Proprietary Name Change as per letter BG/09
Dated: 09 October 2020
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PROFESSIONAL INFORMATION
ADSORBED TETANUS VACCINE BP
Tetanus Toxoid Bio

SCHEDULING STATUS:

S2

PROPRIETARY NAME AND DOSAGE FORM:

Tetanus Toxoid Bio (Suspension for injection)

DESCRIPTION:

Tetanus Toxoid Bio (Adsorbed tetanus vaccine) is a sterile preparation of refined tetanus toxoid.

COMPOSITION:

Tetanus Toxoid Bio

Each 0,5 ml intramuscular dose contains:

- Tetanus toxoid ≥ 40 IU
- Adsorbed on Aluminum phosphate (AlPO4) ≥ 1,5 mg
- Preservative: Thiomersal 0,01 %

The other **inactive** ingredient of **Tetanus Toxoid Bio is**:

- Water for injection

CATEGORY and CLASS:

A 30.2 Antigens

PHARMACOLOGICAL ACTION:

Tetanus is a disease manifested primarily by neuromuscular dysfunction caused by a potent exotoxin released by *Clostridium tetani.*

Tetanus toxoid preparations contain the toxin produced by virulent tetanus bacilli (detoxified growth products of *Clostridium tetani*). The toxin has been modified by treatment with formaldehyde so that it has lost toxicity but still retains its ability to act as an antigen and produce active immunity due to the development of neutralising antibodies to Tetanus toxin. A serum tetanus antitoxin level of at least 0,01 IU/ml, measured by neutralising assay, is considered the minimum protective level.

Summary of Clinical Studies

The immune response was measured in three clinical trials. Immunity was shown after the second injection of Tetanus Toxoid Bio by analysis of antibody titres which showed a >8-fold rise (a minimum of 4-fold required) in the Geometric Mean Titre Values from the baseline values taken before vaccination.

This was reinforced after the third vaccination.

It is recommended, however, that immunisation be completed with reinforcing doses upon starting school and at intervals subsequently of about ten years.

INDICATIONS:

Tetanus Toxoid Bio is indicated for use in:

- Tetanus prophylaxis.
- Post exposure prophylaxis of tetanus.
- Neonatal tetanus prevention.
- Tetanus Prophylaxis in Wound Management.

Tetanus prophylaxis:

Tetanus Toxoid Bio is indicated for active immunisation against tetanus in adults and children over the age of 7 (seven) years.

In children less than 7 years of age, the use of diphtheria, tetanus and pertussis vaccine combination is recommended unless pertussis vaccine is contraindicated.
If pertussis is contraindicated, then the use of diphtheria and tetanus toxoids (**DT**) is recommended.
Tetanus Toxoid Bio is indicated for booster active immunisation for long term prophylaxis of tetanus in adults.

Post exposure prophylaxis of tetanus:

Immunity is not conferred to persons who contract tetanus due to the fact that only a very small amount of toxin is required to produce illness. Persons recovering from tetanus should begin or complete active immunisation with a tetanus-toxoid containing vaccine during convalescence.

Neonatal tetanus prevention:

Neonatal tetanus prophylaxis in countries where neonatal tetanus is common for women of reproductive age.
If vaccination is required, **Tetanus Toxoid Bio** can be used during pregnancy.
Tetanus Toxoid Bio should be given to inadequately immunised pregnant women because it affords protection against neonatal tetanus.
Teratogenic effects have not been reported with tetanus toxoid in humans.
Waiting until the second trimester to administer tetanus vaccine is a reasonable precaution for minimising any concern regarding the theoretical possibility of adverse reactions.

Tetanus Prophylaxis in Wound Management:

Tetanus Toxoid Bio can also be used prophylactically for wound management in persons 7 years of age and older; tetanus and diphtheria toxoid (Td) is preferred, to maintain adequate levels of diphtheria immunity.

CONTRAINDICATIONS:

Tetanus Toxoid Bio is contraindicated for use in:

Patients with a known hypersensitivity to any component of the vaccine, including thiomersal, which is a mercury derivative (see **COMPOSITION**).

Patients who develop any type of neurological symptoms or signs following administration of **Tetanus Toxoid Bio** (see **Warnings and Special Precautions**).

Those patients who develop systemic hypersensitivity or neuralgic reactions to a previous injection with **Tetanus Toxoid Bio**, should only be given passive immunisation using Tetanus Immune Globulin (Human) (TIG).

The attending physician should consider risk/benefit ratio at all times.

Also, routine immunisation should be deferred during an outbreak of poliomyelitis, provided that the patient has not sustained an injury that increases the risk of tetanus.

WARNINGS and SPECIAL PRECAUTIONS:

WARNINGS:

The administration of booster doses more frequently than recommended may be associated with increased incidence and severity of reactions.

