Summary:

- Strong CYP3A4 inhibitors (e.g. clarithromycin, ketoconazole, itraconazole, voriconazole, nefazodone, ritonavir and atazanavir) interact with ticagrelor and increase its plasma level by up to five times.
- This increases the risk of bleeding.
- **The macrolide of choice is azithromycin as it does not interact.**
- Unless there is a strong clinical indication, avoid macrolides or use with caution in patients with cardiovascular history.

Ticagrelor is a widely used antiplatelet medicine that interacts with strong CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, voriconazole, clarithromycin, nefazodone, ritonavir, and atazanavir), increasing its plasma level by up to five times and therefore increasing the risk of bleeding. These antimicrobials should not be given with ticagrelor. Erythromycin (and fluconazole) will probably affect ticagrelor, but both are safe to use in combination with it. There is no interaction with azithromycin.

It would not be possible to stop ticagrelor as it is likely to have an effect for several days after stopping treatment. Therefore an alternative to clarithromycin must be used.

Unless there is a strong clinical indication, avoid macrolides or use with caution in patients with cardiovascular history. If there is no alternative therapy, patients with known QT-interval prolongation, QT-interval prolongation due to electrolyte disturbances or taking medicines which can prolong the QT-interval should have their ECG (QT) monitored.

**Community acquired pneumonia**

- **Low severity:** use oral doxycycline 200 mg loading dose then 100 mg twice daily in place of oral clarithromycin
- **Moderate severity - oral route:** use oral azithromycin 500 mg daily for 3 days only (in combination with oral amoxicillin)
- **Moderate to severe - IV route:** use IV levofloxacin as monotherapy

For other infections, guidance on alternative treatments for patients requiring strong CYP3A4 inhibitors can be provided by Microbiology, Infectious Diseases or the Antimicrobial Pharmacists. Guidance on interactions with other medicines can be provided by The Leeds Medicines Advice Service.

**References and Provenance**

- MiDatabank 148795

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