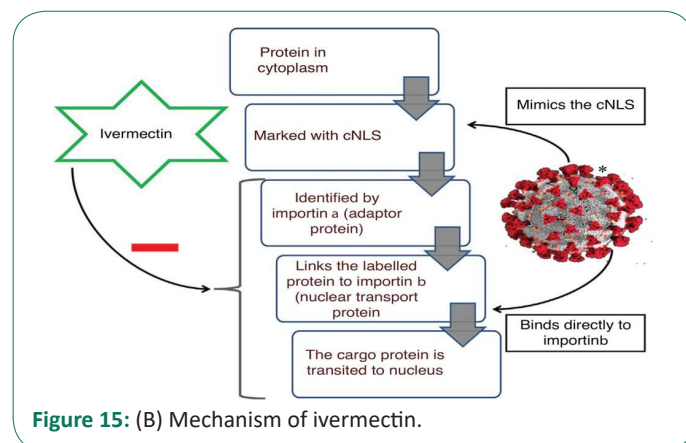


Figure 13: Mechanism of dexamethasone

**D. Mechanism of action:**



**Figure 15: (A) Mechanism of Ivermectin.**



**Figure 15:** (B) Mechanism of ivermectin.

**E. Uses:**

Ivermectin tablets are approved by the FDA to treat people with intestinal strongyloidiasis and onchocerciasis, two conditions caused by parasitic worms. In addition, some topical (on the **skin**) forms of ivermectin are approved to treat external parasites like head lice and for skin conditions such as rosacea

### F. Side effects:

The more common side effects of this drug when it's used to treat intestinal infections include: tiredness, loss of energy, stomach pain, loss of appetite, nausea, vomiting, diarrhea, dizziness, sleepiness or drowsiness, itchiness.

The more common side effects of this drug when it's used to treat intestinal infections include: tiredness, loss of energy, stomach pain, loss of appetite, nausea, vomiting, diarrhoea, dizziness, sleepiness or drowsiness, itchiness.

## 7. Acalabrutinib

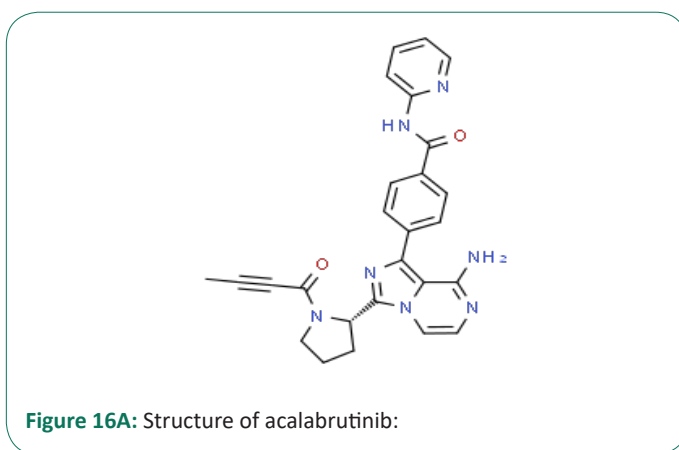
**A. IUPAC name:**

4-{8-amino-3-[(2S)-1-(but-2-ynoyl)pyrrolidin-2-yl]  
imidazo[1,5-a]pyrazin-1-yl}-N-(pyridin-2-yl)benzamide

