

## Drug Dosing Recommendations for Obese COVID-19 Patients



Obesity is highly prevalent in patients who are hospitalised with COVID-19. It is a widely recognised risk factor for severe COVID-19 infection with a greater risk for mortality compared with non-obese patients. With each 1 kg/m<sup>2</sup> increase in body mass index, the risk for severe infection increases by 9% and mortality by 6%.

While there are evidence-based guidelines to treat patients with COVID-19, dosing information specific to patients with obesity is lacking. Obesity can have a significant impact on drug pharmacokinetics. Hence, accounting for these pharmacokinetic alterations in this patient population is important, and failure to do so can lead to underdosing, overdosing, and/or treatment failure.

In this review, the authors provide clinicians with guidance for making dosing decisions for medications used to treat patients with COVID-19:

### Dexamethasone

Dexamethasone is a long-acting corticosteroid widely used in patients with severe COVID-19 infection. The drug has demonstrated significant improvement in mortality in patients requiring mechanical ventilation or supplemental oxygen. So far, the data evaluated for dexamethasone suggests that dosing adjustments secondary to weight are unnecessary, and standard doses of dexamethasone similar to those used in non-obese patients should be utilised in obese patients.

### Janus kinase inhibitors

#### Baricitinib

Baricitinib modulates the immunological and inflammatory response following a COVID-19 infection. The drug has a large volume of distribution. The package insert for the drug states body weight does not have a clinically relevant effect. The effect of weight-based dosing adjustments remains unknown, and therefore, standard doses of baricitinib are suggested in obese and non-obese patients.

#### Tofacitinib

Tofacitinib is used when baricitinib is either unavailable or not feasible. This drug also has a large volume of distribution, but so far, bodyweight differences have not been observed. Standard dosing should thus be utilised for obese patients.

### IL-6 inhibitors

#### Tocilizumab

Tocilizumab has shown a beneficial effect on outcomes in patients with COVID-19. The drug has a small volume of distribution and is hydrophilic. Pharmacokinetic studies have shown linear clearance to be correlated with weight but not in a proportional manner. This could lead to over-exposure with weight-based dosing in patients with obesity. An 800 mg dose cap seems appropriate in patients up to 160 kg. More research is required to evaluate if higher doses may be needed in patients exceeding 160 kg.

#### Sarilumab

This drug is recommended as an alternative to tocilizumab when tocilizumab is not available. It is a hydrophilic compound with a small volume of distribution. The recommended dose for COVID-19 is 400 mg. A 20% reduction in AUC has been reported with a weight change from 71 to 83 kg in one study. Still, body weight was not associated with a change in the pharmacokinetic/pharmacodynamic model in another study. Therefore, no dose adjustments are recommended for this drug based on weight.

### Antiviral therapy

#### Remdesivir

Remdesivir inhibits viral replication by inhibiting SARS-CoV-2 RNA-dependent RNA polymerase. The administration of this drug by IV infusion requires patients to be at least 40 kg, 12 years or older, with an estimated glomerular filtration rate of at least 30 mL/min. The dosing of remdesivir is non-weight based, and there is no information related to dosing in obesity. However, modelling data suggests that the lipophilic

nature of the drug may have pharmacokinetic implications in obese patients. However, with the data that is currently available, the recommended fixed-dose regimen is still valid for patients with less extreme forms of obesity.

Overall, this review makes it evident that clinicians have very little guidance on the applicability of available dosing information for patients with more extreme forms of obesity. There is a need to improve product labelling and conduct future investigations that enrol diverse populations, including patients of more extreme body habitus. In addition, there is a need to provide more details on size descriptors such as weight and BMI.

Source: [Critical Care](#)

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Published on : Mon, 21 Mar 2022