AIFA RECOMMENDATIONS ON MEDICINES to be used in home management of COVID-19 cases Version 9 – Updated 31/05/2022	
SYMPTOMATIC MEDICINES	
Symptomatic therapy	**Paracetamol or NSAIDs** can be used in case of fever or joint or muscle pain (unless there is a clear contraindication to their use). Other symptomatic medicines can be used on clinical judgment.
MEDICINES TO BE USED ONLY IN SPECIFIC STAGES OF THE DISEASE	
Antivirals Remdesivir – Veklury ® information for healthcare professionals https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19 Nirmatrelvir/ritonavir – Paxlovid ® information for healthcare professionals https://www.ema.europa.eu/en/medicines/human/summaries-opinion/paxlovid Molnupiravir – Lagevrio ® information for healthcare professionals https://www.aifa.gov.it/uso-degli-antivirali-orali-per-covid-19	Three antivirals (remdesivir, nirmatrelvir/ritonavir and molnupiravir) have recently become available for the treatment of adults with COVID-19 who do not require supplemental oxygen therapy and who are at increased risk of progression to severe forms of COVID-19. The patient **should not be hospitalised** due to COVID-19, should have a **mild-to-moderate form** and at least one of the following risk factors associated with progression to severe disease: • Oncological/oncohaematological pathology in active phase • Chronic renal insufficiency • Chronic obstructive pulmonary disease and/or other chronic respiratory disease (e.g. subjects with asthma, pulmonary fibrosis or requiring oxygen therapy for reasons other than SARS-CoV-2) • Primary or acquired immunodeficiency • Obesity (BMI ≥30) • Cardio-cerebrovascular disease (heart failure, coronary heart disease, cardiomyopathy, hypertension with concomitant organ damage, stroke) • Diabetes mellitus uncompensated (HbA1c>9.0% 75 mmol/mol) or with chronic complications • Age >65 years • Chronic liver disease • Haemoglobinopathies • Neurodevelopmental and neurodegenerative diseases **Remdesivir** is an antiviral medicine (a propharmaceutical nucleotide analogue of adenosine), already authorised by the EMA for the treatment of COVID-19 with pneumonia requiring supplemental oxygen therapy, which received authorisation in December 2021 for an extension of indication for the treatment of COVID-19 in 'adults who do not require supplemental oxygen therapy and have an increased risk of progression to severe COVID-19'. Treatment should be started as soon as possible after the diagnosis of COVID-19 and within 7 days after the onset of symptoms. The recommended dosage of remdesivir in adults is:

- day 1: single loading dose of remdesivir 200 mg administered by intravenous infusion
- from day 2 onwards: 100 mg administered once daily by intravenous infusion.

The total duration of treatment should be 3 days.
Patients should be monitored during remdesivir treatment.
Administration of the medicine in an outpatient setting should be monitored according to local practice. Use must take place in conditions in which it is possible to treat severe hypersensitivity reactions, including anaphylaxis.
An AIFA web register is to be compiled for prescription and monitoring of outcomes.

Paxlovid® (**nirmatrelvir-ritonavir**) is the first oral antiviral medicine authorised by the EMA for the treatment of COVID-19 in adult, non-hospitalised subjects at high risk of developing severe COVID-19 disease. The medicine contains two active ingredients, nirmatrelvir and ritonavir, in two separate tablets: nirmatrelvir acts 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 acts as a pharmacological booster by prolonging the action of nirmatrelvir.
Paxlovid® should be administered as soon as possible after the diagnosis of COVID 19, no later than 5 days after the onset of symptoms. Treatment consists of taking two nirmatrelvir tablets and one ritonavir tablet, twice daily, for 5 days.
For warnings and precautions for use, see the Summary of Product Characteristics - SmPC
(https://www.ema.europa.eu/en/documents/product-information/paxlovid-epar-product-information_en.pdf).
The attention of prescribers is drawn to the need to thoroughly investigate the patient's drug history as ritonavir has important drug interactions with many drugs, in relation to which 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/ .