**B. Trade name:**

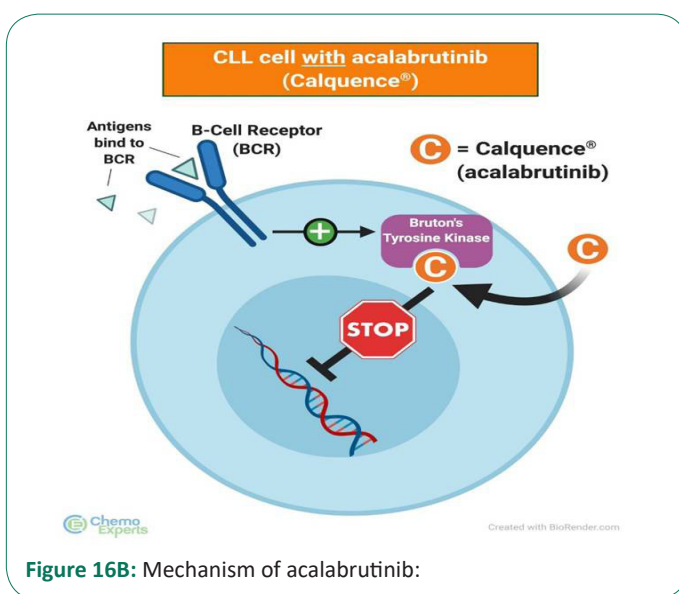
Calquence

### C. Structure:



**Figure 16A:** Structure of acalabrutinib:

**D. Mechanism of action:**



**Figure 16B:** Mechanism of acalabrutinib:

**E. Uses:**

Acalabrutinib blocks the action of certain enzymes in the body, which can interfere with the growth and spread of cancer cells.

Acalabrutinib is used to treat mantle cell lymphoma (a type of non-Hodgkin lymphoma) in adults. acalabrutinib is given after other treatments have failed.

Acalabrutinib was approved by the US Food and Drug Administration (FDA) on an "accelerated" basis. In clinical studies, patients responded to this medicine. However, further studies are needed.

Acalabrutinib may also be used for purposes not listed in this medication guide.

**F. Side effects:**

- unusual bleeding (nose, mouth, vagina, or rectum), or any bleeding that will not stop;
- signs of bleeding inside your body--dizziness, weakness, confusion, problems with speech, prolonged headache, black or bloody stools, pink or brown urine, or coughing up blood or vomit that looks like coffee grounds;

- heart rhythm problems--chest pain, shortness of breath, pounding heartbeats or fluttering in your chest, feeling light-headed;

low red blood cells (anemia)--pale skin, unusual tiredness, feeling light-headed or short of breath, cold hands and feet;

signs of infection--fever, chills, tiredness, flu-like symptoms, cough with mucus, chest pain, trouble breathing; or

signs of a serious brain infection--any change in your mental state, decreased vision, weakness on one side of your body, or problems with walking (may start gradually and get worse quickly).

Your cancer treatments may be delayed or permanently discontinued if you have certain side effects.

Common side effects may include: bruising, headache, muscle pain, diarrhea or feeling tired.

## 8. Oseltamivir

### A. IUPAC name:

ethyl (3R,4R,5S)-5-amino-4-acetamido-3-(pentan-3-yloxy)cyclohex-1-ene-1-carboxylate

### B. Trade name:

1. Tamiflu
2. Ebilfumin
3. Oseltamivir Phosphate Capsules
4. Oseltamivir Powder for Oral Suspension

### C. Structure:

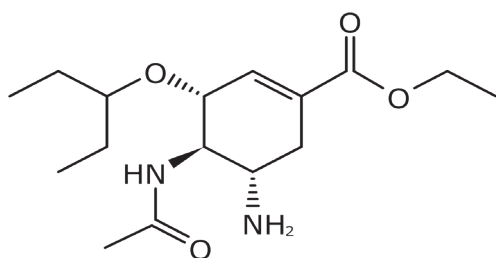


Figure 17: Structure of oseltamivir.

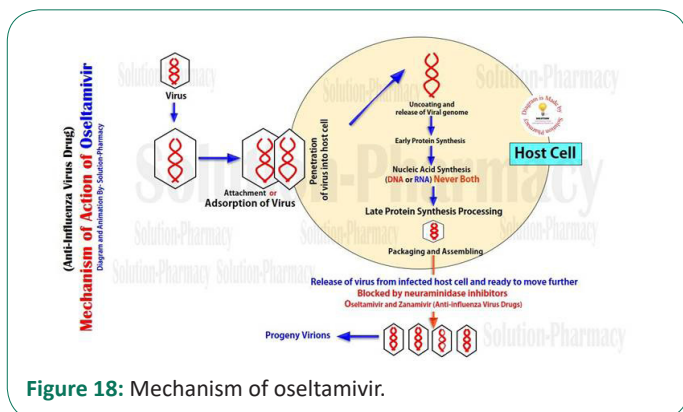


Figure 18: Mechanism of oseltamivir.

