BIOTHRAX

Generic Name: anthrax vaccine adsorbed emergent biosolutions

Brand Name: BioThrax

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BioThrax Side Effects Center

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BioThrax (anthrax) Vaccine Adsorbed is an immunization used to help prevent anthrax disease in people exposed to the bacteria through the skin or lungs. BioThrax vaccine works by exposing you to an antigen protein that causes your body to develop immunity to the disease. BioThrax does not contain live or killed forms of the bacteria that cause anthrax. BioThrax vaccine will not treat an active infection. Common side effects of BioThrax include injection site reactions (pain, redness, swelling, warmth, itching, or tenderness), limited arm movement or stiffness in the injected arm, joint or muscle ache or pain, headache, dizziness, tiredness, weakness, low fever, swelling in your hands or feet, or skin rash.

Immunization with BioThrax consists of a series of 5 intramuscular doses administered at 0 and 4 weeks and 6, 12 and 18 months. Select a different injection site for each sequential injection of this vaccine. Individuals should not be considered protected until they have received the full series of vaccinations. BioThrax may interact with other vaccines, steroids, medicines to treat or prevent organ transplant rejection, or medications to treat psoriasis, rheumatoid arthritis, or other autoimmune disorders. Tell your doctor all medications and supplements you use and all vaccines you recently received. BioThrax is not recommended for use during pregnancy. It may harm a fetus. It is unknown if this medication passes into breast milk. Consult your doctor before breastfeeding.

Our BioThrax (anthrax) Vaccine Adsorbed Side Effects Drug Center provides a comprehensive view of available drug information on the potential side effects when taking this medication.

This is not a complete list of side effects and others may occur. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

BioThrax Consumer Information

You should not receive a booster vaccine if you had a life-threatening allergic reaction after the first shot.

Keep track of any and all side effects you have after receiving this vaccine. When you receive a booster dose, you will need to tell the doctor if the previous shot caused any side effects.

Becoming infected with anthrax is much more dangerous to your health than receiving this vaccine. However, like any medicine, this vaccine can cause side effects but the risk of serious side effects is extremely low.

Get emergency medical help if you have **signs of an allergic reaction**: hives; difficult breathing; swelling of your face, lips, tongue, or throat.

Call your doctor at once if you have:

- a light-headed feeling, like you might pass out;
- fever, chills, body aches, nausea, flu symptoms; or
- severe swelling or a hard lump where the shot was given.

Common side effects include:

- mild redness, swelling, or tenderness where the shot was given;
- trouble moving the injected arm;
- muscle pain;
- tired feeling; or
- headache.

This is not a complete list of side effects and others may occur. Call your doctor for medical advice about side effects. You may report vaccine side effects to the US Department of Health and Human Services at 1 800 822 7967.

BioThrax Professional Information

SIDE EFFECTS

The most common (≥ 10%) local (injection-site) adverse reactions observed in clinical studies were tenderness, pain, erythema, edema, and arm motion limitation. The most common (≥ 5%) systemic adverse reactions were muscle aches, headache, and fatigue.

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a product cannot be directly compared to rates in the clinical trials of another product and may not reflect the rates observed in clinical practice.

In an open-label safety study of 15,907 doses of BioThrax administered by the subcutaneous route to approximately 7,000 textile employees, laboratory workers and other at risk individuals, local and systemic reactions were monitored. Over the course of the 5-year study the following local adverse reactions were reported: 24 (0.15% of doses administered) severe local adverse reactions (defined as edema or induration measuring greater than 120 mm in diameter or accompanied by marked limitation of arm motion or marked axillary node tenderness), 150 (0.94% of doses administered) moderate local adverse reactions (edema or induration greater than 30 mm but less than 120 mm in diameter), and 1,373 (8.63% of doses administered) mild local adverse reactions (erythema only or induration measuring less than 30 mm in diameter). Four cases of systemic adverse reactions were reported during the 5-year reporting period (< 0.06% of doses administered). These reactions, which were reported to have been transient, included fever, chills, nausea, and general body aches.

