Steven W. Schierholt, Esq.
Executive Director

John R. Kasich
Governor

STATE OF OHIO
BOARD OF PHARMACY

**Resolution: Point of Dispensing Locations in a Declared Public Health Emergency**

**Adopted 4/9/2018**

Pursuant to rule 4729-9-05 of the Ohio Administrative Code, the Board hereby authorizes a board of health, as defined in section 3701.048 of the Revised Code, that is licensed as a terminal distributor of dangerous drugs to temporarily remove dangerous drugs upon the governor's declaration of an emergency that affects the public health.

The dangerous drugs removed from a location licensed as a terminal distributor shall be used to establish a point of dispensing location or locations in the event of a declared public health emergency to administer, deliver, dispense, or distribute drugs in accordance with protocols developed pursuant to section 3701.048 of the Revised Code.

The dangerous drugs shall be returned to the board of health within seventy-two hours of the cessation of the public health emergency.

An individual listed in division (B) and (C) of section 3701.048 shall maintain personal supervision and control over the dangerous drugs and any hypodermics removed from the terminal distributor. If personal supervision is not provided, the dangerous drugs and any hypodermics shall be physically secured in a manner to prevent unauthorized access. The drugs shall be stored at temperatures which will ensure the integrity of the drugs prior to their use as stipulated by the USP/NF and/or the manufacturer's or distributor's labeling.

The responsible person on the terminal distributor of dangerous drugs license shall be responsible for compliance with the requirements of this resolution.

ADT Tracking: 122084

# INTER-OFFICE COMMUNICATIONS MEMORANDUM

Date: April 30, 2019

To: Amy Acton, MD
Director of Health

Through: Lance Himes, J.D.
Department of Health

From: Tamara McBride
Chief, Office of Health Preparedness

Subject: Updates to Standing Medical Orders

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Updated Standing Medical Orders to reflect current Director of Health and General Counsel. Updated Centers for Disease Control (CDC) Emergency Use Instructions for Health care Providers in relation to Doxycycline and Ciprofloxacin for Post-Exposure Prophylaxis of Anthrax.

# In Re: Ohio Department of Health Standing Medical Order/Protocol for Ohio Local Health Departments: Prophylactic Use of Antibiotics and Vaccination

## Director's Journal Entry

Recognizing the authority of the United States Food and Drug Administration (FDA) to promulgate an Emergency Use Authorization (EUA) as to the use of antibiotics and vaccine in the Strategic National Stockpile (SNS), in accordance with Ohio Revised Code 3701.13, this standing order for preventing the spread of contagious or infectious diseases is directed to the health officers of Ohio local health departments to establish mass clinics with approved protocols for the rapid and appropriate dispensing and administration of prophylactic antibiotics to persons with known or suspected exposure to *Bacillus anthracis* for the prevention of anthrax disease; *Yersinia pestis* for the prevention of plague; or *Francisella tularensis* for the prevention of tularemia; and for the rapid administration of vaccine to persons with known or suspected exposure to *Bacillus anthracis* for the prevention of anthrax disease.

During a governor's declaration of an emergency that affects the public health, the director of health may issue an order to implement this standing order protocol pursuant to 3701.048.

This medical order does not cover treatment of persons with known or suspected disease from the bioterrorism agents *Bacillus anthracis, Yersinia pestis,* or *Francisella tularensis.* Such persons must be under the care of a physician and public health authorities. All persons with known or suspected disease must be reported immediately to the Ohio local health jurisdiction in which the person resides.

I order public health staff employed in or anyone volunteering for a nationally, state, or locally declared emergency involving the public's health as contemplated and set forth in this medically informed standing public health order to directly, or by delegation and supervision, dispense antibiotic medications herein prescribed by me, to individuals and members of their households, in order to protect against infection by the bioterrorism agents *Bacillus anthracis, Yersinia pestis,* or *Francisella tularensis.*

If the licensed anthrax vaccine adsorbed (AVA) is made available for use under an Emergency Use Authorization and the Centers for Disease Control and Prevention (CDC) releases the vaccine to Ohio for post-exposure prophylaxis, I order public health staff employed in or anyone volunteering for a nationally, state, or locally declared emergency involving the public's health as contemplated and set forth in this medically informed standing public health order to directly, or by delegation and supervision, vaccinate individuals in order to protect them against infection by the bioterrorism agent *Bacillus*

*anthracis*. This part of my order is not in effect if the CDC does not release the vaccine for use in a mass vaccination setting or the AVA is released under an Investigational New Drug protocol.

All medications are prescribed, and must be dispensed in accordance with the national prophylactic treatment recommendations and within the stated restrictions and guidelines of the CDC's Division of Strategic National Stockpile (SNS) Program. When a mass dispensing site is activated and operational in Ohio in response to a public health event involving anthrax, plague or tularemia, one of the attached post-exposure prophylaxis dispensing orders/algorithms must be followed:

1. *Bacillus anthracis* Dispensing Orders and Vaccination Recommendations
2. *Yersinia pestis* Dispensing Orders
3. *Francisella tularensis* Dispensing Orders

Review of this order, and agency policies and procedures related to carrying out this order, will occur at least once a year with changes made as necessary.