Molnupiravir is an antiviral medicine (prodrug metabolized to the ribonucleoside analogue N hydroxycitidine), not yet authorised by the EMA, but made available pursuant to Article 5.2 of Legislative Decree 219/2006 (Ministerial Decree of 26 November 2021).
Molnupiravir should be administered as soon as possible after confirming the diagnosis of COVID 19, no later than 5 days after the onset of symptoms. The recommended dose of molnupiravir is 800 mg (four 200 mg capsules) to be taken orally every 12 hours for 5 days.
For warnings and precautions for use, see the information for health professionals (https://www.aifa.gov.it/uso-degli-antivirali-orali-per-covid-

	19). Attention is drawn to the need to follow appropriate contraceptive measures. In women of childbearing potential, an effective method of contraception (necessarily including a barrier method) should be used for the entire duration of treatment and for at least 4 days after the end of treatment. 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 molnupiravir treatment. For the prescription and monitoring of the results after 30 days, an AIFA web register should be filled in; furthermore, since the medicine is not authorised by EMA, but available in Italy through an emergency procedure, the patient must sign the informed consent.
Monoclonal Antibodies bamlanivimab/etesevimab information for healthcare professionals https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali casirivimab/imdevimab – Ronapreve® (600/600 mg) information for healthcare professionals https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali sotrovimab – Xevudy ® information for healthcare professionals https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali	The monoclonal antibodies available in Italy are: the combination casirivimab/imdevimab, the combination bamlanivimab/etesevimab and sotrovimab. The monoclonal antibodies casirivimab/imdevimab and sotrovimab have been authorised by the EMA, while the combination bamlanivimab/etesevimab has been made available pursuant to Article 5.2 of Legislative Decree 219/2006 (Ministerial Decree of 6 February 2021 and 12 July 2021). The candidate population for therapy with the three treatments is represented by subjects aged 12 years or older (and at least 40 kg), SARS-CoV-2 positive, not hospitalised for COVID-19, not on oxygen therapy for COVID-19, with mild to moderate symptoms and who are at high risk of severe COVID-19. Possible risk factors include the following: • Oncological/oncohaematological pathology in active phase • Chronic renal insufficiency • Chronic obstructive pulmonary disease and/or other chronic respiratory disease (e.g. subjects with asthma, pulmonary fibrosis or requiring oxygen therapy for reasons other than SARS-CoV-2) • Primary or acquired immunodeficiency • Obesity (BMI ≥30) • Cardio-cerebrovascular disease (heart failure, coronary heart disease, cardiomyopathy, hypertension with concomitant organ damage, stroke) • Diabetes mellitus uncompensated (HbA1c>9.0% 75 mmol/mol) or with chronic complications • Age >65 years • Chronic liver disease • Haemoglobinopathies • Neurodevelopmental and neurodegenerative diseases. 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. For all three treatments, a single administration is required at the following dosages: - bamlanivimab (700 mg) + etesevimab (1.400 mg) IV - casirivimab (600 mg) + imdevimab (600 mg) IV; the combination can be administered at the same posology subcutaneously, if intravenous administration is not feasible and involves a delay in treatment. - sotrovimab (500 mg) IV For the methods and duration, see the information for health professionals (https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali). Administration should 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. For the prescription and monitoring of the results after 30 days, an AIFA web register hat to be compiled. For the bamlanivimab/etesevimab association, not yet authorised by EMA, but available in Italy through an emergency procedure, the patient's informed consent is also required. The efficacy of monoclonal antibodies may be reduced with regard to certain viral variants; this must be taken into account in the choice of treatment, also in relation to the local epidemiological situation. In particular, all anti-SARS-CoV-2 antibodies available in Italy (bamlanivimab/etesevimab, casirivimab/imdevimab and sotrovimab) maintain adequate antiviral activity against the alpha (lineage B.1.1.7) and delta (lineage B.1 .617.2), whereas the neutralising activity of the bamlanivimab/etesevimab combination, unlike the other available monoclonal antibodies (casirivimab/imdevimab and sotrovimab), is absent against the beta (B.1.351) and gamma (P.1) variants. Efficacy data on the omicron variant indicate a substantial inefficacy of the bamlanivimab/etesevimab and casirivimab/imdevimab combinations against the BA.1 subvariant, with respect to which sotrovimab appears to maintain adequate efficacy. On the other hand, sotrovimab also has a reduced neutralising capacity against subvariant BA.2, in respect of which data of even residual caserivimab/imdevimab activity is emerging. In general, based on the advancement of knowledge, diagnostic availability, any logistical-organizational difficulties and the epidemiological situation, the opportunity to determine the viral variant involved in the infection may be considered before deciding on which monoclonal antibody or combination of monoclonal antibodies should be directed the choice of therapy. Please note that these data are constantly evolving and that therefore the indication for the use of specific monoclonal antibodies may vary over time depending on the variant of SARS-CoV-2 prevalent in the country and its sensitivity to the different products available.