In a randomized, double-blinded, placebo-controlled, and active-controlled multi-center clinical study, [NCT00119067] 1,564 healthy subjects were enrolled. The objective of this study was to evaluate the effect of (1) changing the route of vaccine administration from subcutaneous (SC) to intramuscular (IM), and (2) of reducing the number of doses on the safety and immunogenicity of BioThrax. The dosing schedules and routes studied are provided in Table 1. [See **Clinical Studies**]

Group A (8SC) (N=259) received BioThrax via the SC route of administration at Weeks 0, 2, 4, and Months 6, 12, 18 followed by 2 annual boosters (original U.S. licensed route/schedule). Group A served as the active control in this study.

Group B (8IM) (N=262) received BioThrax via the IM route of administration at Weeks 0, 2, 4, and Months 6, 12, 18 followed by 2 annual boosters.

Group C (COM) (N=782) received BioThrax via the IM route of administration at Weeks 0, 4 (no Week 2 dose), and Month 6 with various schedules thereafter. (Group C represents data from 3 randomized groups [Groups D, E, and F] combined for the analysis through Month 7 because the schedules are identical through the Month 6 dose.)

Group D (7IM) (N=256) received BioThrax via the IM route of administration at Weeks 0, 4 (no Week 2 dose), and Months 6, 12, 18 followed by 2 annual boosters.

Group E (5IM) (N=258) received BioThrax via the IM route of administration at Weeks 0, 4 (no Week 2 dose), and Months 6, 18 followed by 1 booster dose at Month 42 (2 year interval).

Group F (4IM) (N=268) received BioThrax via the IM route of administration at Weeks 0, 4 (no Week 2 dose), and Month 6 followed by 1 booster dose at Month 42 (3 year interval).

Table 1: Vaccination Schedules and Routes Evaluated

Group/Route	Weeks			Months				
	0	2	4	6	12	18	30	42

Group A (8SC)*	V	V	V	V	V	V	V	V
Group B (8IM)	V	V	V	V	V	V	V	V
Group D (7IM)	V	S	V	V	V	V	V	V
Group E (5IM)	V	S	V	V	S	V	S	V
Group F (4IM)	V	S	V	V	S	S	S	V
Placeboˆ	S	S	S	S	S	S	S	S

SC: subcutaneous; IM: intramuscular; V: vaccine, S: saline.

*Active Control.

ˆSubjects randomized to the control group were then re-randomized (1:1) to receive saline by the IM or SC route. The IM and SC placebo groups are combined in analyses.

Subjects were instructed to complete a 14-day post-vaccination diary card after the first 2 doses and a 28-day diary card after the subsequent doses to capture solicited and unsolicited adverse reactions. Adverse reaction data were also collected from in-clinic exams, which were performed prior to, and 15 to 60 minutes after each injection, at 1 to 3 days after each injection, and at 28 days after injections 3 through 8. The mean age, gender ratio, and race distribution were not significantly different across treatment groups among the vaccinated cohort (N=1563). The mean age was 39 years (range 18 to 62 years). Fifty-one percent of participants were female and 49% were male. Seventy-four percent were white, 21% were black and 5% were categorized as “other”.

Shown in Table 2 are the rates (percentage) of prospectively defined local and systemic solicited adverse reactions observed in the in-clinic exams for doses 1-4 as well as the rates (percentage) of local and systemic solicited adverse reactions observed in the in-clinic exams for doses 5-8.

Analysis of injection site (local) adverse reactions by study group was performed after each dose. It was observed that groups receiving BioThrax by the IM route had a statistically significantly lower incidence of any (one or more) local adverse reactions compared to the BioThrax SC route, by dose in the in-clinic data set, in almost all analyses. Injection site adverse reactions, including warmth, tenderness, itching, erythema, induration, edema, and nodule occurred at lower frequencies in participants given BioThrax by the IM route after each dose, in almost all comparisons. However, by dose, the incidence of arm motion limitation was usually higher in each BioThrax IM group compared to the 8SC group (excluding doses where IM groups received a placebo). The incidence of any moderate or severe local adverse reactions was consistently lower in BioThrax IM groups, compared to the 8SC group after each dose. Route of administration did not affect the occurrence of systemic adverse reactions, with the exception of muscle ache (increased incidence in the BioThrax IM groups after most doses). There was no clear pattern for differences in the incidence of any moderate or severe systemic adverse reactions for BioThrax IM groups compared to the 8SC group after each dose. The proportion of participants with severe local or systemic adverse reactions reported by adverse reaction category after each dose was very low (generally < 1%).

