| AIFA RECOMMENDATIONS ON MEDICINES<br>to be used in home management of COVID-19 cases<br>Vers. 7 – Updated 09/02/2022 | |
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| **SYMPTOMATIC MEDICINES** | |
| **Symptomatic therapy** | **Paracetamol or NSAIDs** can be used in case of fever or joint/muscle pain (unless there is a clear contraindication to use). Other symptomatic medicines can be used upon clinical judgment. |
| **MEDICINES TO BE USED ONLY IN SPECIFIC STAGES OF THE DISEASE** | |
| **Antivirals**<br><br>Remdesivir – Veklury ®<br>information for healthcare professionals<br>https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19<br><br>Nirmatrelvir/ritonavir – Paxlovid ®<br>Information for healthcare professionals<br>https://www.ema.europa.eu/en/medicines/human/summaries-opinion/paxlovid<br><br>Molnupiravir – Lagevrio ®<br>information for healthcare professionals<br>https://www.aifa.gov.it/uso-degli-antivirali-orali-per-covid-19 | Three antivirals (remdesivir, nirmatrelvir/ritonavir and molnupiravir) have recently been made available for treatment of adults with COVID-19 not requiring supplemental oxygen therapy and at increased risk of progression to severe forms of COVID-19.<br>The patient **should not be hospitalised** due to COVID-19, should have a **mild to moderate** form and show at least one of the following risk factors associated with development to severe disease:<br>• Oncological/oncohematological pathology in the active phase<br>• Chronic renal failure<br>• Severe pulmonary disease<br>• Primary or acquired immunodeficiency<br>• Obesity [(Body Mass Index, BMI) ≥30]<br>• Severe cardiovascular disease (heart failure, coronary artery disease, cardiomyopathy)<br>• Uncompensated diabetes mellitus<br><br>**Remdesivir** is an antiviral drug (adenosine nucleotide analog prodrug), already authorized by the EMA for treatment of COVID-19 with pneumonia requiring supplemental oxygen therapy; in December 2021 it was granted the authorization for the extension of indication related to treatment of COVID-19 in "adults who do not require supplemental oxygen therapy and with an increased risk of progression to severe COVID-19".<br>Treatment should be started as soon as possible after the diagnosis of COVID-19 and within 7 days of the onset of symptoms.<br>The recommended dosage of remdesivir for adults is:<br>• day 1: single loading dose of remdesivir 200 mg administered by intravenous infusion<br>• from day 2 onwards: 100 mg administered once a day by intravenous infusion.<br><br>The total duration of treatment should be 3 days.<br>Patients should be monitored during treatment with remdesivir.<br>Administration of the drug in an outpatient setting should be monitored according to local practice. Use should be in settings where it is possible to treat severe hypersensitivity reactions, including anaphylaxis.<br>An AIFA web register shall be compiled for the prescription and monitoring |

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| | of the outcomes.<br><br>Paxlovid® (**nirmatrelvir-ritonavir**) has been the first oral antiviral drug to be authorized by the EMA for the treatment of COVID-19 in non-hospitalised adults, with an high risk of developing severe COVID-19 disease. The medicine contains two active ingredients, nirmatrelvir and ritonavir, in two separate tablets: nirmatrelvir works by reducing the ability of SARS-CoV-2 to replicate in the body, while ritonavir (a drug that has long been used in the treatment of HIV infection) has no antiviral activity but works as a pharmacological booster by prolonging the action of nirmatrelvir.<br>Paxlovid® should be administered as soon as possible after the diagnosis of COVID-19 and no later than 5 days of the onset of symptoms. Treatment consists of taking two nirmatrelvir tablets and one ritonavir tablet, twice a day, for 5 days.<br>For warnings and precautions for usesee the Summary of Product Characteristics - SmPC (https://www.ema.europa.eu/en/documents/product-information/paxlovid-epar-product-information_en.pdf).<br>Prescribers are recommended to thoroughly investigate the patient's drug history as ritonavir has remarkable interactions with many drugs, so that warnings and recommendations have been included in the product information for Paxlovid. For further support in the evaluation of possible drug interactions it is advisable to consult the website: https://www.covid19-druginteractions.org/ .<br><br>**Molnupiravir** is an antiviral drug (prodrug metabolised to the ribonucleoside analogue N-hydroxycitidine), not yet authorized by the EMA, but made available pursuant to Article 5.2 of Legislative Decree 219/2006 (Ministerial Decree of 26 November 2021).<br>Molnupiravir should be administered as soon as possible after the diagnosis of COVID-19 and no later than 5 days of symptom onset.<br>The recommended dose of molnupiravir is 800 mg (four 200 mg capsules) to be administered orally every 12 hours for 5 days.<br>For warnings and precautions for use, see the information for health professionals (https://www.aifa.gov.it/uso-degli-antivirali-orali-per-covid-19). Please pay attention to the need to follow appropriate contraceptive measures.<br>In women of childbearing potential, use an effective method of contraception (which necessarily includes a barrier method), for the entire duration of treatment and for at least 4 days after the end of the treatment itself.<br>In men who are partners of women of childbearing potential, contraception should be performed for the entire duration of treatment and for at least 3 months after the end of treatment with molnupiravir.<br>Prescription and monitoring of the outcomes at 30 days requires the compilation of an AIFA web register; moreover, since the drug is not authorised by the EMA, but is available in Italy through an emergency |

