1. NAME OF THE MEDICINAL PRODUCT.

- Tetanus vaccine (Adsorbed) I.P.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Pharma ingredient (API) i.e. Antigen tetanus toxoid added at the time of formulation in vaccine contains ≥ 5 Lf to ≤ 25 Lf/ single human dose, whereas the limit is ≤ 25 Lf / single human dose as per I.P.2010/2014 and WHO TRS 840.

Aluminium phosphate gel as adjuvant for tetanus toxoid (antigen) vaccine contains 0.35 mg/ human dose of Al $^{3+}$ as Aluminium phosphate gel, were as the limit of Al $^{3+}$ as Aluminium phosphate gel as per I.P. 2010 & WHO TRS 800, NMT 1.25 mg/ human dose.

Preservative as 2-Phenoxyethanol added at the time of formulation in vaccine contains 2.5 mg/single human dose, as per reference - David A. Geier et.al. The relative toxicity of compounds used as preservatives in vaccines and biologics, Med. Sci. Monit., 2010; 16(5): SR21-27)

Sodium chloride solution 0.85% is used for Isotonicity.

The final formula is as per Pharmacopoeia and WHO TRS 840.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Ingredient</th>
<th>UOM</th>
<th>Specification</th>
<th>Target Concentration</th>
<th>Used as</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Tetanus toxoid</td>
<td>Lf</td>
<td>5 – 25</td>
<td>7.5</td>
<td>Antigen/ Immunogen</td>
</tr>
<tr>
<td>2.</td>
<td>Sodium Chloride</td>
<td>%</td>
<td>0.85</td>
<td>0.85</td>
<td>Isotonicity</td>
</tr>
<tr>
<td>3.</td>
<td>2-Phenoxyethanol</td>
<td>mg</td>
<td>2.12 – 2.87</td>
<td>2.5</td>
<td>Preservative</td>
</tr>
<tr>
<td>4.</td>
<td>Aluminum Phosphate</td>
<td>mg</td>
<td>≤ 1.25</td>
<td>0.35</td>
<td>Adjuvant</td>
</tr>
<tr>
<td></td>
<td>equivalent Al$^{3+}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Final pH</td>
<td>Range</td>
<td>6.0 – 7.0</td>
<td>6.5 ± 0.3</td>
<td>---</td>
</tr>
</tbody>
</table>
3. PHARMACEUTICAL FORM

Drug substance(s)

- Bulk Purified Tetanus toxoid I.P. has been developed as per WHO TRS 840 and Indian pharmacopoeia 2010 & 2014.

Drug product

- Tetanus vaccine (Adsorbed) I.P. has been developed as per WHO TRS 840 and Indian pharmacopoeia 2010 & 2014.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

As Tetanus can occur in cases of even minor injuries it is advisable to actively immunize every person in general. With this aim in view, tetanus toxoid is desirable;

- To actively immunize all children from the age of 6 weeks onwards
- To protect infants against the risks of tetanus neonatorum by immunizing pregnant mothers
- To actively immunize civil population particularly those who are exposed to occupational risks such as road workers, athletes, agricultural workers, industrial workers etc.
- To actively immunize civil and defense personnel, home guards and police personnel.

4.2 Posology and method of administration:

The full basic course of immunization against tetanus toxoid consists of three primary doses of 0.5 ml at least four weeks apart, followed by booster doses at 18 months, 5 years, 10 years and 16 years. To maintain a high level of immunity further 0.5 ml booster doses are recommended at every feasible interval (for adults usually 5 to 10 years).

Protection of the new born against tetanus: -
For the prevention of neonatal tetanus, tetanus toxoid is recommended for immunization of women of childbearing age, and especially pregnant women. Tetanus toxoid may be safely administered during pregnancy and should be given to the mother at first contact or as early as possible in pregnancy.

Pregnancy: After completing the full basic course of 7 doses, there is no need for additional doses during pregnancy at least for the next 10 years; thereafter a single booster would be sufficient to extend immunity for another 10 years. For pregnant woman who have not had
previous immunization, at least 2 doses of tetanus toxoid at four weeks interval with the 2nd
dose at least 2 weeks before delivery should be given during pregnancy so that protective
antibody would be transferred to the infant in order to prevent neonatal tetanus.

**Vaccination of injured persons:**
For those subjects who have proof of either completing their course of primary immunization
containing tetanus toxoid and receiving a booster dose within the previous 5 years, no
additional dose of tetanus toxoid is recommended.
If more than 5 years have elapsed, and infection with tetanus because of injury or other cause
is suspected, 0.5 ml of the adsorbed tetanus toxoid should be given immediately. Where the
immunization history is inadequate 1500 IU tetanus antiserum and 0.5 ml tetanus toxoid
should be injected, with separate syringes, to different body sites. (If available, 250 units of
tetanus immune globulin (human origin) can be substituted for the tetanus antiserum).

