Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 12/1/12**
(See policy history boxes for previous effective dates)

Title: Anthrax Vaccine

Description / Background

Anthrax is an infectious disease caused by the spores of the bacterium, *Bacillus anthracis*. It occurs most commonly in wild and domestic animals, such as cattle, sheep, goats, camels and antelope. The spores are highly resistant to inactivation and may be present in the soil for decades and occasionally infect grazing animals that ingest the spores. Human infection may occur by three routes of exposure to anthrax spores:

- Cutaneous (through the skin)
- Gastrointestinal (by ingestion)
- Pulmonary (by inhalation)

Cutaneous anthrax is the most commonly reported form in humans, comprising >95% of all anthrax cases. It occurs when spores enter a cut or abrasion on the skin. An itchy papule develops within 12 days after contact and progresses to a vesicle which ruptures, leaving an ulcer with a black eschar and surrounding edema. Systemic symptoms such as lymphadenopathy, fever, myalgia, malaise, vomiting and headache often accompany the skin lesions. This type is curable with antibiotic treatment; the fatality rate without treatment is estimated to be 20%.

Gastrointestinal anthrax begins with acute gastrointestinal inflammation within 7 days after the ingestion of contaminated meat. Initial symptoms are nausea, anorexia, vomiting and fever, followed by abdominal pain, hematemesis and bloody diarrhea. The case fatality rate is unknown but estimated to be 25-60%.

Pulmonary anthrax is the most severe form, with an estimated fatality rate of up to 90%. After an indeterminate incubation period, symptoms of sore throat, mild fever, myalgias, cough and chest discomfort appear, lasting a few days. The illness progresses to an abrupt onset of high

fever and acute respiratory distress with pulmonary edema and pleural effusions ensuing. Cyanosis, shock, coma and often meningitis may follow.

In North America, human cases of anthrax are infrequent. However, the United States military views anthrax as a potential biological terrorism threat because the spores are resistant to destruction and can be easily spread by release into the air. The development of anthrax as a biological weapon by several foreign countries has been documented.

Immediately after the bioterrorist attacks on the United States began in 2001, officials at the Centers for Disease Control and Prevention in Atlanta started working to ensure that they would have the anthrax vaccine available to treat soldiers who might be exposed to anthrax during biological warfare. It was felt that if the attacks continued, antibiotics might not be effective.

The only known effective prevention against anthrax is the anthrax vaccine. The vaccine was developed from an attenuated strain of *B. anthracis*. The licensed anthrax vaccine, termed Anthrax Vaccine Adsorbed (AVA), is recommended for individuals who may come in contact with animal products that may be contaminated with the *Bacillus anthracis* spores and for individuals engaged in diagnostic or investigational activities which may bring them in contact with *Bacillus anthracis* spores.

Regulatory Status:

AVA is marketed as BioThrax (Emergent BioSolutions, Lansing, Michigan) and is licensed by the Food and Drug Administration (FDA). It is indicated for the active immunization for the prevention of disease caused by *Bacillus anthracis*, in persons 18 through 65 years of age at high risk of exposure. The safety and efficacy of BioThrax in a post-exposure setting have not been established.

Medical Policy Statement

Anthrax vaccination is not a medically necessary therapy as routine prophylaxis for the general public. The federal government does not recommend vaccination for the general public at this time.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

N/A

CPT / HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

N/A

Other codes (investigational, not medically necessary, etc.):

90581

Rationale

According to the ACIP (2010), "Human anthrax is best controlled through prevention, including preexposure vaccination for persons at high risk for encountering aerosolized *B. anthracis* spores, reduction of animal illness by vaccination of livestock at risk for anthrax, and environmental controls to decrease exposure to contaminated animal products, such as imported hair and skins. After a person is exposed to aerosolized *B. anthracis* spores, a combination of antimicrobials and vaccine provides the best available protection."

Recommendations of the Advisory Committee on Immunization Practices (ACIP), state that AVA may be used
1) Via the licensed schedule to prevent infection by priming the immune system before exposure to *B. anthracis* (pre-event or preexposure vaccination) and
2) After exposure to aerosolized *B. anthracis* spores under an IND or possibly under an EUA (PEP vaccination) (Tables 2 and 3).

