

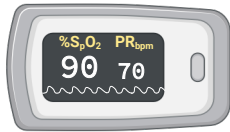



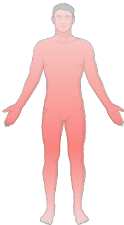




Clozapine initiation (week 1-4)

- **Pre-exposure minimum:** high-sensitivity troponin, CRP, FBC, vital parameters, ECG
- **Pre-exposure enhanced:** + TTE, + NT-proBNP¹
- **Starting dose of clozapine:** 12.5 mg

Minimum and enhanced monitoring requirements in weeks 1-4 (clozapine initiation)

| | Heart rate | Temperature | SpO ₂ | ECG | postural BP | hs troponin | CRP | NT-proBNP ¹ | FBC ² |
|-----------|--|--|--|--|--|--|--|--|--|
| | Clinical | | | Instrumental | | Laboratory parameters | | | |
| Parameter |  |  |  |  |  |  |  |  |  |
| Minimum | twice weekly | twice weekly | weekly | every 2 weeks | weekly | weekly | weekly | - | weekly |
| Enhanced | daily | daily | twice weekly | weekly | twice weekly | weekly | weekly | weekly | weekly |












Dose range for clozapine at **day 7**: 25-50mg

Dose range for clozapine at **day 14**: 100-125mg

Supplementary Table 2: Minimum and enhanced monitoring requirements in weeks 1-4 (clozapine initiation) and recommended clozapine dose ranges. Created with biorender

Week 5-8 (clozapine initiation)

| | Heart rate | Temperature | SpO ₂ | ECG | postural BP | hs troponin | CRP | NT-proBNP ¹ | FBC ² |
|----------------------|---|---|---|---|---|---|---|---|---|
| | Clinical | | | Instrumental | | Laboratory parameters | | | |
| Parameter |  |  |  |  |  |  |  |  |  |
| Minimum/ Enhanced | weekly | weekly | weekly | every 4 weeks | weekly | every 2 weeks | every 2 weeks | - | weekly |

Legend

¹ if available in the respective jurisdiction

² only for cardiac monitoring irrespective of regular ANC monitoring

³ clinical symptoms highly suggestive of myocarditis in individuals treated with clozapine are: fever, chest pain or dyspnoea and flu-like symptoms

⁴ i.e. new ST-segment and T-wave deviations

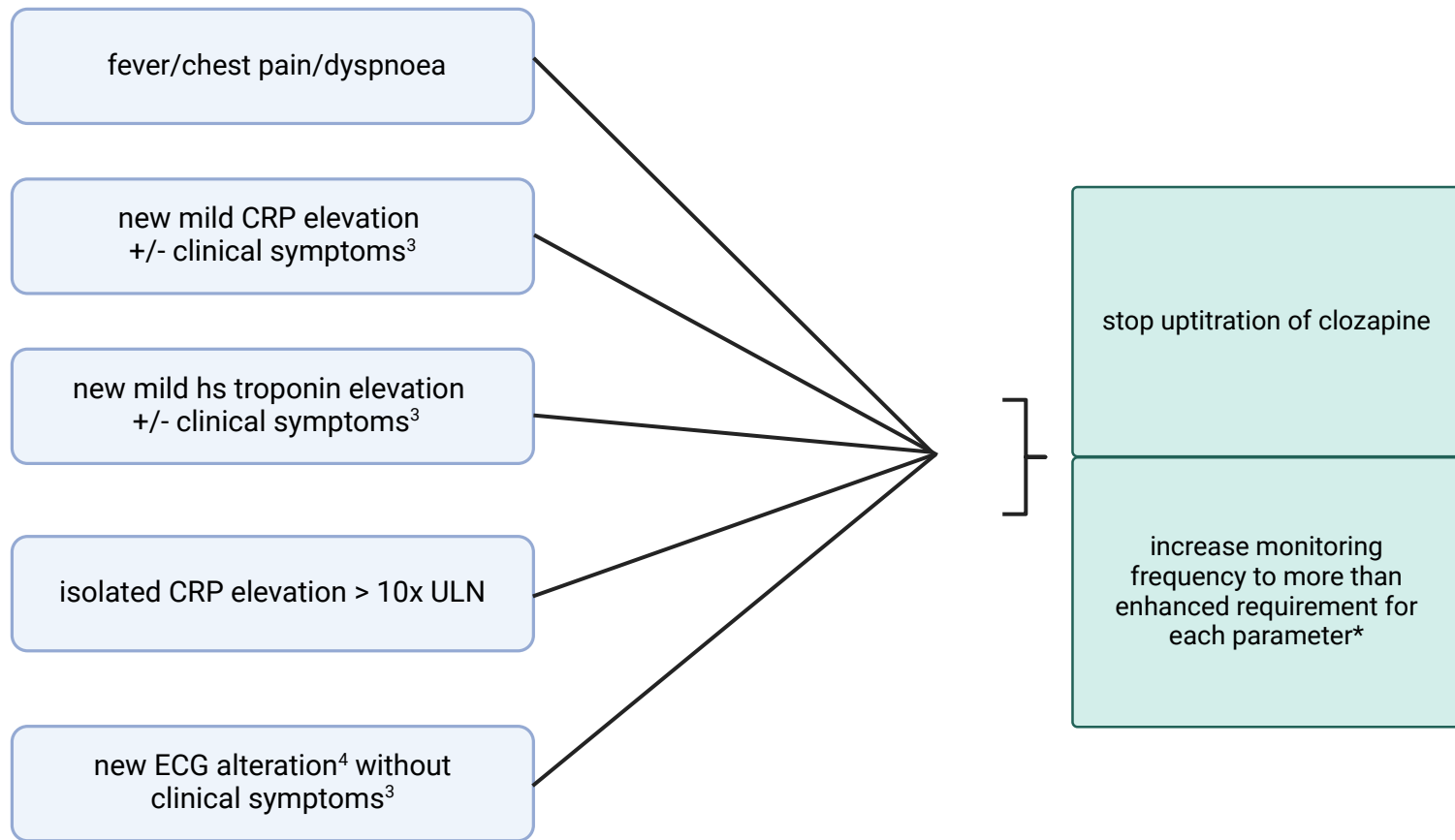
⁵ potentially life-threatening conditions (such as torsades de points, cardiogenic shock, etc) would trigger clozapine discontinuation before laboratory results are confirmed

⁶ add NT-proBNP if cardiac imaging is not immediately available

⁷ cardiac MRI shall be performed in cases when hs troponin I/T > 99th percentile, NT-proBNP ≥ 125 pg/ml or new significant rise from baseline beyond the biological and analytical variation of the assay used.

Supplementary Table 3: Minimum and enhanced monitoring requirements in weeks 5-8 (clozapine initiation).

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General rules:

- waiting period of at least 4 weeks after a mRNA vaccination and at least 2-3 weeks (after resolution of the fever) after a viral/bacterial infection to minimize CAM risk
- Caveat: special requirements (see Table 2)
- additional therapeutic drug monitoring with clozapine/norclozapine ratio in week 2 can help guide understanding around potential slow metabolizers