Amy Acton, MD, Director
Ohio Department of Health

5/29/19
Date

I hereby certify this to be a true and correct copy of the Journal Entry of the Director of the Ohio Department of Health.

5-30-19
Date

Custodian of the Director's Journals
Ohio Department of Health

**RECORD OF CHANGE AND REVIEW**

| DATE | CHANGE/REVIEW | BY |
|---|---|---|
| 3/7/2013 | Annual Review<br>Tularemia recommendations updated<br>Record of change/review document added | Rebecca Sandholdt |
| 6/30/14 | Annual Review by Dr. Wapner<br>Updated si211atures | Viola Webber |
| 3/20/15 | Annual Review, Update to Peds | Viola Webber |
| 2/11/16 | Annual Review, Update to Pediatric. Changed Pediatrics dosing to be consistently maximum per dose. | Viola Webber |
| 7/7/2016 | Update to Table 1, included Ciprofloxacin and Doxycycline EUI and Doxycycline EUI Crushing Instructions, March 28, 2016 | Viola Webber |
| 9/28/2017 | Update to include ORC 3701.048,<br>Update to include current medical director and director of health | Ryan Morrison |
| 4/30/2019 | Update to reflect current Director of Health and General Counsel.<br>Update of CDC's Emergency Use Instructions for Doxycycline and Ciprofloxacin. | Ryan Morrison |

***Bacillus anthracis* Dispensing Orders and Vaccination Recommendations**

Recommended initial antimicrobial agent and anthrax vaccine adsorbed (AVA) dosages for post-exposure prophylaxis (PEP) after exposure to aerosolized *Bacillus anthracis* spores

| TABLE 1 | | |
|---|---|---|
| | | |
| Population | Antimicrobials for 60-day* PEP | AVA dosage and route†,∞ |
| **Adults (≥ 18 years)** | ***One of the following for 60 days:***<br>Ciprofloxacin,§ One tablet (500 mg) by mouth every 12 hours (one tablet in the morning and one tablet in the evening with a full glass of water) each day<br>*or*<br>Doxycycline, one tablet (100 mg) by mouth every 12 hours (one tablet in the morning and one tablet in the evening with a full glass of water) each day | In conjunction with antimicrobial therapy. 3-dose subcutaneous (SC) series: first dose administered as soon as possible, second and third doses administered 2 and 4 weeks after the first dose. |

<table>
<tr>
<td>Children (<18 years)††</td>
<td>One of the following for 60 days:<br>Doxycycline,††, ¶¶ (maximum of 100 mg/dose)<br>• Children ≥ 35 kg (76 lbs.): one tablet (100mg) by mouth every 12 hours (one tablet in the morning and one tablet in the evening with a full glass of water) each day<br>• < 35 kg (76 lbs.) crushed doxycycline mixed with food or drink, dosed by weight every 12 hours (one dose in the morning and one dose in the evening) each day. See brochure, In an Emergency: How to Prepare Doxycycline Hyclate for Children and Adults Who Cannot Swallow Pills, Doxycycline EUI Crushing Instructions March 28, 2016<br>• < 14 kg (30 lbs.) priority for using suspension, dosed by weight (See table below; dose is specific to doxycycline oral suspension in 25 mg/5 ml concentration only) every 12 hours (one dose in the morning and one dose in the evening) each day.
<table>
<tr><th>Weight in pounds (kilograms)</th><th>Dose in ml (based on 25 mg/5 ml concentration)</th><th>Number of 60 ml bottles (25 mg/5 ml concentration) needed for 10-day supply for one patient</th></tr>
<tr><td>0-5 lbs (0-2 kg)</td><td>1 ml (5mg)</td><td rowspan="3">ONE (1) Bottle</td></tr>
<tr><td>6-10 lbs (3-4 kg)</td><td>2 ml (10 mg)</td></tr>
<tr><td>11-15 lbs (5-7 kg)</td><td>3 ml (15 mg)</td></tr>
<tr><td>16-20 lbs (8-9 kg)</td><td>4 ml (20mg)</td><td rowspan="3">TWO (2) Bottles</td></tr>
<tr><td>21-25 lbs (10-11 kg)</td><td>5 ml (25 mg)</td></tr>
<tr><td>26-30 lbs (12-14 kg)</td><td>6 ml (30 mg)</td></tr>
</table>
</td>
<td>Recommendations for use of AVA in children are made on an event-by-event basis</td>
</tr>
</table>

