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Investigational Drug Available Directly from CDC for the Treatment of Free-Living Ameba Infections

Summary: CDC now has an expanded access investigational new drug (IND) protocol in effect with the Food and Drug Administration (FDA) to make miltefosine available directly from CDC to clinicians for treatment of free-living ameba (FLA) infections in the United States.

Background

Infections caused by FLA are severe and life-threatening. These infections include primary amebic meningoencephalitis (PAM) caused by *Naegleria fowleri** and granulomatous amebic encephalitis caused by *Balamuthia mandrillaris*[†] and *Acanthamoeba* species.[§] Although several drugs have in vitro activity against FLA, mortality from these infections remains greater than 90% despite treatment with combinations of drugs.

Miltefosine is a drug used to treat leishmaniasis and also has shown in vitro activity against FLA (1), but as an investigational drug, it has not been readily available in the United States. With CDC assistance, however, miltefosine has been administered in combination with other drugs since 2009 for FLA infections as single-patient emergency use with permission from the Food and Drug Administration. Although the number of *B. mandrillaris* and *Acanthamoeba* species infections treated with a miltefosine-containing regimen is small, it appears that a miltefosine-containing treatment regimen does offer a survival advantage for these usually fatal infections (2). Miltefosine has not been used successfully to treat a *Naegleria* infection, but the length of time it has taken to import miltefosine from abroad has made timely treatment of fulminant *Naegleria* infections with miltefosine difficult.

CDC now has an expanded access IND protocol in effect with the Food and Drug Administration to make miltefosine available directly from CDC for treatment of FLA in the United States. The expanded access IND use of miltefosine for treatment of FLA is partly supported by 26 case reports of FLA infection from around the world during the period of 2008–2012 in which miltefosine was part of the treatment regimen (Unpublished data, Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC, 2013). Miltefosine is generally well-tolerated, with gastrointestinal symptoms as the most commonly reported adverse effects.

Recommendation

Clinicians who suspect they have a patient with FLA infection who could benefit from treatment with miltefosine should contact CDC to consult with an FLA expert. See the **For More Information** section below for information on contacting a CDC FLA expert.

For More Information

- For diagnostic assistance, specimen collection guidance, specimen shipping instructions, treatment recommendations, and information on obtaining miltefosine from CDC, clinicians should contact the CDC Emergency Operations Center at 770-488-7100 to request to speak to an FLA expert.

- For more information on diagnostic assistance specimen collection guidance and specimen shipping instructions, see <http://www.cdc.gov/parasites/naegleria/diagnosis-hcp.html>.
- For *Naegleria fowleri* treatment recommendations, see <http://www.cdc.gov/parasites/naegleria/treatment-hcp.html>.
- For the MMWR Notice to Readers on this topic, see http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6233a4.htm?s_cid=mm6233a4_w.

References

1. Schuster FL, Guglielmo BJ, Visvesvara GS. In-vitro activity of miltefosine and voriconazole on clinical isolates of free-living amebas: *Balamuthia mandrillaris*, *Acanthamoeba* spp., and *Naegleria fowleri*. J Eukaryot Microbiol 2006;53:121–6.
2. Cope JR, Roy SL, Yoder JS, Beach MJ. Improved treatment of granulomatous amebic encephalitis and other infections caused by *Balamuthia mandrillaris* and *Acanthamoeba* species [Poster]. Presented at CSTE Annual Conference, Pasadena, CA, June 9–13, 2013. Available at <http://www.cste2.org/confpresentations/uploadedfiles/cste%202013%20miltefosine%20Poster%20final.pdf>.

Endnotes

* Additional information available at <http://www.cdc.gov/parasites/naegleria>.

† Additional information available at <http://www.cdc.gov/parasites/balamuthia>.

§ Additional information available at <http://www.cdc.gov/parasites/acanthamoeba>.

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