## E. Uses:

Oseltamivir is used to treat symptoms caused by the flu virus (influenza). It helps make the symptoms (such as stuffy nose, cough, sore throat, fever/chills, aches, tiredness) less severe and shortens the recovery time by 1-2 days. This medication may also be used to prevent the flu if you have been exposed to someone who already has the flu (such as a sick household member) or if there is a flu outbreak in the community. Talk to your doctor for more details. This medication works by stopping the flu virus from growing. It is not a substitute for the flu vaccine

## F. Side effects:

Oseltamivir may cause side effects: nausea, vomiting, stomach pain, diarrhoea, headache, rash, hives, or blisters on the skin, mouth sores, itching, swelling of the face or tongue, difficulty breathing or swallowing, hoarseness, confusion, speech problems, shaky movements, Hallucinations (seeing things or hearing voices that do not exist)

## 9. Colchicine

### A. IUPAC name:

N-{3,4,5,14-tetramethoxy-13-oxotricyclo[9.5.0.0<sup>2,7</sup>]hexadeca-1(16),2(7),3,5,11,14-hexaen-10-yl}acetamide

### B. Trade name: Colchicine

### C. Structure:

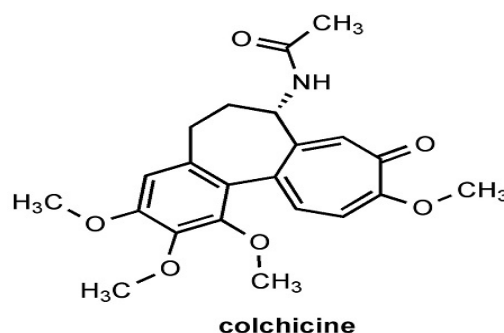


Figure 19: Structure of colchicine.

## D. Mechanism of action:

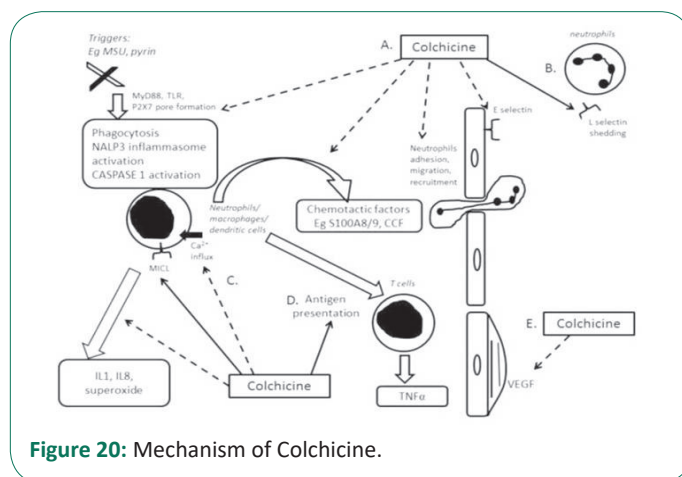


Figure 20: Mechanism of Colchicine.



## E. Uses:

This medication is used to prevent or treat gout attacks (flares). Usually gout symptoms develop suddenly and involve only one or a few joints. The big toe, knee, or ankle joints are most often affected. Gout is caused by too much uric acid in the blood. When uric acid levels in the blood are too high, the uric acid may form hard crystals in your joints. Colchicine works by decreasing swelling and lessening the build up of uric acid crystals that cause pain in the affected joint(s). This medication is also used to prevent attacks of pain in the abdomen, chest, or joints caused by a certain inherited disease (familial Mediterranean fever). It is thought to work by decreasing your body's production of a certain protein (amyloid A) that builds up in people with familial Mediterranean fever. Colchicine is not a pain medication and should not be used to relieve other causes of pain.