*Or*

Ciprofloxacin,§,††, §§

- Children ≥31kg(67lbs.): one tablet (500 mg) by mouth every 12 hours (one tablet in the morning and one tablet in the evening with a full glass of water) each day
- Children< 31 kg (67 lbs.): Ciprofloxacin oral suspension dosed by weight (see table below) every 12 hours (one dose in the morning and one dose in the evening) each day

Ciprofloxacin oral suspension comes in two strengths: 5% (250 mg/5 ml) and 10% (500 mg/5 ml)

- Ciprofloxacin oral suspension is supplied in two components (ciprofloxacin microcapsules and diluent). Followthe instructions provided with the oral suspension to mix the microcapsules in the diluent before dispensing the drug to the recipient. Write the dose on the bottle and mark the dose with a line on the graduated teaspoon or oral syringe.
- Tell the recipient to shake the oral suspension very well (for 15 seconds) before each use.

| Weight in pounds (kilograms) | Dose* in milliliters (ml) 250 mg/5ml strength | Dose* in milliliters (ml) 500 mg/5 ml strength | Number of 100 ml bottles needed for 10-day Supply for one patient | |
|---|---|---|---|---|
| | | | 250 mg/5 ml strength | 500 mg/5 ml strength |
| 0-7 lbs ( 0-3k g) | 1 ml (50 mg) | 0.5 ml (50 mg) | One (1) Bottle | One (1) Bottle |
| 8-14 lbs (4-6 kg) | 2 ml (100 mg) | 1 ml (100 mg) | | |
| 15-22 lbs (7-10 kg) | 3ml (150 mg) | 1.5 ml (150 mg) | | |
| 23-29 lbs (11-13 kg) | 4 ml (200 mg) | 2 ml (200 mg) | | |
| 30-36 lbs (14-16 kg) | 5 ml (250 mg) | 2.5 ml (250 mg) | | |
| 37-44 lbs (17-20 kg) | 6 ml (300 mg) | 3 ml (300 mg) | Two (2) Bottles | |
| 45-51 lbs (21-23 kg) | 7 ml (350 mg) | 3.5 ml (350 mg) | | |
| 52-58 lbs (24-26 kg) | 8 ml (400 mg) | 4 ml (400 mg) | | |
| 59-66 lbs (27-30 kg) | 9 ml (450 mg) | 4.5 ml (450 mg) | | |
| >67 lbs (>31 kg) | 10 ml (500 mg) | 5 ml (500 mg) | | |

*Dosage adjustment *is* needed for individuals with severe renal impairment.

If **isolate is proved susceptible:**

Amoxicillin ,** 75mg/kg/day, orally, divided every 8 hours (not to exceed 1 g dose) for 60 days:

| | | |
|---|---|---|
| **Pregnant women, ¶,*** ** | ***One of the following for 60 days:*** Ciprofloxacin, 500 mg orally twice daily for 60 days *or* Doxycycline, 100 mg orally twice daily for 60 days **Alternate choice (if isolate is proved susceptible):** Amoxicillin, 1g orally every 8 hours for 60 days | In conjunction with antimicrobial therapy. 3-dose SC series; first dose administered as soon as possible, second and third doses administered 2 and 4 weeks after the first dose. |

Table 1 was adapted from: Use of Anthrax Vaccine in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009; Morbidity and Mortality Weekly Report (MMWR), 59(RR6); July 23, 2010. NOTE: Web version indicates the article is "archived" only because it was published in MMWR before January 2013. This IS a current recommendation., Ciprofloxacin for Post-Exposure Prophylaxis of Anthrax, Emergency Use Instructions for Health Care Providers-March 28, 2016., Doxycycline for Post-Exposure Prophylaxis of Anthrax, Emergency Use Instructions for Health Care Providers- March 28, 2016., Doxycycline Emergency Use Crushing Instructions- March 28, 2016., The American Academy of Pediatrics Red Book: 2012 Report of the Committee on Infectious Diseases, P 228 to 232, PEDIATRICS Volume 133, Number 5, May 2014, Pediatric Anthrax Clinical Management., CDC Emerging Infectious Disease journal, Volume 20, Number 2-February 2014, Special Considerations for Prophylaxis for and Treatment of Anthrax in Pregnant and Postpartum Women.

* Antimicrobials should continue for 14 days after administration of the third dose of vaccine.

† AVA used for PEP must be administered subcutaneously.

Data on the safety of AVA are only available for persons aged 18-65 years; no information is available on the safety of this vaccine in children or older adults (>65 years).

§ Levofloxacin is a second-line antimicrobial agent for PEP for persons aged :2:6 months with medical issues (e.g. tolerance or resistance to ciprofloxacin) that indicate its use. *Children:* 16 mg/kg/day divided every 12 hours; each dose should not exceed 250 mg. *Adults:* 500 mg every 24 hours. Safety data on extended use of levofloxacin in any population for >28 days are limited; therefore, levofloxacin PEP should only be used when the benefit outweighs the risk.

