Clinically relevant Drug-Drug interaction between AEDs and medications used in the treatment of COVID-19

The Liverpool Drug Interaction Group (based at the University of Liverpool, UK), in collaboration with the University Hospital of Basel (Switzerland) and Radboud UMC (Netherlands) (http://www.covid19-druginteractions.org/) is constantly updating a list of interactions for many co-medication classes. This table is adapted from their valuable work, summarize treatments in epilepsy and includes other drugs.

In light of pharmacological considerations, single cases management is mandatory.

Drugs reported (constantly updated): ANK, anakinra; ATV, atazanavir; AZT, azithromycin; CLQ, chloroquine; DRV/c, darunavir/cobicistat; EMP, emapalumab FAVI, favipiravir; HCLQ, hydroxychloroquine; IFN-β-1a, interferon β-1a; LPV/r, lopinavir/ritonavir; NITA, nitazoxanide; RBV, ribavirin; RDV, remdesivir/ GS-5734; OSV, oseltamivir; SAR, sarilumab; TCZ, tocilizumab.
↑ Potential increased exposure of the AED; ↓ Potential decreased exposure of the AED; ◊ Potential increased exposure of COVID drug; ◊◊ Potential decreased exposure of COVID drug; ↔ No significant effect; ♥ One or both drugs may cause dysrhythmia.

1 An increase in IL-6, as well as other cytokines (e.g., IL-1), can improve plasmatic concentration of administered drugs reducing hepatic metabolism (CYP-mediated), a treatment with Tocilizumab, Sarilumab (both IL6Ra), Anakinra (IL1Ra) or Emapalumab (IFNγ-a) could reduce plasmatic concentrations of other previous co-treatments due to hepatic metabolism normalization.

2 QT prolongations can occur with Azithromycin, Chloroquine and Hydroxychloroquine. Pay particular attention in case of co-administration of these drugs.

3 No specific studies have been performed in humans to assess drug-drug interactions.

4 Chloroquine should not be administered in patients with epilepsy. Hydroxychloroquine can lower the seizure threshold.


6 Recently, a randomized clinical trial has observed no benefits of the lopinavir/ritonavir treatment compared to standard care ([https://www.nejm.org/doi/full/10.1056/NEJMoa2001282](https://www.nejm.org/doi/full/10.1056/NEJMoa2001282)).

7 Some data on drug interactions of Remdesivir are not yet available.

**Notes:**

- **Ritonavir** is a strong inhibitor of CYP3A and 2D6 per se, independently to co-administered antiviral. Carbamazepine, phenobarbital and phenytoin are not recommended in co-treatment.
- **Cobicistat** is a strong inhibitor of CYP3A4 per se; carbamazepine, phenobarbital and phenytoin should not be used in co-treatment.
- Atazanavir can increase midazolam plasmatic concentration until 4-fold.
- Also refer to SmPC for further information.
