



## Position statement from the Brazilian Society of Nephrology regarding chloroquine and hydroxychloroquine drug dose adjustment according to renal function


Nota da Sociedade Brasileira de Nefrologia em relação ao ajuste das drogas cloroquina e hidroxicloroquina pela função renal

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### ABSTRACT

Chloroquine and hydroxychloroquine have shown promising preliminary results and have been discussed as therapeutic options for patients with Covid-19. Despite the lack of robust evidence demonstrating the benefits and justifying the use of one of these drugs, the final decision is the responsibility of the attending physician and should be individualized and shared, whenever possible. This position statement recommends dosage adjustment for these drugs in the context of renal impairment.

**Keywords:** Chloroquine; Hydroxychloroquine; Antimalarials; Posology; Drug Dosage Calculation; Renal Failure.

### RESUMO

Em razão de resultados preliminares promissores, a hidroxicloroquina e a cloroquina têm sido discutidas como opção terapêutica para pacientes com Covid-19. Apesar da ausência de estudos robustos que evidenciem o benefício e justifiquem o uso de uma dessas drogas, a decisão final compete ao médico assistente, devendo ser individualizada e, sempre que possível, compartilhada. A presente nota pretende orientar o ajuste posológico dessas drogas no contexto da disfunção renal.

**Palavras-chave:** Cloroquina; Hidroxicloroquina; Antimaláricos; Posologia; Cálculos da Dosagem de Medicamento; Insuficiência Renal.

On the first day of April 2020, Informative Note n° 6/2020-DAF/SCTIE/MS was published, establishing that the Brazilian Ministry of Health (MS) would make the medications available for use, in confirmed cases and at medical criteria, chloroquine and hydroxychloroquine as adjunctive therapy in the treatment of severe forms in hospitalized patients, without other supportive measures being neglected in their favor<sup>1</sup>. On April 6, the MS published “Guidelines for the diagnosis and treatment of Covid-19”, in which it also instructed on the use of chloroquine and hydroxychloroquine as adjuvant therapy in severe forms of the disease, in confirmed cases and upon medical discretion<sup>2</sup>.

On April 23, the Federal Board of Medicine (CFM) published its Note No. 04/2020, which establishes criteria and conditions for the prescription of chloroquine and hydroxychloroquine for

patients with a confirmed diagnosis of Covid-19<sup>3</sup>. The CFM, in its understanding, concluded that there is no solid evidence that these drugs have a confirmed effect on the prevention and treatment of this disease. However, considering the exceptional nature of the situation, and during the declared period of the Covid-19 pandemic, CFM considered it possible to prescribe these drugs in three specific situations:

1. The use of chloroquine or hydroxychloroquine in patients with mild symptoms, in the onset of the clinical picture, after other viruses (such as influenza, H1N1, dengue) and a confirmed diagnosis of Covid-19 can be considered.
2. Patients with important symptoms, but still without the need for intensive care, with or without a recommendation for hospitalization.

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3. Patients in critical condition receiving intensive care, including mechanical ventilation.

In these situations, the principle that must, mandatorily, guide the treatment of the patient is that of the physician's autonomy, as well as upholding the doctor-patient relationship, "this being the closest possible, with the objective of offering the best treatment currently available to the patient". In all contexts, the prescription of drugs will be the responsibility of the attending physician, in a decision shared with the patient<sup>3</sup>.

### USE OF CHLOROQUINE AND HYDROXYCHLOROQUINE IN PATIENTS WITH CHRONIC KIDNEY DISEASE

The Brazilian Society of Nephrology understands that there is no solid evidence that these drugs have a confirmed effect on the prevention and treatment of Covid-19. If the doctor chooses to use one of these drugs in the population with Chronic Kidney Disease, especially in dialysis patients, he/she must consider its long half-life (up to 40-50 days). Both are not excreted by dialysis and have renal excretion of around 40-50%, with 50% protein binding<sup>4-7</sup>. Therefore, chloroquine and hydroxychloroquine should be used with extreme caution in patients with chronic or acute renal dysfunction, especially due to the arrhythmogenic potential of the drug.

While the manufacturer and some sources do not advise on dose adjustment for renal function, other recommendations suggest a 50% dose reduction in patients with glomerular filtration rate  $<10 \text{ mL/min/1.72m}^2$  on hemodialysis, hemodiafiltration, peritoneal dialysis or under conservative treatment<sup>6,8</sup>.

Given the above and the associated risks, the Brazilian Society of Nephrology advises its associate doctors to prescribe one of these drugs according to the recommendations established by CFM and MS, which recommend a 50% reduction in the recommended dose of chloroquine and hydroxychloroquine in patients with glomerular filtration rate  $<10 \text{ mL/min/1.72 m}^2$ , in dialysis or conservative treatment. The doctor should also note that, regardless of the modality of renal replacement therapy, no additional dose of the drug is required after dialysis.

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