¶ The antimicrobial of choice for initial prophylactic therapy among pregnant women is ciprofloxacin. Doxycycline should be used with caution in asymptomatic pregnant women and only when other appropriate antimicrobial drugs are contraindicated. Although tetracyclines are not recommended during pregnancy, their use might be indicated for life-threatening illness.

** If susceptibility testing demonstrates an amoxicillin MIC .:S:0.125 µg/mL, oral amoxicillin should be used to complete therapy.

†† Use of tetracyclines and fluoroquinolones in children can have adverse effects. These effects must be weighed carefully against the risk for developing life-threatening disease. If exposure to *B. anthracis* is confirmed, children may be treated initially with ciprofloxacin or doxycycline as prophylaxis. However, amoxicillin is preferred for antimicrobial PEP in children when susceptibility testing indicates that the *B. anthracis* isolate is susceptible to penicillins.

§§ Each ciprofloxacin dose should not exceed 500 mg, or 1 g/day.

¶¶ In 1991, the American Academy of Pediatrics (AAP) amended the recommendation to allow treatment of young children with tetracyclines for serious infections such as Rocky Mountain spotted fever for which doxycycline might be indicated. Doxycycline is preferred for its twice daily dosage and low incidence of gastrointestinal side effects.

•• Because of the lack of data on amoxicillin dosages for treating anthrax (and the associated high mortality rate), AAP recommends a higher dosage of 80 mg/kg/day, divided into 3 daily doses; each dose should not exceed 500 mg. If this higher dosage of amoxicillin is used, recipients should be carefully monitored for side effects from long-term treatment.

••• Antimicrobial drug use in pregnant women in the setting of anthrax must be viewed in the context of the high mortality risk and the benefits of treatment for the mother and fetus, as well as possible effects on the fetus resulting from the infection or from administration of antimicrobial drugs to the mother. Although safety and pharmacokinetic data for pregnant women are limited, antimicrobial drugs used for anthrax post-exposure prophylaxis and treatment for pregnant/postpartum/ lactating women are generally the same as those for non-pregnant adults.

***Yersinia pestis* Dispensing Orders**

Prescribed Post-exposure Prophylaxis for Pneumonic Plague¥

| TABLE2 | |
|---|---|
| Patient Category | Recommended Therapy |
| **Adults** | ***Preferred choices:***<br>Doxycycline, 100 mg orally twice daily for seven days<br>**IF adult is allergic to doxycycline, THEN**<br>Ciprofloxacin, 500 mg orally twice daily for seven days € |
| Children | ***Preferred choices:***<br>Doxycycline<br>• If child's weight is ≥45 kg, give adult dosage (100 mg orally twice daily) for seven days<br>• If child's weight is <45 kg, give 2.2 mg/kg orally twice daily for seven days (not to exceed 100 mg/dose)<br>**If child is allergic to doxycycline, THEN**<br>Ciprofloxacin, 20 mg/kg orally twice daily for seven days € |
| **Pregnant women and breastfeeding mothers** | ***Preferred choices:***<br>Ciprofloxacin, 500 mg orally twice daily for seven days €<br>**If individual is allergic to Ciprofloxacin THEN,**<br>Doxycycline, 100 mg orally twice daily for seven days |

Table 2 adapted from: Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a Biological Weapon: Medical and Public Health Management, *JA1 A* 2000; 283:2281-90, (Page last reviewed: April 25, 2014).

¥ Recommendations were reached by consensus of the Working Group on Civilian Biodefense and may not necessarily be approved by the United States Food and Drug Administration (FDA).

t Although fetal toxicity may occur with doxycycline use and toxic effects on the liver in pregnancy have been noted with the tetracycline class, the Working Group on Civilian Biodefense recommend doxycycline or ciprofloxacin for post-exposure prophylaxis of pregnant women.

€ Other fluoroquinolones may be substituted at doses appropriate for age. Ofloxacin (and possibly other quinolones) may be acceptable alternatives to ciprofloxacin or levofloxacin; however, they are not approved for use in children. Each ciprofloxacin dose should not exceed 500 mg and maximum daily dosage for ciprofloxacin should not exceed 1 g.

## *Francisella tularensis* Dispensing Orders

Prescribed Post-exposure Prophylaxis for Tularemia

| Table 3 | |
|---|---|
| Patient Category | Recommended Therapy+ |
| **Adults (including pregnant women)** | **One of the following:**<br>Ciprofloxacin, 500 mg orally twice daily for 14 days<br>or<br>Doxycycline, 100 mg orally twice daily for 14 days € |
| **Children** | ***Preferred** choices:*<br>Doxycycline<br>• If child's weight is ≥45 kg, give adult dosage (100 mg orally twice daily) for 14 days<br>• If child's weight is <45 kg, give 2.2 mg/kg orally twice daily for 14 days (not to exceed 100 mg/dose)<br>If child is **allergic to doxycycline, THEN**<br>Ciprofloxacin, 15 mg/kg orally twice daily for 14 days § |

Table 3 adapted from the following reference for the recommended therapy information for adults: Dennis DT, Inglesby TV, Henderson DA, et al. Tularemia as a Biological Weapon: medical and public health management. *JAMA* 2001; 285(21): 2763-2773. Table 3 adapted from the following reference for the recommended therapy information for children: A National Consensus Conference for "Pediatric Preparedness for Disasters and Terrorism", March 2007, convened by the Mailman School of Public Health at Columbia University: http://www.ncdp.mailman.columbia.edu/files/peds2.pdf.