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| | procedure, the patient is expected to sign the informed consent. |
| **Monoclonal antibodies**<br><br>bamlanivimab/etesevimab information for healthcare professionals https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali<br><br>casirivimab/imdevimab – Ronapreve® (600/600 mg) information for healthcare professionals https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali<br><br>sotrovimab – Xevudy ® information for healthcare professionals https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali | The monoclonal antibodies available in Italy are as follows: casirivimab/imdevimab in combination, bamlanivimab/etesevimab in combination and sotrovimab.<br>The monoclonal antibodies casirivimab/imdevimab and sotrovimab have been authorized by the EMA, while the combination bamlanivimab/etesevimab was made available pursuant to Article 5.2 of Legislative Decree 219/2006 (Ministerial Decree of 6 February 2021 and 12 July 2021).<br>The population eligible to treatment is represented by subjects aged >12 (at least 40 kg in weight), SARS-CoV-2 positive, **non-hospitalised** for COVID-19, not on oxygen therapy due to COVID-19, with **mild to moderate** symptoms and at high risk of severe COVID-19. Possible risk factors include the following:<br>• age> 65 years;<br>• a Body Mass Index (BMI) ≥30, or >95% percentile by age and gender;<br>• chronic renal failure, including peritoneal dialysis or hemodialysis;<br>• uncontrolled diabetes mellitus (HbA1c ≥9.0% or 75 mmol/mol) or with chronic complications;<br>• primary or secondary immunodeficiency;<br>• cardio-cerebrovascular disease (including hypertension with concomitant organ damage)<br>• chronic obstructive pulmonary disease and/or other chronic respiratory disease (eg. people with asthma, pulmonary fibrosis or requiring oxygen therapy for reasons other than SARS-CoV-2);<br>• Chronic liver disease<br>• Hemoglobinopathies<br>• Neurodevelopmental and neurodegenerative diseases.<br>COVID-19 must be of recent onset (in any case no later than 7 days). Treatment is possible beyond seven days from onset only in subjects with immunodeficiency who have negative serology for SARS-CoV-2 and prolonged positivity to the molecular swab.<br>For all three treatments, a single administration is required with the following doses:<br>- bamlanivimab (700 mg) + etesevimab (1,400 mg) IV<br>- casirivimab (600 mg) + imdevimab (600 mg) IV; the combination can be administered with the same posology subcutaneously, if intravenous administration is not feasible and involves a delay in treatment.<br>- sotrovimab (500 mg) IV<br>For methods and duration, see the information for health professionals (https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali).<br>Administration must be monitored for up to one hour after the end of the infusion by an adequately trained healthcare professional, able to manage any serious adverse reactions.<br>An AIFA web register shall be compiled for the prescription and monitoring |

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| | of the outcomes after 30 days. For the combination bamlanivimab/etesevimab and sotrovimab, not yet authorized by the EMA, but available in Italy through an emergency procedure, the patient is also expected to sign the informed consent.<br><br>The effectiveness of monoclonal antibodies may be reduced in patients who have antibodies to SARS-COV-2 or for some viral variants; this must be considered in the therapeutic choice also in relation to the local epidemiological situation. Based on the available data, the table below shows the efficacy against VOCs for each of the monoclonal antibodies available in Italy |
| **Corticosteroids**<br><br>AIFA information sheet: https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19 | Use of **corticosteroids** is recommended in subjects with severe COVID-19 disease requiring oxygen supplementation. This recommendation is based on current evidence of a clinical benefit of such medicines only in this patient setting/disease stage. It should also be underlined that in the initial phase of the disease (with prevailing events related to viral replication), use of cortisone may have a negative impact on the immune response.<br>**Use of corticosteroids at home can be considered in patients with risk factors for disease progression to severe forms, in the presence of worsening pulse oximetry parameters requiring oxygen therapy and if immediate hospitalisation is not possible due to hospital overload.**<br>The study showing reduced mortality with low-dose corticosteroids used dexamethasone at a dosage of 6 mg once a day for up to 10 days. Any other corticosteroids should be used at equivalent dosages (methylprednisolone 32 mg, prednisone 40 mg, hydrocortisone 160 mg).<br>Finally, it is important to consider that in many people with chronic diseases, use of cortisone may cause important adverse events with a risk of complicating the course of the viral disease. A well-known example is diabetic subjects, in whom both the presence of an infection and the use of cortisone can seriously destabilise glycaemic control. |