There is evidence that the incidence of allergic reactions is higher in individuals with high titres of tetanus antitoxin antibody at time of reimmunisation

Persons who experience Arthus-type hypersensitivity reactions or temperature greater than 39 °C after a previous dose of tetanus toxoid usually have very high

serum tetanus antitoxin levels and should not be given even emergency doses of tetanus toxoid more frequently than every 10 years, even if they have a wound that is neither clean nor minor.

Evidence mainly from case reports and uncontrolled studies favoured a causal relationship between vaccination with single-antigen tetanus vaccines and Guillain-Barré Syndrome. The data came primarily from immunocompromised patients. However, a later analysis of active epidemiological studies of Guillain-Barré and tetanus vaccination history concluded that if an association exists, it must be extremely rare and not of public health significance.

Should not be given to individuals with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection, unless the potential benefit clearly outweighs the risk of administration.

Patients with impaired immune responsiveness may have a reduced antibody response to active immunisation procedures.

Special care should be taken to ensure that the injection does not enter into a blood vessel.

SPECIAL PRECAUTIONS:

General precautions regarding Tetanus Toxoid Bio:

Patients with any acute infection or any febrile illness.

Immunisation should be deferred in these patients. A minor afebrile illness such as a mild upper respiratory infection is not usually a contraindication to defer immunisation and may be considered when indicated based on clinical judgment.

Prior to administration of any dose of vaccine, the parent, guardian, or adult patient should be asked about the recent health status and immunisation history of the patient to be immunised in order to determine the existence of any contraindication to immunisation.

When the patient returns for the next dose in a series, the parent, guardian, or adult patient should be questioned concerning occurrence of any symptom and/or sign of an adverse reaction after the previous dose.

Before the injection of any biological product, the physician should take all precautions known for prevention of allergic or any other side reactions. This should include: a review of the patient's history regarding possible sensitivity, the ready availability of epinephrine 1:1000 and other appropriate agents used for control of immediate allergic reactions.

A separate sterile syringe and needle or a sterile disposable unit should be used for each individual patient to prevent transmission of hepatitis or other infectious agents from one person to another (see **Dosage and Directions for use**).

Shake vigorously before withdrawing each dose to re-suspend the contents of the vial.

Special Precautions in certain population groups:

Human Immunodeficiency Virus (HIV) infected persons:

HIV-infected persons, both asymptomatic and symptomatic, should be immunised with **Tetanus Toxoid Bio** according to standard schedules.

Effects on the ability to drive and use machinery:

The safety of **Tetanus Toxoid Bio** on the ability to drive and operate machinery has not been established.

INTERACTIONS:

General:

There is no evidence of safety and immunogenicity following concomitant use with other vaccines and medications.

Patients receiving immunosuppressant therapy, including antineoplastics or therapeutic doses of corticosteroids, may also display a reduced response to vaccines and deferral of immunisation is advised.

If possible, delay the administration of vaccines in immunosuppressed patients. However, the clinical judgment of the responsible physician should prevail. It should be noted that the benefits of vaccination will outweigh any risks in the management of a tetanus prone wound.

Tetanus immunoglobulins will neutralise tetanus toxoid and should not be injected into the same site or in the same syringe as a tetanus vaccine.

The following medicines may also cause an inadequate immunological response to **Tetanus Toxoid Bio**:

Chloramphenicol.

Cyclosporine.

It should be noted that the benefits of vaccination with **Tetanus Toxoid Bio** will outweigh any risks in the management of a tetanus prone wound.

When using chloramphenicol, administer **Tetanus Toxoid Bio** either before or after chloramphenicol therapy.

When possible, immunisation should occur two to four weeks before initiating therapy with cyclosporine.

HUMAN REPRODUCTION:

Tetanus Toxoid Bio:

Animal reproductive studies have not been conducted.

There is no evidence that the vaccine is teratogenic.

The vaccine should be given to inadequately immunised pregnant woman because it affords protection against neonatal tetanus (see **Dosage and Directions for use**).

Waiting until the second trimester is a reasonable precaution to minimise any theoretical concern.

The effect on the nursing infant is unknown.

DOSAGE AND DIRECTIONS FOR USE:

Tetanus Toxoid Bio:

The vaccine vial should be shaken before use to homogenise the suspension. A sterile needle and a sterile syringe should be used for each injection (see **Warnings and Special Precautions**).

Immunisation schedule of Tetanus Toxoid Bio:

FOR TETANUS PROPHYLAXIS:

The **primary** immunising course for unimmunised individuals 7 years of age or older consists of two intramuscular (IM) doses of 0,5 ml each.

These doses should be given 4 to 8 weeks apart followed by a third (reinforcing) dose of 0,5 ml. This dose should be given 6 to 12 months after the second dose.