Corticosteroids AIFA Information Sheet: https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19	The use of **corticosteroids** is recommended in hospitalised patients with severe COVID-19 disease who need oxygen supplementation. This recommendation is based on the fact that there is currently evidence of a clinical benefit of such medicines only in this setting of patients/stage of disease. Please note that in the initial phase of the disease (in which phenomena related to viral replication prevail) the use of cortisone could have a negative impact on the developed immune response. **The use of corticosteroids at home may be considered in patients who present risk factors for disease progression to severe forms, in the presence of a worsening of pulse oximetry parameters requiring oxygen therapy, and if hospitalisation is not immediately possible due to overload.** The study that demonstrated a reduction in mortality with low doses of corticosteroids used dexamethasone at a dosage of 6 mg for up to 10 days. Any other corticosteroids should be used at equivalent dosages (methylprednisolone 32 mg, prednisone 40 mg, hydrocortisone 160 mg). Finally, it is important to remember that in many chronically ill individuals, the use of corticosteroids may lead to major adverse events that risk complicating the course of the disease. A well-known example is that of diabetic subjects in whom both the presence of an infection and the use of cortisone can seriously destabilise glycaemic control.
Heparins AIFA Information Sheet: https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19	The use of **heparins (usually low-molecular-weight heparins)** in the prophylaxis of thrombo-embolic events in the medical patient with acute respiratory infection and reduced mobility is recommended by the main guidelines and should continue throughout the period of immobility. 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 clinical benefit in this patient setting/disease phase. In the case of the bedridden subject, prophylactic dosages of the various available heparin compounds may be used. It is important to remember that SARS-CoV-2 infection is not a contraindication to continuing oral anticoagulant therapy (with AVK or NAO) or even dual antiplatelet therapy already underway.
MEDICINES NOT RECOMMENDED FOR TREATMENT OF COVID-19	
Antibiotics AIFA Information Sheet	**The use of antibiotics is not recommended for the treatment of SARS-CoV-2 infection.** Recent well-conducted randomised clinical trials (which in most cases evaluated the efficacy of azithromycin) have shown that the use of an antibiotic, alone or combined with other drugs, with particular reference to hydroxychloroquine, does not change the clinical course of the disease. The use of an antibiotic can only be considered when the presence of bacterial overlap is suspected, in relation to the patient's general clinical picture.

(relating to azithromycin): https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19	An unjustified use of antibiotics can also determine the onset and spread of bacterial resistance that could impair the response to future antibiotic therapies.
Hydroxychloroquine AIFA Information Sheet: https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19	**The use of chloroquine or hydroxychloroquine is not recommended either to prevent or to treat infection.** The randomised clinical trials published to date conclude for substantial ineffectiveness of the medicine in the face of an increase in adverse events, albeit not serious ones. This makes the balance between the benefits and risks of using this medicine negative.
Lopinavir / ritonavir **Darunavir / ritonavir o cobicistat** AIFA Information Sheet: https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19	**The use of lopinavir/ ritonavir or darunavir/ ritonavir or cobicistat is not recommended either for the purpose of preventing or curing infection.** The randomised clinical studies published to date all conclude for an inefficacy of these pharmacological approaches.
The recommendations provided reflect the existing literature and indications and will be updated in relation to rapidly evolving scientific evidence. For more details on the individual sheets, please consult the 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 exclude oxygen therapy, which represents an essential therapeutic aid in the presence of respiratory insufficiency and for the correct use of which please refer to the specific recommendations. In addition to these recommendations, it should be pointed out that subjects undergoing chronic treatment (e.g. with antihypertensives, ACE inhibitors or statins) are recommended to continue their treatment until otherwise ordered by their doctor. Individuals undergoing chronic immunosuppressive treatment due to a previous solid organ transplant rather than due to immune-mediated pathogenesis will be able to continue their current drug treatment unless otherwise instructed by their treating specialist.	