+ Recommendations were reached by consensus of the Working Group on Civilian Biodefense and may not necessarily be approved by the FDA.

€ Although fetal toxicity may occur with doxycycline use, the Working Group on Civilian Biodefense recommended doxycycline or ciprofloxacin for post-exposure prophylaxis of pregnant women.

§ Other fluoroquinolones may be substituted at doses appropriate for age. Ofloxacin (and possibly other quinolones) may be acceptable alternatives to ciprofloxacin or levofloxacin; however, they are not approved for use in children. Each ciprofloxacin dose should not exceed 500 mg and maximum daily dosage for ciprofloxacin should not exceed 1 g.

# Doxycycline for Post-Exposure Prophylaxis of Anthrax

## Emergency Use Instructions for Healthcare Providers

This fact sheet provides instructions for the use of doxycycline for post-exposure prophylaxis (PEP) during an emergency involving anthrax (referred to as Emergency Use Instructions (EUI) fact sheet). Doxycycline is FDA-approved for PEP of inhalation anthrax – to reduce the incidence or progression of disease following exposure to aerosolized *Bacillus anthracis (B. anthracis)*.[1] The Food and Drug Administration (FDA) has also issued an order permitting the emergency dispensing of oral formulations of doxycycline without a prescription during an anthrax emergency to individuals who may have been exposed to *B. anthracis*.[2]

**What is inhalation anthrax?**

Anthrax is a serious disease caused by the spore-forming bacterium *B. anthracis*. Inhalation anthrax is the most deadly form of the disease, with a historical mortality rate of approximately 90% for untreated cases. Inhalation anthrax occurs when an individual inhales aerosolized spores. It is not spread from person to person. Early symptoms include fever, chills, fatigue, cough or headache. Later symptoms include shortness of breath, chest pain, confusion or nausea. Symptoms usually occur within 7 days of inhaling anthrax spores, but can occur as soon as 24 hours after exposure or may take up to 6 to 7 weeks to appear (animal data show symptoms can occur more than 50 days after exposure).

**Who should NOT take doxycycline?**

Do not give doxycycline to anyone who is allergic to doxycycline or another antibiotic in the tetracycline class.

**What is the usual dose of doxycycline for PEP of anthrax?**

The full PEP regimen is 60 days. During an anthrax emergency, recipients may receive an initial 10-day supply to begin doxycycline therapy; public health officials will announce whether recipients need more doxycycline and how to get additional quantities of the drug.

- **Children weighing 76 lbs (35 kg) or more and Adults (≥ 18 years):** Take one tablet (100 mg) by mouth every 12 hours (one tablet in the morning and one tablet in the evening) each day with a full glass of water (with or without food or milk). For those who **cannot swallow tablets**, provide the crushing and mixing directions (which can also be found by searching "doxycycline crushing instructions" on www.cdc.gov). These instructions are appropriate **only** for 100 mg **tablets**.
- **Children weighing less than 76 lbs (35 kg):** Weight-based dosing (2.2 mg/kg) every 12 hours (one dose in the morning and one dose in the evening) each day. Provide the crushing and mixing instructions (which can also be found by searching "doxycycline crushing instructions" on www.cdc.gov). These instructions are appropriate **only** for 100 mg **tablets**.
- **Children weighing less than 30 lbs (14kg):** Children weighing less than 30 lbs (14 kg) should receive priority for doxycycline oral suspension, dosed by weight every 12 hours (one dose in the morning and one dose in the evening) each day. For convenience, the table below provides dosing by weight-range based on 2.2 mg/kg derived calculation.[3] Doses in the table below are specific to **doxycycline powder for oral suspension in the 25 mg/5 mL concentration only**.
  - ➢ Follow the instructions provided with the oral suspension to mix the doxycycline powder with water before dispensing the drug to the recipient. Write the dose on the bottle and mark the dose with a line on the oral syringe.
  - ➢ Tell the recipient to shake the oral suspension very well (15 seconds) before each use.

| Weight in pounds (kilograms) | Dose in mL based on 25 mg/5 mL concentration (mg) | Number of 60-mL bottles (25 mg/5 mL concentration) needed for 10-day supply for one child |
|---|---|---|
| ≤ 5 lbs (≤ 2 kg) | 1 mL (5mg) | ONE (1) Bottle |
| 6–10 lbs (3–4 kg) | 2 mL (10 mg) | |
| 11–15 lbs (5–7 kg) | 3 mL (15 mg) | |
| 16–20 lbs (8–9 kg) | 4 mL (20 mg) | TWO (2) Bottles |
| 21–25 lbs (10–11 kg) | 5 mL (25 mg) | |
| 26–30 lbs (12–14 kg) | 6 mL (30 mg) | |

**What are common side effects of doxycycline?**

Inform recipients that mild gastrointestinal side effects such as nausea, vomiting, and/or diarrhea, a mild sunburn or a vaginal yeast infection may be experienced but to continue taking doxycycline. If these side effects become severe, over-the-counter or prescription drugs can help to relieve the symptoms.