TABLE 1. Recommended initial antimicrobial agent and anthrax vaccine adsorbed (AVA) dosages for postexposure prophylaxis (PEP) after exposure to aerosolized *Bacillus anthracis* spores

Population	Antimicrobials for 60-day* PEP	AVA dosage and route†
Adults (18--65 yrs)	*One of the following for 60 days:* Ciprofloxacin,§ 500 mg orally twice daily Doxycycline, 100 mg orally twice daily	3-dose subcutaneous (SC) series: first dose administered as soon as possible, second and third doses administered 2 and 4 wks after the first dose
Pregnant women¶	*One of the following for 60 days:* Ciprofloxacin, 500 mg orally twice daily Doxycycline, 100 mg orally twice daily Amoxicillin,** 500 mg every 8 hrs	3-dose SC series; first dose administered as soon as possible, second and third doses administered 2 and 4 wks after the first dose
Children (<18 yrs)††	*One of the following for 60 days:* Ciprofloxacin,§,††,§§ 15 mg/kg every 12 hrs Doxycycline,††,¶¶ (maximum of 100 mg/dose) >8 yrs and >45 kg: 100 mg every 12 hrs >8 yrs and ≤45 kg: 2.2 mg/kg every 12 hrs ≤8 yrs: 2.2 mg/kg every 12 hrs Amoxicillin,**,*** 45 mg/kg/day orally divided into 3 daily doses given every 8 hrs; each dose should not exceed 500 mg	Recommendations for use of AVA in children are made on an event-by-event basis.

* Antimicrobials should continue for 14 days after administration of the third dose of vaccine.
† AVA used for PEP must be administered subcutaneously.

§ Levofloxacin is a second-line antimicrobial agent for PEP for persons aged ≥6 mos with medical issues (e.g., tolerance or resistance to ciprofloxacin) that indicate its use. *Children:* 16 mg/kg/day divided every 12 hrs; each dose should not exceed 250 mg. *Adults:* 500 mg every 24 hrs. 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 ≤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.

TABLE 2. Recommended preexposure and postexposure vaccination schedules for anthrax vaccine adsorbed

Type of prophylaxis	Schedule	Route	Dose
Preexposure	5 doses (0 wks, 4 wks, 6 mos, 12 mos, and 18 mos) Annual booster to maintain immunity	Intramuscular	0.5 mL
Postexposure*	3 doses (0, 2, and 4 wks)†,§	Subcutaneous	0.5 mL

* For previously unvaccinated persons.
† In conjunction with 60-day antimicrobial postexposure prophylaxis.
§ Administered under an Investigational New Drug (IND) protocol or an Emergency Use Authorization (EUA).

TABLE 3. Recommendations for use of anthrax vaccine adsorbed, by type of population

Population	Pre-event*	Postexposure prophylaxis (PEP)†
General public	Not recommended	Recommended

Special populations in the general public		
Pregnant women	Not recommended	Recommended
Breastfeeding women	Not recommended	Recommended
Children (aged <18 yrs)	Not recommended	Determined on an event-by-event basis
Medical professionals	Not recommended	Recommended
Populations at risk for occupational exposure		
Persons who handle animals or animal products	Not routinely recommended§	Recommended
Persons who perform certain types of laboratory work	Recommended¶	Based on pre-event vaccination status
Persons who work in postal facilities	Not recommended	Recommended
Military personnel	As recommended by the Department of Defense	As recommended by the Department of Defense
Persons involved in environmental investigations or remediation efforts	Recommended	Based on pre-event vaccination status
Persons involved in emergency response activities**	Not routinely recommended; may be offered on a voluntary basis under the direction of a comprehensive occupational health and safety program	Recommended

* Five 0.5-mL doses administered intramuscularly at 0 wks, 4 wks, 6 mos, 12 mos, and 18 mos; annual boosters are required to maintain immunity.