Overall, women had a higher incidence of any local adverse reaction than did men, by dose, within BioThrax groups, regardless of the route of administration. Overall, women also had a higher incidence of any systemic adverse reaction than men, within BioThrax groups, regardless of the route of

administration. A brief pain or burning sensation, felt immediately after vaccine injection, and distinct from injection site pain, was reported by 45 - 97% of all study participants receiving BioThrax. Reporting frequency and event intensity varied with route of administration and vaccine dose. Up to 11% of subjects rated the brief pain or burning they experienced immediately after vaccine injection as 8 out of 10 or greater. Female participants generally experienced a higher pain scale rating than male participants.

Eight serious adverse events (SAEs) were reported with 6 subjects and determined to be possibly related to the administration of BioThrax: (1) a case of generalized allergic reaction, (2) a case of ANA positive autoimmune disorder manifesting as a moderate bilateral arthalgia of the metacarpophalangeal (MCP) joints, (3) a right shoulder supraspinatus tendon tear, (4) a case of bilateral pseudotumor cerebri with bilateral disc edema, (5) a case of generalized seizure and hospitalization for evaluation of hydrocephalus and endoscopic fluid ventriculostomy, (6) a case of bilateral ductal carcinoma of the breast. No SAEs were determined by the investigator to be probably or definitely related to administration of BioThrax. The percent of serious adverse events was similar between the BioThrax combined groups (193/1303 or 1.5%) and the placebo group (38/260 or 1.5%).

Out of a total of 51 pregnancies reported in this study, no distinct patterns of infant outcome were seen, with the majority of pregnancies uncomplicated and healthy term infants delivered. Of women who received vaccine within 90 days of the estimated date of conception (n = 14), 2 spontaneous abortions and a first trimester intra-utero fetal death were reported, along with one report of a healthy term infant with mild right clubbed foot abnormality.

Table 2: Adverse Reactions: In-Clinic Day 0 - 3, Solicited by Dose Number*

	STUDY GROUP																							
	Group D BioThrax 7IM (BioThrax Doses 1, 3-8) Weeks-0-4-26† Months 12-18-30-42								Placebo‡ Control SC/IM (Doses 1-8) Weeks-0-2-4-26 Months 12-18-30-42								Group A BioThrax 8SC (BioThrax Doses 1-8) Weeks-0-2-4-26 Months 12-18-30-42							
Number of Subjects (N)**	256								260								259							
	Dose								Dose								Dose							
	1	2†	3	4	5	6	7	8	1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8
	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%
Local Adverse Reactions																								
Presence of any local adverse reaction	60	23	68	68	69	77	76	73	22	22	19	27	25	29	25	18	81	89	80	84	81	84	84	92
Warmth	4	1	8	10	11	13	14	19	1	0	0	0	0	0	1	1	29	41	32	39	34	40	51	49

Tenderness	46	37	51	47	41	44	44	48	6	8	7	10	6	7	7	4	64	72	48	65	53	57	61	63
Itching	1	0	2	4	7	7	7	10	0	0	0	0	1	0	0	0	3	16	23	20	17	22	25	26
Pain	16	4	20	15	16	13	16	15	4	2	3	4	4	2	3	2	16	22	12	19	16	14	18	20
Arm motion limitation	14	1	15	11	10	10	15	9	1	0	2	1	1	1	1	0	8	12	5	11	10	5	8	5
Erythema	15	10	20	30	35	48	40	37	11	12	7	13	14	17	14	11	53	64	57	65	64	64	68	71
Induration	7	7	12	16	21	23	15	17	1	3	2	3	4	4	3	3	26	35	28	40	38	36	38	35
Edema	5	2	11	20	15	23	30	25	3	4	4	4	4	7	8	5	17	33	31	33	31	35	37	46
Nodule	3	0	4	5	8	9	6	5	0	2	0	1	2	0	2	0	39	42	36	26	26	23	21	27
Bruise	5	4	5	3	2	4	3	2	4	5	1	4	3	5	5	4	6	7	6	6	3	6	5	6
Presence of any moderate/severe local adverse reactions§	5	1	8	7	4	5	6	4	0	0	0	0	0	0	0	0	7	16	8	13	10	7	12	14
Presence of any large local adverse reaction‖	0	0	0	2	2	4	2	2	0	0	0	0	0	0	0	0	0	1	4	2	1	2	2	4
Systemic Adverse Reactions																								
Presence of any systemic adverse reaction	18	12	24	19	15	19	10	9	10	10	13	11	13	8	13	4	16	20	18	21	18	14	20	17
Fatigue	9	4	12	10	9	11	4	6	5	4	7	7	8	5	10	3	9	12	8	12	12	10	10	13
Muscle ache	8	4	13	6	5	5	3	5	2	2	3	4	5	3	1	1	5	8	4	5	4	3	9	5
Headache	6	6	9	7	8	8	5	4	4	6	5	4	7	4	6	1	7	9	8	11	7	5	9	2
Fever ≥ 100.4°F	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0