[1] See the FDA-approved package insert for doxycycline at www.dailymed.nlm.nih.gov and search for doxycycline.
[2] FDA's emergency dispensing order applies to all FDA-approved oral dosage forms of doxycycline products for the post-exposure prophylaxis of inhalation anthrax during an emergency involving *B. anthracis*. For details, see www.fda.gov.
[3] Weight-range dosing table is provided as exact dose calculation (based on 2.2 mg/kg) may not be feasible during an emergency.

**What are possible serious side effects of doxycycline?**

Tell recipients to **STOP** the doxycycline and get medical help immediately if they develop any of the following:

- Serious allergic/hypersensitivity reactions (anaphylactic and/or severe rashes)
- Severe stomach cramps with high fever or bloody diarrhea (antibiotic-associated diarrhea and pseudomembranous colitis)
- Liver problems (anorexia, jaundice, dark brown or tea-colored urine, pruritus or tender abdomen)
- Pain when swallowing (esophageal ulcers)
- Unusual bleeding or bruising
- Severe headaches, dizziness or double vision

**What should recipients avoid while taking doxycycline?**

- If a recipient is taking multivitamins, supplements or antacids that contain aluminum, calcium, magnesium, or iron, or drugs containing bismuth subsalicylate, instruct the recipient to take doxycycline at least 2 hours before or 2 hours after taking any of these products.
- Doxycycline can interact with certain drugs like blood thinners (increased blood thinning) or seizure drugs (decreased doxycycline concentration). If a recipient is taking these or other drugs with known interaction with doxycycline, consider changing the dose of these drugs or recommending alternative drugs. For more information on doxycycline drug interactions, please see package insert.

**What additional information should be provided to recipients taking doxycycline?**

- Tell recipients to take with food or milk if they have gastrointestinal upset with doxycycline. Co-administration of doxycycline with food or milk does not significantly reduce doxycycline absorption.
- Doxycycline is recommended as antimicrobial PEP for anthrax during pregnancy and while breastfeeding, but if taken during the last half of pregnancy or possibly when nursing, infants may have permanent tooth discoloration (yellow-gray-brown) and poor enamel formation. This may also occur in children under 8 years old who take doxycycline.
- Slowed bone growth may occur in children who take doxycycline.
- Doxycycline can cause sun sensitivity. Instruct recipients to use sunscreen and cover exposed skin.
- The effectiveness of birth control pills may be reduced with doxycycline use. Recommend a second form of birth control while taking doxycycline.
- Instruct recipients to keep doxycycline tablets dry and to store them at room temperature (between 68–77°F or 20–25°C).
- If you have been asked to dispense doxycycline with an expired date on the container, please note that FDA is allowing for the use of certain lots of doxycycline beyond the labeled expiration date during an anthrax emergency based on scientific review. For more information, go to the FDA website at www.fda.gov (search for "doxycycline expiration").
- The Countermeasures Injury Compensation Program (CICP) is a federal program created to help pay for related costs of medical care and other specific expenses for eligible people seriously injured by the administration or use of certain medical countermeasures. Medical countermeasures may include vaccines, medications, devices or other items used to prevent, diagnose or treat the public during a public health emergency or security threat. For more information about CICP, visit www.hrsa.gov/cicp or call: 1-855-266-2427.

**Risk-Benefit Statement**

Although doxycycline has some potential and serious adverse events, the expected benefit of doxycycline to help prevent disease and death associated with anthrax exposure outweighs these risks.

**Available Alternatives**

During an anthrax emergency, you will be informed of any alternative antibiotics that are available, such as ciprofloxacin, levofloxacin or amoxicillin. The risks and benefits of available alternative antibiotics will be explained in their own fact sheets.

**Reporting Adverse Event or Medication Errors**

Report adverse events or medication errors to MedWatch (www.fda.gov/medwatch) by completing a MedWatch Form 3500 or by calling 1-800-FDA-1088.