† Three 0.5-mL doses administered subcutaneously at 0, 2, and 4 wks after exposure to aerosolized *Bacillus anthracis* spores for persons who have not completed the pre-event vaccination schedule.
§ Recommended only if handling potentially infected animals in research settings or in areas with a high incidence of enzootic anthrax or when standards and restrictions are insufficient to prevent exposure to *B. anthracis* spores.

¶ Laboratorians who work 1) with high concentrations or pure cultures of *B. anthracis* spores, 2) with environmental samples associated with anthrax investigations, or 3) in spore-contaminated areas or other settings with exposure to aerosolized *B. anthracis* spores. Laboratorians who do not work in these settings are not recommended for pre-event vaccine.

** Persons involved in emergency response activities might include persons who work in police departments, fire departments, hazardous material units, and the National Guard, as well as other government responders. These persons might perform site investigations, respond to suspicious substance reports (also known as white powder incidents), and perform other related activities, such as evacuation procedures or other activities critical to the maintenance of infrastructure.

TABLE 4. Postexposure prophylaxis (PEP) for persons with repeated occupational exposures to aerosolized *Bacillus anthracis* spores, by preexposure anthrax vaccine adsorbed vaccination status		
Vaccination status	**Vaccination recommendation**	**Duration of antimicrobial PEP***
No previous vaccine	Use PEP schedule of 3 subcutaneous doses (0, 2, and 4, wks); resume the licensed vaccination schedule† at 6 mos	60 days; continue for 14 days after the third dose of vaccine, even if initial vaccine administration is delayed and therefore antimicrobial is used for >60 days
Partially vaccinated§	Continue with licensed vaccination schedule†	At least 30 days after any type of disruption of respiratory protection¶
Fully vaccinated**	Continue with annual boosters as scheduled	At least 30 days after any type of disruption of respiratory protection¶

* Because antimicrobial PEP is the primary intervention, do not delay initiation if vaccine is not available.

† Licensed vaccination schedule: 5 doses intramuscularly (IM) (0 wks, 4 wks, 6 mos, 12 mos, and 18 mos), with annual boosters thereafter.

§ Partially vaccinated persons have either received <5 IM priming doses or have not received all annual boosters indicated by the licensed vaccination schedule.

¶ Because respiratory protection can be disrupted in numerous ways (e.g., a face-seal leak in a respirator or not wearing personal protective equipment when entering an area presumed to be uncontaminated that is later determined to be contaminated) and such disruptions are not always detected, the threshold for assuming such a disruption has occurred should be extremely low.

** Fully vaccinated workers have completed the 5-dose IM series and have received all annual booster doses indicated by the licensed vaccination schedule.

Government Regulations

National:

There is no national coverage determination.

Local:

There is no local coverage determination.

Michigan Department of Community Health:

Medicaid does not have any information on this topic.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

N/A

References

1. Centers for Disease Control, "MMWR: Use of Anthrax Vaccine in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP)," 2009 July 23, 2010 / 59(rr06);1-30, Accessed from: http://www.bt.cdc.gov/agent/anthrax/vaccination/#guidelines, Date 6/25/12.
2. Emergent BioSolutions, BioThrax® (Anthrax Vaccine Adsorbed), Prescribing Information, Accessed from: http://www.biothrax.com/prescribinginformation_biothrax_us.pdf, Date 6/25/12.
3. U.S. Food and Drug Administration, "Authorization of Emergency Use of Anthrax Vaccine," *Department of Health and Human Services*, Federal Register, Vol. 70, No. 148, August 3, 2005.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through June 25, 2012, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
10/30/03	10/30/03	10/3/03	Joint medical policy established
5/1/07	3/1/07	4/30/07	Routine maintenance
5/1/08	2/19/08	1/28/08	Routine maintenance
5/1/09	2/10/09	2/10/09	Routine maintenance
12/1/12	9/27/12	9/27/12	Routine maintenance; policy retired.

This is an established policy and no longer subject to routine review.

BLUE CARE NETWORK BENEFIT COVERAGE POLICY: ANTHRAX VACCINE

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Not covered
BCNA (Medicare Advantage)	Not covered
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.
Blue Cross Complete of Michigan	Not covered

II. Administrative Guidelines:

N/A