**F. Side effects:** Stomach pain, nausea, vomiting, diarrhoea, unusual bruising or bleeding, sore throat, fever, chills, and other signs of infection, paleness or grayness of the lips, tongue, or palms, slowed breathing, slowed or stopped heartbeat.

## 10. Convalescent plasma

In the absence of drugs to cure Coronavirus infection or vaccines to prevent COVID-19, currently, plasma therapy is being seen as a potential treatment for critically ill-patients. It has also got a stamp of approval from the Food and Drug Administration (FDA) of United States. In India, states like Delhi, Maharashtra, Punjab, among others have already started using Convalescent Plasma Therapy (CPT) as a treatment for serious COVID-19 patients.

### What is plasma therapy?

Plasma Therapy involves transfusion of antibodies from someone who has recovered from COVID-19 (convalescent coronavirus patient) into a critical patient. The therapy is based on the principle that the blood of a recovered patient is rich in antibodies needed to combat COVID-19. Antibodies are Y shaped proteins produced by a human body and used by the immune system to identify and neutralise foreign objects such as bacteria and viruses. These antibodies are expected to help critical patients recover.

### How does plasma therapy work?

Blood plasma, a yellowish liquid is a component of blood and consists of protein, minerals and antibodies. If someone has recovered from COVID-19 there are chances that the person's body has developed antibodies that helped him/her to fight the virus. The same antibodies, if infused into a critical patient may provide passive immunity and help in the recovery process.

### What is the procedure of convalescent plasma therapy?

First blood is drawn from the potential donor to check for the presence of antibodies. Once it is clear that an individual can donate plasma, the blood is extracted and plasma is separated from the blood. The point to be noted is, only plasma is taken from the blood and at the end, blood is transfused back into the body of the donor.

### Who can donate plasma?

Patients who have gone through the cycle of Coronavirus and have recovered from COVID-19 can donate plasma. 500 ml of plasma can be donated after 14 days of recovering from the disease. According to the information available on Delhi's

plasma bank website, there are seven categories of people who cannot donate plasma. This includes diabetics on insulin, pregnant women, people having body weight less than 50 kg, cancer survivor, among others.

### At What stage of COVID-19 is plasma therapy recommended?

According to Dr Sandeep Budhiraja, Group Medical Director, Max Healthcare who did the first plasma therapy in India for a COVID patient back in April, the best stage to give plasma is 'moderate severity' - when the patient's requirement of oxygen increases. He says, 'The convalescent plasma therapy is not much effective when a patient is on a ventilator.'

Dr Suresh Kumar, Medical Director at LNJP (Lok Nayak) Hospital in Delhi says that plasma therapy benefits people more who:

- Are under 65 years of age.
- Have only SARI (severe acute respiratory infections).
- Have acute respiratory failure because of COVID.
- Have oxygen saturation is less than 90.

### Are there any risks involved in plasma therapy?

Blood transfusion related infections can be transmitted, therefore, before plasma transfusion, test for HIV and other diseases, which are usually done for all transfusions are conducted.

## 11. Monoclonal antibodies

The body's immune system generates antibodies as a defense mechanism against unfamiliar molecules. The scientific term for such unfamiliar molecules is antigens. Molecules from bacteria and viruses can act as antigens, prompting the production of antibodies.

Antibodies bind to antigens. This tells specialized cells of the immune system to kill the invading pathogen.

The bodies of the majority of people who recover from COVID-19 produce antibodies to the SARS-CoV-2 virus. Scientists have found that these antibodies persist for at least 5–7 months after the infection.

However, scientists can also produce these antibodies in a laboratory setting to be infused into the blood.

Monoclonal antibodies Trusted Source are identical copies of an antibody that targets one specific antigen. Scientists can make monoclonal antibodies by exposing white blood cells to a particular antigen.

They can then select a single white blood cell or clone and use this as the basis to produce many identical cells, making many identical copies of the monoclonal antibody.