**Give recipients "Anthrax Emergency: How to Take Doxycycline to Prevent Anthrax" instructions.**

| Space Reserved for State/Local Public Health Information |
|---|
| |

# Ciprofloxacin for Post-Exposure Prophylaxis of Anthrax
## Emergency Use Instructions for Healthcare Providers

This fact sheet provides instructions for the use of ciprofloxacin for post-exposure prophylaxis (PEP) during an emergency involving anthrax (referred to as Emergency Use Instructions (EUI) fact sheet). Ciprofloxacin is FDA-approved for PEP of inhalation anthrax – to reduce the incidence or progression of disease following exposure to aerosolized *Bacillus anthracis (B. anthracis)*.[1] The Food and Drug Administration (FDA) has also issued an order permitting the emergency dispensing of oral formulations of ciprofloxacin without a prescription during an anthrax emergency to individuals who may have been exposed to *B. anthracis*.[2]

**What is inhalation anthrax?**
Anthrax is a serious disease caused by the spore-forming bacterium *B. anthracis*. Inhalation anthrax is the most deadly form of the disease, with a historical mortality rate of approximately 90% for untreated cases. Inhalation anthrax occurs when an individual inhales aerosolized spores. It is not spread from person to person. Early symptoms include fever, chills, fatigue, cough or headache. Later symptoms include shortness of breath, chest pain, confusion or nausea. Symptoms usually occur within 7 days of inhaling anthrax spores, but can occur as soon as 24 hours after exposure or may take up to 6 to 7 weeks to appear (animal data show symptoms can occur more than 50 days after exposure).

**Who should NOT take ciprofloxacin?**
Do not give ciprofloxacin to anyone who is allergic to a quinolone antibiotic (including ciprofloxacin) or has a history of myasthenia gravis. Avoid concomitant administration of ciprofloxacin and Zanaflex (tizanidine) since ciprofloxacin can increase effects of tizanidine (e.g., bradycardia, hypotension); consider switching either ciprofloxacin or tizanidine to an alternative drug.

**What is the usual dose of ciprofloxacin for PEP of anthrax?**
The full PEP regimen is 60 days. During an anthrax emergency, recipients may receive an initial 10-day supply to begin ciprofloxacin therapy; public health officials will announce whether recipients need more ciprofloxacin and how to get additional quantities of the drug.

- **Children weighing 67 lbs (31 kg) or more and Adults (≥ 18 years):** Take one tablet (500 mg) by mouth every 12 hours (one tablet in the morning and one tablet in the evening) each day with a full glass of water (with or without food). For those who **cannot swallow tablets**, consider an oral suspension/liquid form (of ciprofloxacin or alternative drug) or a drug that can be mixed with food or liquid (such as doxycycline).
- **Children weighing less than 67 lbs (31 kg):** Weight-based dosing of ciprofloxacin oral suspension every 12 hours (one dose in the morning and one dose in the evening) each day. For convenience, the table below provides dosing by weight-range based on 15 mg/kg derived calculation.[3] Ciprofloxacin oral suspension comes in two concentrations [5% (250 mg/5 mL) and 10% (500 mg/5 mL)] and is supplied as ciprofloxacin microcapsules with diluent.
  - ➢ Follow the instructions provided with the oral suspension to mix the microcapsules in the diluent before dispensing the drug to the recipient. Write the dose on the bottle and mark the dose with a line on the graduated teaspoon or oral syringe.
  - ➢ Tell the recipient to shake the oral suspension very well (15 seconds) before each use.

| Weight in pounds (kilograms) | Dose* in mL (mg) | | Number of 100-mL bottles needed for 10-day supply for one child | |
|---|---|---|---|---|
| | 250 mg/5 mL Concentration | 500 mg/5 mL Concentration | 250 mg/5 mL Concentration | 500 mg/5 mL Concentration |
| ≤ 7 lbs (≤ 3 kg) | 1 mL (50 mg) | 0.5 mL (50 mg) | ONE (1) Bottle | ONE (1) Bottle |
| 8–14 lbs (4–6 kg) | 2 mL (100 mg) | 1 mL (100 mg) | | |
| 15–22 lbs (7–10 kg) | 3 mL (150 mg) | 1.5 mL (150 mg) | | |
| 23–29 lbs (11–13 kg) | 4 mL (200 mg) | 2 mL (200 mg) | | |
| 30–36 lbs (14–16 kg) | 5 mL (250 mg) | 2.5 mL (250 mg) | | |
| 37–44 lbs (17–20 kg) | 6 mL (300 mg) | 3 mL (300 mg) | TWO (2) Bottles | |
| 45–51 lbs (21–23 kg) | 7 mL (350 mg) | 3.5 mL (350 mg) | | |
| 52–58 lbs (24–26 kg) | 8 mL (400 mg) | 4 mL (400 mg) | | |
| 59–66 lbs (27–30 kg) | 9 mL (450 mg) | 4.5 mL (450 mg) | | |
| > 67 lbs (> 31 kg) | 10 mL (500 mg) | 5 mL (500 mg) | | |

*Dosage adjustment is needed for individuals with severe renal impairment (see package insert).[1]

**What are common side effects of ciprofloxacin?**
Inform recipients that mild gastrointestinal side effects such as nausea, vomiting, and/or diarrhea, a mild sunburn or a vaginal yeast infection may be experienced but to continue taking ciprofloxacin. If these side effects become severe, over-the-counter or prescription drugs can help to relieve the symptoms.

