



August 1, 2022

Dear Colleague -

Overview and Summary

This letter is in follow up to the letter of June 21, 2022 about tuberculosis (TB) screening in the Uniting for Ukraine program ([Dear Colleague Letter June 21](#)). In the Uniting for Ukraine program, Ukrainian parolees are required to undergo testing with a TB-specific interferon-gamma release assay (IGRA) and subsequent TB diagnostic studies as needed. Parolees are also required to be vaccinated for several other infections. On July 14, the U.S. Department of Homeland Security extended the time period for completing the TB requirement from 14 days to 90 days ([USCIS Uniting for Ukraine Vaccine Attestation](#)).

The Division of Tuberculosis Elimination (DTBE), Centers for Disease Control and Prevention (CDC), has received questions about preventive treatment regimens for Ukrainian parolees who are diagnosed with latent TB infection (LTBI) following post-arrival testing because of reports of prevalent drug-resistant TB in Ukraine. The data from CDC and the World Health Organization (WHO) indicate a prevalence rate of multidrug-resistant (MDR) TB among Ukrainians who had culture-confirmed TB in the United States or in Ukraine of 13% to 32.6%. These rates underlie concerns that have been raised that drug resistance could be common among persons coming from Ukraine who have LTBI.

LTBI in Ukrainian parolees should be treated in accordance with current guidelines from the National Tuberculosis Controllers Association (NTCA) and CDC ([NTCA and CDC: Treatment of LTBI](#)), unless drug susceptibility test results for the presumed source case support a conclusion of drug-resistant LTBI. If drug-resistant LTBI is suspected, clinical consultation should be obtained for assistance in selecting drugs in an empirical LTBI treatment regimen. TB disease must be excluded before any regimen for treating LTBI is started. When Ukrainian parolees are being examined for possible TB disease, microbiological testing should include rapid molecular methods for detecting drug resistance.

Drug Resistance Data from the World Health Organization

In the World Health Organization (WHO) 2020 TB profile for Ukraine, 17,533 new and relapse cases were reported. Of those, 4,257 cases were MDR TB or at least rifampin resistant and 1,172 were extensively drug resistant (XDR) or pre-XDR TB ([WHO TB Profile: Ukraine 2020](#)). WHO projected that TB was approximately 50% underreported in Ukraine, and testing and reporting for drug resistance in Ukraine are not systematic ([Int J Tuberc Lung Dis 2018 ;22:197-205](#)). Of culture-confirmed cases, 32.6% were MDR TB, including XDR and pre-XDR TB ([WHO TB High Burden Countries, ECDC WHO Information Note](#)).

Drug Resistance Data from the Centers for Disease Control and Prevention

For 2014–2020 in CDC's National TB Surveillance System, 122 cases of TB were reported in non-U.S.-born persons with Ukraine as the place of birth. Of these cases, 104 (85%) were culture confirmed, and 102 had susceptibility results for at least isoniazid and rifampin. Any isoniazid resistance was reported for 24 (24%), any rifampin resistance for 13 (13%), and MDR TB for 13 (13%), which included XDR or pre-XDR TB for 3 (3%). The pre-2021 definitions for XDR and pre-XDR TB were used.

From U.S. immigration panel sites in Ukraine during 2016–2021, the results of medical examinations ([TB Technical Instructions for Panel Physicians](#)) for 54,493 Ukrainians who were applying for immigrant or refugee admission to the United States were reported to CDC’s Division of Global Migration and Quarantine: 36 applicants had Class A Active TB, for a prevalence rate of 66/100,000 persons examined. Of the 36 cases, 31 (86%) were culture confirmed: 6 (19%) were drug resistant besides MDR or XDR TB, and 7 (23%) were MDR TB, which included 2 (6%) XDR TB. Two of the five cases that were not culture confirmed were diagnosed with rapid molecular tests that indicated rifampin resistance.

The TB epidemiology of the United for Ukraine parolees might be dissimilar to that of the Ukraine-born persons already in the United States or to that of the applicants at the immigration panel sites in Ukraine. Still, the data from WHO and CDC indicate that drug resistance could be common among the parolees who have LTBI or TB disease.

Treatment of Latent Tuberculosis Infection when Background Drug Resistance is Prevalent

The influence of prevalent drug resistance on the effectiveness of preventive therapy for a national population has not been determined. In a U.S. observational study during an outbreak of isoniazid- and streptomycin-resistant TB, the infected contacts who were treated with only isoniazid were more likely to have TB disease during follow up than persons who were treated with rifampin-based regimens, and the breakthrough cases were isoniazid resistant ([Am J Respir Crit Care Med 1996;154:1473-1477](#)). In an overseas observational study during an MDR TB outbreak, fluoroquinolone-based regimens that were selected from the drug susceptibility for the source cases appear to have prevented TB disease in infected contacts ([HHS Public Access doi:10.5588/ijtld.13.0028](#)).

Treatment Regimen Recommendations

CDC has not published LTBI treatment guidance that is specific to a country of origin or to a background prevalence of drug resistance. The recommended regimens that have been studied in randomized clinical trials ([NTCA and CDC: Treatment of LTBI](#)) should be prescribed for Ukrainian parolees who have LTBI, unless the drug-susceptibility results for the presumed source case are known and indicate that drug-resistant LTBI is likely. The selection of drugs for empirical regimens that have not been studied in randomized clinical trials should be guided by the susceptibility results of a presumed source case. For Ukrainian parolees who have LTBI and who describe being exposed to drug-resistant TB when drug susceptibility test results are unavailable, consultation from a TB control official ([TB Control Offices](#)) or a clinician at a regional TB Center of Excellence ([TB Centers of Excellence](#)) is advisable.

TB disease must be excluded with chest radiography and other studies as guided by clinical findings before any regimen for treating LTBI is started. When Ukrainian parolees are being examined for possible TB disease, microbiological testing should include rapid molecular methods for early detection of drug resistance.

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