Efficacia in vitro rispetto alle VOC circolanti degli anticorpi monoclonali disponibili in Italia (https://www.idsociety.org/covid-19-real-time-learning-network/emerging-variants/emerging-covid-19-variants/ )

| **Variante** (WHO label/ Pango lineage) | **Bamlanivimab + etesevimab** | **casirivimab + imdevimab (Ronapreve)** | **Sotrovimab (Xevudy)** |
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| **Omicron B.1.1.529** | Attività neutralizzante assente | Attività neutralizzante assente | Attività neutralizzante conservata |
| **Delta B.1.617.2** | Attività neutralizzante conservata | Attività neutralizzante conservata | Attività neutralizzante conservata |
| **Gamma P.1** | Attività neutralizzante marcatamente ridotta | Attività neutralizzante conservata | Attività neutralizzante conservata |
| **Beta B.1.351** | Attività neutralizzante marcatamente ridotta | Attività neutralizzante conservata | Attività neutralizzante conservata |
| **Alpha B.1.1.7** | Attività neutralizzante conservata | Attività neutralizzante conservata | Attività neutralizzante conservata |

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| **Heparins**<br><br>AIFA information sheet:<br>https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19 | Use of **heparins (usually low molecular weight heparins)** in the prophylaxis of thrombo-embolic events in patients with acute respiratory infection and reduced mobility is recommended by the main guidelines and must continue for the entire period of immobility.<br>Routine use of heparins is **not recommended** in non-hospitalised and non-bedridden subjects due to the infectious episode, as there is no evidence of a clinical benefit in this patient setting/disease stage. In the case of a bedridden subject, the prophylactic dosages of the various available heparin compounds can be used.<br>It should be highlighted that SARS-CoV-2 infection is not a contraindication to continuing an ongoing oral anticoagulant therapy (with AVK or NOA) or even double antiplatelet therapy already in progress. |
| **MEDICINES NOT RECOMMENDED FOR TREATMENT OF COVID-19** | |
| **Antibiotics**<br><br>AIFA information sheet (relating to azithromycin):<br>https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19 | **Use of antibiotics is not recommended for treatment of SARS-CoV-2 infection.**<br>Recent well-conducted randomised clinical trials (which in most cases evaluated the efficacy of azithromycin) have shown that the use of an antibiotic, plain or in association with other drugs, with particular reference to hydroxychloroquine, does not change the clinical course of the disease.<br>The use of an antibiotic can only be considered when the presence of bacterial superinfextion is suspected, in relation to the patient's general clinical condition.<br>An unjustified use of antibiotics can also determine the onset and spread of bacterial resistance, which could jeopardise the response to future antibiotic therapies. |
| **Hydroxychloroquine**<br><br>AIFA information sheet:<br>https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19 | **Use of chloroquine or hydroxychloroquine is not recommended neither to prevent nor to treat the infection.**<br>The randomised clinical trials published to date conclude that the drug is substantially ineffective, against an increase in adverse events, albeit not serious. This entails a negative risk/benefit ratio for using this medicine. |
| **Lopinavir/ritonavir**<br>**Darunavir/ritonavir or cobicistat**<br>AIFA information sheet:<br>https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19 | **Use of lopinavir/ritonavir or darunavir/ritonavir or cobicistat is not recommended neither to prevent nor to treat the infection.**<br>All randomised clinical trials published to date conclude<br>that such treatments are ineffective. |

The recommendations provided reflect existing literature and indications and will be updated in relation to the rapidly evolving scientific evidence. For further details on the individual sheets, please visit AIFA institutional website at the following link: https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19 .

The guidelines provided do not include oxygen therapy, which represents an essential therapeutic aid in the presence of respiratory failure. For its correct use, please refer to the specific recommendations. In addition to these recommendations, it should be noted that subjects on chronic treatment (for example with antihypertensives, ACE inhibitors or statins) are recommended to continue their treatment up to different instructions from their doctor. Subjects on chronic immunosuppressive treatment due to a previous solid organ transplant or to diseases with immune-mediated pathogenesis shall continue their ongoing pharmacological treatment unless otherwise indicated by their treating practitioner.