Interim Treatment Guidance for Central Nervous System (CNS) and/or Parameningeal Infections Associated with Injection of Potentially Contaminated Steroid Products

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These recommendations are based upon growing evidence that *Exserohilum rostratum* (a brown-black mold) is the predominant pathogen in this outbreak, and expert opinion and published literature indicating that voriconazole may be effective in treating infections due to brown-black molds, as well as infections due to *Aspergillus* species. Recommendations are also based on considerations related to the anatomic site of infection and pharmacokinetics of antifungal agents. CDC continues to consult with national experts on treatment options for fungal CNS and/or parameningeal infections in patients associated with this cluster.

This is interim guidance for treatment of adult patients with CNS and/or parameningeal infections associated with injections of potentially contaminated steroid products from the New England Compounding Center. Interim guidance may change as new information becomes available.

- Consult an infectious disease physician to assist with diagnosis, management, and follow-up, which may be complex and prolonged.
- Initiate empiric antifungal therapy after collecting cerebrospinal fluid for culture using the following regimen in addition to routine empiric treatment protocols to cover for potential bacterial pathogens until the etiology of the patient’s CNS and/or parameningeal infection has been identified:
  - **Voriconazole**, preferably at a dose of 6 mg/kg every 12 hours:
    - Voriconazole should be continued at a dose of 6 mg/kg every 12 hours, whenever possible, for the duration of treatment. This dose is recommended because ensuring adequate penetration of voriconazole into the CNS is critical.
    - Regular monitoring of serum voriconazole concentrations (e.g., at a weekly interval) is recommended, aiming for trough levels of 2-5 mcg/ml.
    - Patients with more severe disease should be started on voriconazole IV.
    - Patients with mild disease may be started on oral voriconazole at the provider’s discretion. The above target serum levels of voriconazole are readily achievable using the oral form but may require a slightly higher dose and make take longer to achieve if unforeseen problems with gastro-intestinal intolerance or poor absorption are encountered.
    - If provider wants to transition patients initially started on IV voriconazole therapy to oral therapy, this should be done only after a patient is clinically stable or improving, as long as no contraindications to oral therapy exist.
    - Providers and patients should be aware of and monitor for potential adverse effects of voriconazole, including (but not limited to) hepatic toxicity and neurotoxicity.
    - Providers should carefully consider and manage the potential for voriconazole drug interactions in all patients.
  - Providers should consider giving **liposomal amphotericin B in addition to voriconazole** to patients who present with severe disease, and patients started...