Antibody treatments in themselves are not new. Healthcare professionals have used monoclonal antibodies, for example, to treat viral infections such as Ebola Trusted Source and HIV.

Each monoclonal antibody is specific to its matching antigen. For COVID-19, there are several authorized monoclonal antibody therapies.

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## **Anti-SARS-CoV-2 monoclonal antibodies**

The SARS-CoV-2 virus's spike glycoprotein, which sits on its surface, functions to facilitate the virus's entry into the body's cells. Some SARS-CoV-2 antibodies bind to the spike protein and prevent the virus from entering the cell.

Currently, all the monoclonal antibodies for COVID-19 for which the FDA have issued emergency use authorization target the spike protein.

### **Bamlanivimab and etesevimab**

Eli Lilly and Company developed two different antibody therapies: Bamlanivimab monotherapy and combination bamlanivimab and etesevimab therapy.

On February 9, 2021, the FDA authorized Trusted Source the emergency use of combined bamlanivimab and etesevimab for people with mild-to-moderate COVID-19. The EMA are currently reviewing the data behind these antibodies.

The FDA also authorized Trusted Source bamlanivimab therapy on November 10, 2020. However, on March 24, 2021, Eli Lilly and Company halted distribution of the bamlanivimab monotherapy, noting:

Given the sustained increase in SARS-CoV-2 viral variants in the United States that are resistant to bamlanivimab administered alone, and the availability of other authorized monoclonal antibody therapies that are expected to retain activity.

Eli Lilly and Company recently announced their phase 3 clinical trial data in a press release. They said that the combined bamlanivimab and etesevimab therapy reduced the risk of COVID-19 hospitalizations and death by 87% in people with mild-to-moderate symptoms at high risk of severe disease.

However, these beneficial results were in outpatients who were not experiencing severe COVID-19. Dr. Lundgren stated that Eli Lilly and Company are currently investigating the efficacy of these monoclonal antibodies in hospitalized patients through a National Institutes of Health (NIH)-sponsored inpatient clinical trial called ACTIV-3Trusted Source.

Initial results with bamlanivimab have not indicated any particular efficacy for inpatients variants, the U.S. government, in coordination with Eli Lilly and Company, will stop the distribution of bamlanivimab."

The FDA advise the use of alternative monoclonal treatments in light of the increase in the prevalence of SARS-CoV-2 variants against which bamlanivimab has shown reduced efficacy.

### **REGN-COV2: Casirivimab and imdevimab**

Regeneron developed a "combination antibody cocktail" called REGN-COV2, which contains the antibodies casirivimab and imdevimab.

On November 21, 2020, the FDA authorized Trusted Source the emergency use of REGN-COV2 for mild-to-moderate COVID-19. The EMA have concluded that healthcare professionals can use this treatment for COVID-19 patients at risk of developing severe disease but who do not require oxygen treatment. The agency will continue their rolling review to support national health authorities in European Union countries, who issue authorization for use individually.

The NIH, on the other hand, have stated that there is not enough evidence to support its use and that there is a need to review phase 3 trial data, which were released on March 23, 2021.

According to Regeneron's phase 3 clinical trial data, the combined casirivimab and imdevimab antibodies reduced the risk of COVID-19 hospitalizations and death by 70% in people with mild-to-moderate symptoms.

Like Eli Lilly and Company, Regeneron are conducting trials to test the efficacy of these antibodies in inpatients-particularly those who need oxygen or a mechanical ventilator as a result of COVID-19.

However, in October 2020, Regeneron received advice to halt enrollment for people on high flow oxygen or mechanical ventilators until further data had been collected. This was due to a possible safety risk. They are continuing enrollment for people receiving no or low flow oxygen.

### **Anti-interleukin-6 receptor monoclonal antibodies**

There are concerns that the immune system may overreact in response to COVID-19 and lead to a cytokine storm, in which excessive amounts of inflammatory proteins called cytokines can cause life threatening levels of inflammation.

Interleukin 6 (IL-6) is a type of inflammatory cytokine. Antibodies that block this cytokine from binding to other cells may alleviate the danger of COVID-19-related inflammation.