Tender/painful axillary adenopathy	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	1	0	1	2	1	1	0	1	0
Presence of any moderate/severe systemic adverse reactions††	2	2	6	3	3	5	4	3	1	2	2	1	3	1	2	1	2	5	4	3	3	2	3	2

*Per-dose, statistical assessment performed on Intent-to-Treat population data. Evaluations performed at 15-60 minutes and 1-3 days following each injection and prior to the next scheduled injection.

**N is the highest number per treatment arm (received at least one dose); denominator (N) varied with dose number due to attrition over time.

†Subjects received saline (instead of BioThrax) for the Week 2 dose. Placebo dose data for 7IM group is in italics.

‡The two saline groups (SC and IM) were combined.

§ Moderate = causes discomfort and interferes with normal daily activities; Severe = incapacitating and completely prevents performing normal daily activities. This is based on the local AE categories of warmth, tenderness, itching, pain, and arm motion limitation.

Large = an occurrence of induration, erythema, edema, nodule, and bruise with a largest diameter greater than 120 mm.

†† Moderate = causes discomfort and interferes with normal daily activities; Severe = incapacitating and completely prevents performing normal daily activities. This is based on the systemic AE categories of fatigue, muscle ache, headache, and fever.

Solicited and unsolicited adverse reactions observed from Day 0 through month 43 at a higher frequency (by at least 5%) in the BioThrax groups (IM and SC) as compared to the placebo (P) group were: headache (70.4% IM, 78.4% SC, 68.1% P); myalgia (72% IM, 76.1% SC, 50% P); and fatigue (70.1% IM, 76.8% SC, 60.8% P).

Postmarketing Experience

The following adverse events, not previously listed in Section 6.1, have been identified during post-approval use of BioThrax. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The reports included below are listed due to one or more of the following factors: (1) seriousness of the event, (2) number of reports, or (3) strength of causal relationship to the drug.

Blood and Lymphatic System Disorders

Lymphadenopathy

Gastrointestinal Disorders

Nausea

Immune System Disorders

Allergic reactions (including anaphylaxis, angioedema, rash, urticaria, pruritus, erythema multiforme, anaphylactoid reaction, and Stevens Johnson syndrome)

Nervous System Disorders

Paresthesia syncope, dizziness, tremor, ulnar nerve neuropathy

Musculoskeletal, Connective Tissue, and Bone Disorders

Arthralgia, arthropathy, myalgia, rhabdomyolysis, alopecia

General Disorders and Administration Site Conditions

Malaise, pain, cellulitis, flu-like symptoms

Psychiatric Disorders

Insomnia

Skin and Subcutaneous Disorders

Pruritis, rash, urticaria

Vascular Disorders

Flushing

Infrequent reports were also received of multisystem disorders defined as chronic symptoms involving at least two of the following three categories: fatigue, mood-cognition, and musculoskeletal system.

Related Resources for BioThrax

RELATED HEALTH

- Vaccination and Immunization Safety Information

RELATED DRUGS

- Adoxa
- Atridox
- Cipro

- Cipro XR
- Oracea
- Proquin XR
- Sumycin
- Vibramycin

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