(A note of caution: if tetanus antiserum from heterologous origin is used in prophylaxis, the
patient should be tested for sensitivity to horse serum protein prior to its administration. It is
desirable to have 1 ml of Epinephrine Hydrochloride solution (1:1000) immediately available
and the normal precautions followed when injecting antitoxins).

**Method of Administration**

The vaccine should be administered by deep intramuscular injection. Tetanus toxoid should
be injected intramuscularly into the deltoid muscle in adults and older children. If there are
indications for the use of tetanus toxoid in younger children the preferred site for
intramuscular injection is the anterolateral aspect of the upper thigh since it provides the
largest muscular area.

Only sterile needles and syringes should be used for injection. The vaccine should be shaken
well before use to make uniform suspension. Each injection of the primary immunization
series should be made into a different site.

The vaccine should be visually inspected for any foreign particulate matter and / or variation
of physical aspect prior to administration. In event of either being observed, discard the
vaccine.

**4.3 Contraindications:**

Tetanus vaccine (adsorbed) should not be given to persons who showed a severe reaction to a
previous dose of tetanus toxoid. Immunization should be deferred during the course of any
febrile illness or acute infection. A minor febrile illness such as a mild upper respiratory
infection should not preclude immunization.
4.4 Special warnings and precautions for use:

Individuals receiving corticosteroids or other immunosuppressive drugs may not develop an optimum immunologic response.

The possibility of allergic reactions in individuals sensitive to any component of the product should be borne in mind. Adrenaline injection (1:1000) must be immediately available should an acute anaphylactic reaction occur due to any component of the vaccine. The mainstay in the treatment of severe anaphylaxis is the prompt use of adrenaline, which can be lifesaving. It should be used at the first suspicion of anaphylaxis.

As with the use of all vaccines, the vaccine should remain under observation for not less than 30 minutes for possibility of occurrence of immediate or early allergic reactions. Hydrocortisone and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation.

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

Intramuscular injections should be given with great care in patients suffering from thrombocytopenia or other coagulation disorders.

A separate sterile syringe should be used for each individual patient to prevent the transmission of hepatitis or other infectious agents.

4.5 Interaction with other medicinal products and other forms of interaction:

Immunosuppressive therapies may reduce the immune response to tetanus toxoid vaccine. As with other Intramuscular injections, use with caution in patients on anticoagulant therapy.

4.6 Pregnancy and lactation:

There is no evidence that tetanus toxoid is teratogenic. Tetanus toxoid should be given to inadequately immunize pregnant women because it affords protection against neonatal tetanus. In fact, it is recommended to give the vaccine to pregnant women with greater coverage. Waiting until the second trimester is a reasonable precaution to minimize any theoretical teratogenic concern.

Tetanus toxoid does not affect the safety of mothers who are breastfeeding or their infants. Breastfeeding does not adversely affect immune response and is not a contraindication for vaccination.

4.7 Effects on ability to drive and use machines:

Tetanus toxoid is not reported to have any influence on the ability to drive and use machines.
4.8 Undesirable effects:

Mild local reactions consisting of pain, erythema, tenderness and induration at the injection site are common and may be associated with systemic reactions including mild to moderate transient fever and irritability. Persistent nodules at the site of injection have occurred following the use of an adsorbed vaccine, but this complication is unusual. There is an increased incidence of local and systemic reactions to booster doses of tetanus toxoid when given to previously immunized persons.

4.9 Overdose:

- Not Known

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

➤ Not applicable

5.2 Pharmacokinetic properties

➤ Not applicable

5.3 Preclinical safety data

➤ Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Aluminium Phosphate Gel (Adjuvant)
- 2-Phenoxyethanol (preservative)

6.2 Incompatibilities

- This product must not be mixed with other medicinal products.

6.3 Shelf life

- 2 Years
6.4 Special precautions for storage

- Store between +2°C to +8°C. Not to be frozen. Shake well before use to make uniform suspension.

6.5 Nature and contents of container

Tetanus Vaccine (Adsorbed) I.P. - Container closure system

- 1 ml Clear glass ampoule - USP Type I

6.6 Special precautions for disposal

- Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION

Cadila Healthcare Ltd
Plot Survey No. 23, 25/P, 37, 40/P, 42 to 47 Changodar road, Opp. Ramdev Masala,
Sarkhej- Bavla N.H. 8A,
Taluka: Sanand, Dist. Ahmedabad – 382 213
Phone: +91-2717- 664600

8. MARKETING AUTHORISATION NUMBER(S)

- G/28D/VAC/03 (Manufacturing License Form 28-D)

9. DATE OF FIRST AUTHORISATION

- License No. G/28D/VAC/03 in Form 28D issued dated on 05/08/2015 & Valid up to dated 04/08/2020