### **Levilimab (Ilsira)**

The Russian biotechnology company BIOCAD developed the antibody levilimab (Ilsira) to prevent cytokine storm-related complications caused by COVID-19. The Russian Federation's Ministry of Health approved its use for COVID-19 treatment on June 5, 2020.

According to Dmitry Morozov, BIOCAD's general director, "The results of clinical trials of the drug, initiated on April 24, demonstrate that levilimab therapy can significantly reduce mortality among [people] with COVID-19 and the burden on the health system."

However, the data supporting the use of levilimab have not been published.

### **Anti-CD6 monoclonal antibodies**

These antibodies also work to prevent cytokine storms, but instead of targeting cytokines, they target specific molecules on the cell surface, or cluster of differentiation (CD) antigens, that are involved in regulating the immune response.

### **Itolizumab**

Indian biopharmaceutical company Biocon tested their anti-CD6 monoclonal therapy itolizumab as a treatment for COVID-19. The Drugs Controller General of India authorized the antibody for use in India in June 2020.

In contrast to the FDA-authorized antibodies for treating mild-to-moderate COVID-19, this antibody is intended for people with moderate-to-severe COVID-19.

Some physicians have raised concerns about Biocon's small trial size of 30 participants, stating that it does not provide enough data to support the treatment's efficacy. Regardless,

the regulatory agency have deemed it safe and plan to continue studies to evaluate the evidence.

### Eligibility criteria for antibody treatment

Healthcare professionals currently administer monoclonal antibodies *via* intravenous infusions in specialized medical facilities. As noted in the clinical trials, most of the treatments work most effectively for non-hospitalized patients in the early stages of COVID-19.

- Currently, the FDA have authorized treatments for mild-to-moderate COVID-19 in patients at “high risk [of] progression to severe disease.” The FDA define this as meeting at least one of the following criteria Trusted Sourhaving a body mass index (BMI) equal to or greater than 35.
- Having chronic kidney disease, diabetes, or an immunosuppressive condition.
- Being older than 65 years.
- Being older than 55 years and having cardiovascular disease, hypertension, chronic obstructive pulmonary disease, or another chronic respiratory disease
- Being aged 12–17 years and having a BMI equal to or greater than the 85th percentile for one’s age and sex (according to Centers for Disease Control and Prevention [CDC] clinical growth charts Trusted Source), sickle cell disease, heart disease, a neurodevelopmental disorder, medical-related technological dependence, asthma, or another chronic respiratory disease requiring daily medication

### Potential side effects

Both Eli Lilly and Company and Regeneron state that their combined antibody therapies may cause hypersensitivity reactions, with the most common side effects including infusion-related reactions and allergic reactions: Infusion-related reactions include: Fever, Nausea, Chills, Fatigue, Chest pain, Difficulty breathing, An irregular heartbeat, Headache, Low or high blood pressure, Throat pain, Rash, Dizziness, Allergic reactions include anaphylaxis.

If a person experiences any of these side effects, the companies recommend that the healthcare professional administering the treatment consider slowing or stopping the infusion and providing appropriate care.

### Antibody-dependent enhancement

There have been concerns that the use of monoclonal antibodies may cause Antibody-Dependent Enhancement (ADE) Trusted Source.

This occurs when the bound antibody further promotes, rather than prevents, the virus’s entry into cells. As a result, the virus can replicate more effectively within the cell.

So far, there is no evidence to suggest that COVID-19 monoclonal antibodies can cause this phenomenon.

This is also the case with similar risks. The bamlanivimab and etesevimab fact sheet Trusted Source notes that the antibodies could potentially weaken the body’s immune system against future infection, but no studies have examined this yet.