[1] See the FDA-approved package insert for ciprofloxacin at www.dailymed.nlm.nih.gov and search for ciprofloxacin.
[2] FDA's emergency dispensing order applies to all FDA-approved oral dosage forms of ciprofloxacin products for the post-exposure prophylaxis of inhalation anthrax during an emergency involving *B. anthracis*. For details, see www.fda.gov.

**What are possible side effects of ciprofloxacin?**
Tell recipients to **STOP** the ciprofloxacin and get medical help immediately if they develop any of the following:

- Tendon rupture, tendinitis or joint problems
- Serious allergic/hypersensitivity reactions (anaphylactic and/or severe rashes)
- Liver problems (anorexia, jaundice, dark brown or tea-colored urine, pruritus or tender abdomen)
- Central nervous system effects (seizures, tremors, paranoia, anxiety)
- Serious heart rhythm changes (QT prolongation and torsade de pointes)
- Severe stomach cramps with high fever or bloody diarrhea (antibiotic-associated diarrhea and pseudomembranous colitis)
- Changes in sensation and possible nerve damage (peripheral neuropathy)

**What should recipients avoid while taking ciprofloxacin?**

- If a recipient is taking Carafate (sucralfate), Videx (didanosine), phosphate binders or multivitamins, supplements or antacids containing magnesium, calcium, aluminum, iron or zinc, instruct the recipient to take ciprofloxacin at least 2 hours before or 6 hours after taking any of these products.
- Ciprofloxacin can interact with certain drugs such as blood thinners (increased blood thinning), oral antidiabetic drugs (increased glucose-lowering effect), phenytoin (loss of seizure control), theophylline (increased theophylline concentration), or clozapine (irregular heartbeat). If a recipient is on these or other drugs with known interaction with ciprofloxacin, consider changing the dose of these drugs or recommending alternative drugs. For more information on ciprofloxacin drug interactions, please see package insert.

**What additional information should be provided to recipients taking ciprofloxacin?**

- Ciprofloxacin can exacerbate myasthenia gravis symptoms. It can also greatly potentiate effects of Zanaflex (tizanidine) (e.g., bradycardia, hypotension). Instruct those with a history of myasthenia gravis or taking tizanidine to avoid taking ciprofloxacin.
- Instruct recipients not to take ciprofloxacin with dairy products (like milk or yogurt) or calcium-fortified juices.
- Ciprofloxacin can cause sun sensitivity. Instruct recipients to use sunscreen and cover exposed skin.
- Ciprofloxacin, while not generally recommended for use in pregnancy, is recommended as antimicrobial PEP for anthrax during pregnancy and while breastfeeding due to the risks of anthrax. The very limited data available on ciprofloxacin use in pregnancy suggest the benefits of ciprofloxacin outweigh the risks.
- Recipients may wish to cut back on their caffeine intake, as the caffeine half-life may be prolonged.
- Instruct recipients to keep ciprofloxacin tablets dry and to store tablets and reconstituted oral suspension at room temperature (68–77°F or 20–25°C). Reconstituted oral suspension may be stored at room temperature up to 14 days.
- If you have been asked to dispense ciprofloxacin with an expired date on the container, please note that FDA is allowing for the use of certain lots of ciprofloxacin beyond the labeled expiration date during an anthrax emergency based on scientific review. For more information, go to the FDA website at www.fda.gov (search for "ciprofloxacin expiration").
- The Countermeasures Injury Compensation Program (CICP) is a federal program created to help pay for related costs of medical care and other specific expenses for eligible people seriously injured by the administration or use of certain medical countermeasures. Medical countermeasures may include vaccines, medications, devices or other items used to prevent, diagnose or treat the public during a public health emergency or security threat. For more information about CICP, visit www.hrsa.gov/cicp or call: 1-855-266-2427.

**Risk-Benefit Statement**
Although ciprofloxacin has some potential and serious adverse events, the expected benefit of ciprofloxacin to help prevent disease and death associated with anthrax exposure outweigh these risks.

**Available Alternatives**
During an anthrax emergency, you will be informed of any alternative antibiotics that are available, such as doxycycline, levofloxacin or amoxicillin. The risks and benefits of available alternative antibiotics will be explained in their own fact sheets.

**Reporting Adverse Event or Medication Errors**
Report adverse events or medication errors to MedWatch (www.fda.gov/medwatch) by completing a MedWatch Form 3500 or by calling 1-800-FDA-1088.

**Give recipients "Anthrax Emergency: How to Take Ciprofloxacin to Prevent Anthrax" instructions.**

| Space Reserved for State/Local Public Health Information |
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