The reinforcing dose is an integral part of the primary immunising course.

Individuals who have not completed primary immunisation against tetanus, or whose immunisation history is unknown or uncertain, should be immunised with a tetanus-toxoid containing product.

FOR NEONATAL TETANUS PREVENTION:

Antenatal immunisation is recommended for the prevention of neonatal tetanus in the previously unimmunised mother (see **Human reproduction**).

A previously unimmunised pregnant woman who may deliver her child under non hygienic circumstances and/or surroundings should receive two doses of a tetanus toxoid-containing preparation before delivery (4 to 8 weeks apart), preferably during the last 2 trimesters.

Incompletely immunised pregnant women should complete the 3-dose series.

Those immunised more than 10 years previously should have a booster dose.

Table: Tetanus toxoid immunisation schedule for pregnant women and women of childbearing age

Recommended Schedule	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5
Pregnant women with no previous immunisation (or unreliable immunisation)	TT or Td	TT or Td	TT or Td	TT or Td	TT or Td
	As early as possible in first pregnancy	At least 4 weeks later	At least 6 months later	At least 1 year later	At least 1 year later
Pregnant women with 3 childhood DTP doses	TT or Td	TT or Td	TT or Td	TT or Td	TT or Td
	As early as possible in first pregnancy	At least 4 weeks later	At least 1 year later or in next pregnancy		
Pregnant women with 4 childhood DTP doses	TT or Td	TT or Td	TT or Td	TT or Td	TT or Td
	As early as possible in first pregnancy	At least 1 year later or in next pregnancy			
Supplementary immunisation activities in high-risk areas (women of childbearing age)	TT or Td	TT or Td	TT or Td	TT or Td	TT or Td
	During round 1	During round 2, at least 4 weeks after round 1	During round 3, at least 6 months after round 2	At least 1 year later (in next pregnancy)	At least 1 year later (in next pregnancy)

IN TETANUS PROPHYLAXIS IN WOUND MANAGEMENT:

The need for active immunisation with a tetanus toxoid-containing preparation, with or without passive immunisation with **TIG** (Human tetanus immune globulin) depends on both the condition of the wound and the patient's vaccination history.

Tetanus Toxoid Bio is used alone (1 dose) in low-risk wounds (clean or minor wounds) in individuals in whom primary immunisation is incomplete or uncertain, or in individuals who have had full primary immunisation but who have received no booster dosage for 10 years.

Tetanus Toxoid Bio used in conjunction with tetanus immune globulin is recommended for prophylactic contaminated wound management in unimmunised, uncertain, or incomplete immunisation status patients.

A thorough attempt must be made to determine whether a patient has completed primary immunisation.

Individuals who have completed primary immunisation against tetanus, and who sustain wounds which are minor and uncontaminated, should receive a booster dose of a tetanus toxoid-containing preparation only if they have not received tetanus toxoid within the preceding 10 years.

For tetanus prone wounds (e.g., wounds contaminated with dirt, faeces, soil, and saliva, puncture wounds; avulsions and wounds resulting from missiles, crushing, burns, and frostbite), a booster is appropriate if the patient has not received a tetanus toxoid-containing preparation within the preceding 5 years.

Interruption of the recommended schedule with a delay between doses does not interfere with the final immunity achieved, nor does it necessitate starting the series over again, regardless of the length of time elapsed between doses.

BOOSTER DOSES OF TETANUS TOXOID BIO:

A tetanus booster dose of 0,5 ml of tetanus toxoid is given 10 years after completion of primary immunisation and every 10 years thereafter.

If a booster dose is given sooner than 10 years as part of wound management, the next routine booster should not be given for 10 years thereafter.

Method of administration with Tetanus Toxoid Bio:

Shake vigorously before withdrawing each dose to re-suspend the contents of the vial or ampoule.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

Tetanus toxoid and tetanus toxoid adsorbed should be given preferably into the anterolateral aspect of the mid-thigh in younger children or deltoid muscle in older children and adults.

Because of the risk of nerve injury, the gluteal area or areas where there may be a major nerve trunk should be avoided.

It has been suggested that the same muscle site should not be used more than once during the course of primary immunisation.

For IM injection, it is recommended that a needle at least 1 inch (2,54 cm) long be used since shorter needles may be insufficient length to penetrate muscle tissue in certain adults and older children.

The vaccine should be injected intramuscularly, preferably into deltoid muscle, with care to avoid major peripheral nerve trunks.

Before injection, the skin at the injection site should be cleansed and prepared with a suitable germicide.

After insertion of the needle, aspirate to help avoid inadvertent injection into a blood vessel.

SIDE EFFECTS:

Tetanus Toxoid Bio may have side effects.