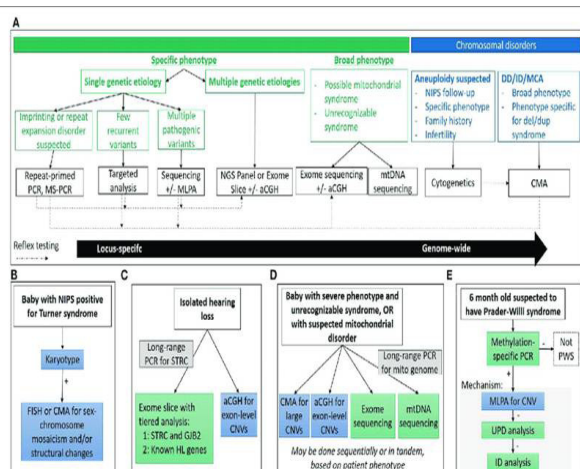
Coronavirus Disease 2019 Testing Basics			
You’ve probably heard a lot about coronavirus disease (COVID-19) testing. If you think you have COVID-19 and need a test, contact your health care provider or local health department immediately. You can also find a community testing site in your state, or buy an FDA-authorized at-home test. Some FDA-authorized at-home tests give you results within minutes. Others require you to mail the sample to a lab for analysis.			
There are two different types of tests – diagnostic tests and antibody tests.			
 <b>Diagnostic tests</b> can show if you have an active COVID-19 infection and need to take steps to quarantine or isolate yourself from others. <b>Molecular</b> and antigen tests are types of diagnostic tests that can detect if you have an active COVID-19 infection. Samples for diagnostic tests are typically collected with a nasal or throat swab, or saliva collected by spitting into a tube.	 <b>Antibody tests</b> look for antibodies in your immune system produced in response to SARS-CoV-2, the virus that causes COVID-19. <b>Antibody tests should not be used to diagnose an active COVID-19 infection.</b> Antibodies can take several days or weeks to develop after you have an infection and may stay in your blood for several weeks or more after recovery. Samples for antibody tests are typically blood from a finger stick, or blood drawn by your doctor or other medical personnel.		
	MOLECULAR TEST	ANTIGEN TEST	ANTIBODY TEST
<b>Also known as...</b>	Diagnostic test, viral test, molecular test, nucleic acid amplification test (NAAT), RT-PCR test, LAMP test	Diagnostic test, viral test, rapid test	Serological test, serology, blood test, serology test
<b>How the sample is taken...</b>	Nasal swabs, either shallow or deep (most tests). Saliva (some tests)	Nasal or nasopharyngeal swab (most tests)	Blood from a fingerstick or vein
<b>How long it takes to get results...</b>	Less than an hour (at home tests and some point-of-care locations), same day (some point-of-care locations) or 1–3 days (tests sent to a lab for processing). Some tests may take longer in some locations, depending on testing capacity.	Some may be very fast (15–30 minutes), depending on the test	Same day (some point-of-care locations) or 1–3 days (tests sent to a laboratory for processing)
<b>Is another test needed...</b>	Not usually. This type of test is typically highly accurate and usually does not need to be repeated. Some may indicate the need to re-test in certain circumstances.	Maybe. Positive results are usually highly accurate, but false positives can happen, especially in areas where very few people have the virus. Negative results may need to be confirmed with a molecular test.	Sometimes a second antibody test is needed for accurate results.
<b>What it shows...</b>	Diagnoses active COVID-19 infection. (Some tests may also diagnose influenza or other respiratory viruses)	Diagnoses active COVID-19 infection. (Some tests may also diagnose influenza or other respiratory viruses)	Shows if you’ve been infected by the virus that causes COVID-19 in the past
<b>What it can’t do...</b>	It cannot show if you ever had COVID-19 or were infected with the virus that causes COVID-19 in the past	It may not detect an early COVID-19 infection. Your health care provider may order a molecular test if your antigen test shows a negative result, but you have symptoms of COVID-19. It also cannot show if you ever had COVID-19 or were	It cannot diagnose COVID-19 at the time of the test or show that you do not have COVID-19

Figure 21: Diagnostic methods of COVID virus.



### Limitations and challenges

Newly emerging variants of SARS-CoV-2 - such as the ones that scientists first identified in the United Kingdom, South Africa, and Brazil - may be resistant to some of the currently available antibodies.

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