Clinical Guidance from the MGH-McLean-NSMHA Clozapine Working Group

On Clozapine Prescribing During the COVID-19 Public Health Emergency for Clinicians and Pharmacists

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The current COVID-19 public health emergency (PHE) poses particular access problems for patients treated with clozapine due to registry-based and prescriptive “no blood, no drug” rules for prescribing and dispensing this essential psychiatric medication. With social distancing and staying home the current orders of the day, the risk of obtaining blood work to monitor the absolute neutrophil count (ANC), according to the FDA-mandated monitoring schedule, may outweigh the benefit – or may not be possible at all. On March 22, 2020, the FDA offered the following guidance regarding medications covered by certain Risk Evaluation and Mitigation Strategy (REMS)-required testing during this PHE, including laboratory testing of ANC for clozapine:

For drugs subject to these REMS with laboratory testing [...], health care providers prescribing and/or dispensing these drugs should consider whether there are compelling reasons not to complete these tests [...] during the PHE, and use their best medical judgment in weighing the benefits and risks of continuing treatment in the absence of laboratory testing [...]. Health care providers should also communicate with their patients regarding these judgments, including the risks associated with it.

The wording of the FDA guidance has led to many questions about how it should be applied. We offer the following clinical guidance for our clinicians and pharmacists for clozapine dispensing during the COVID-19 public PHE which is in accordance with the spirit of the FDA guidance and which will be in effect for the duration of the PHE. This guidance does not address clozapine prescribing in general:

- Clinicians may determine that obtaining mandated clozapine blood work (i.e., ANC) during the COVID-19 pandemic is only possible at unacceptably high risk for patients or providers – or practically not possible at all. Patients may, for example, be in isolation, in quarantine, or at high risk for mortality were they to be infected while traveling to a clinic or laboratory for blood work.
- In determining whether to waive ANC testing consistent with the new FDA guidance, clinicians should consider the duration of clozapine treatment. Long-term clozapine patients (12 months or longer) in particular are at very low risk for clozapine-associated severe neutropenia, with the peak incidence occurring at one month of clozapine exposure and a decline to negligible risk levels after one year of treatment.
- Pharmacists, in collaboration with the patient’s physician and using their professional judgement should dispense the most appropriate number of pills without a current ANC on file. For many patients on long-term treatment, this may simply be an additional 30-day supply of
clozapine, assuming an ANC can be obtained in a month. There may, however, be situations
where a 60-day or 90-day supply may be prudent, depending on how the pandemic evolves over
the next few months. For patients newly started on clozapine, more cautious dispensation of
clozapine would be prudent.

- Pharmacists and clinicians may determine that having a one-month emergency supply on hand
may be prudent.
- Pharmacists are encouraged to dispense additional clozapine even if payment is not guaranteed.
Hopefully, retroactive payments would be forthcoming in such cases.
- The decision to continue clozapine treatment in the absence of scheduled ANC monitoring
should be made in collaboration with patients and family members (or legal guardian),
explaining the rational for proceeding without ANC monitoring and weighing the risks and
benefits of this approach.
- Patients who develop a sore throat and fever, among other symptoms, during a period without
ANC monitoring should be medically assessed for clozapine-associated neutropenia, including
obtaining an ANC. They should not simply be isolated at home under the assumption that they
may have a viral illness like COVID-19.
- Inpatient units should discharge patients with the maximum clozapine supply deemed clinically
safe to avoid gaps during the transition to outpatient care. This may be 30 days for established
clozapine patients. Inpatient units should obtain an ANC at the time of discharge (and enter it
into REMS) to “buy” more time.
- While patients should not be told to go to APS for the sole purposes of obtaining an ANC,
clozapine patients already in the ED should have an ANC drawn (and entered into REMS) so a
recent one is on file.

References

1. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-certain-rem-
requirements-during-covid-19-public-health-emergency-guidance-industry-and


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