Immune system disorders:

Frequency unknown: Severe anaphylactic reactions (with skin erythema and generalised pruritus accompanied by sweating, dizziness and dyspnoea with subsequent loss of consciousness) and immune hypersensitivity reactions (consisting of pain, oedema, erythema and local adenopathy); Influenza-like symptoms; systemic reactions such as fever, chills, malaise, arthralgia, and lymphadenopathy; granulomatous disorder.

Nervous system disorders:

Frequency unknown: Neurological complications such as convulsions, encephalopathy, headache, various mono and polyneuropathies including Guillain-Barré syndrome optic neuritis, acute transverse myelitis and brachial myelitis and neuritis.

Ear and labyrinth disorders:

Frequency unknown: Ototoxicity.

Skin and subcutaneous tissue disorders:

Frequency unknown: Local reactions such as erythema, induration, warmth, oedema and tenderness (usually self-limiting and require no therapy).
Arthus type hypersensitivity reactions or high fever may occur in patients who have very high serum antitoxin antibodies due to frequent injections of toxoid.
Urticaria, erythema multiforme or other rashes and a severe anaphylactic reaction (i.e., urticaria with swelling of the mouth, difficulty in breathing, hypotension, or shock) have. been reported.

Musculoskeletal, connective tissue and bone disorders:

Frequency unknown: Arthralgias.

Renal and urinary disorders:

Frequency unknown: Haematuria.

General disorders and administrative site conditions:

Frequency unknown: Nodule, sterile abscess formation or subcutaneous atrophy.

KNOWN SYMPTOMS OF OVER DOSAGE AND PARTICULARS OF ITS TREATMENT:

Tetanus Toxoid Bio:

In case of overdose, it is recommended that the vaccinee should be monitored in accordance with established medical practice. There is no information on the effects of overdose.

IDENTIFICATION:

Tetanus Toxoid Bio:

The vaccine is a white turbid suspension in which the mineral carrier tends to settle down slowly on keeping.

PRESENTATION:

Tetanus Toxoid Bio is available in the following:

3 ml vial contains 1 dose of 0,5 ml

5 ml vial contains10 doses of 0,5 ml

10 ml vial contains 20 doses of 0,5 ml

Each of these are made up of:

Glass vials - USP type 1, Clear and transparent; grey Bromobutyl Rubber Stoppers; green Flip off Aluminium Seals. The vial/vials are packaged in an outer cardboard carton.

STORAGE INSTRUCTIONS:

Tetanus Toxoid Bio:

Store in a refrigerator at a temperature ranging between 2 °C to 8 °C.

Do not freeze.

Discard if the vaccine has been frozen.

Should be used on or before the expiry date stated on the pack.

KEEP OUT OF THE REACH OF CHILDREN.

Incompatibilities:

Tetanus Toxoid Bio has no known incompatibilities.

HANDLING OF MULTI DOSE VIAL ONCE OPENED:

Tetanus Toxoid Bio:

Once opened, multi-dose vials can be re-used in subsequent immunisation sessions, but for up to a maximum of 28 days only provided that the following conditions are fully met:

1. The expiry date has not passed.
2. The vaccine is stored under appropriate cold chain conditions.
3. The vaccine vial septum has not been submerged in water.
4. Aseptic technique has been used to withdraw all doses.
5. The vaccine vial monitor (VVM) has not reached the discard point.

Presentations available with or without vaccine vial monitor.

	The vaccine vial monitor
	Inner square lighter than outer circle. **if the expiry date has not passed,** **USE the vaccine.**
	At a later time, inner square still lighter than outer circle. **If the expiry date has not been passed,** **USE the vaccine.**
	Discard point: Inner square matches colour of outer circle. **DO NOT use the vaccine**.
	Beyond the discard point: Inner square darker than outer ring. **DO NOT use the vaccine.**

VVM:

Vaccine Vial Monitor (VVM) is part of the label.

The colour dot which appears on the label of the vial, is a VVM.

This is a time temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed.

It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple.

Focus on the central square. Its colour will change progressively.

As long as the colour of this square is lighter than the colour of the ring, the vaccine can be used.

As soon as the colour of the central square becomes the same colour as the ring or a darker colour than the ring, then the vial should be discarded.

INSTRUCTIONS FOR USE, HANDLING AND DISPOSAL:

Tetanus Toxoid Bio:

Shake vial vigorously before withdrawal and use.

Withdraw 0,5 ml of the vaccine into separate sterile needle and syringe for each immunisation.

The vaccine should be administered shortly after withdrawal from the vial.

Unused portions of multi-dose vial may be refrigerated at between 2 °C to 8 °C

Rotate stock so that the earliest dated material is used first.

All used injection equipment should be placed in a **sharp disposal container or safety box** immediately after use. These containers are waterproof and tamper-proof and needles cannot easily pierce them.

REGISTRATION NUMBER:

52/30.2/0244

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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