Translation from the Slovak language

Approved text for the decision on transfer, file No.: 2017/02477-TR

Rectangular stamp with the text:
State Institute for Drug Control
825 08 Bratislava, Kvetná 11
-7/4-
(illegible signature)

SUMMARY OF CHARACTERISTICS OF THE MEDICINE

17 July 2017

1. MEDICINE NAME

VACDITE
injection suspension
vaccine (adsorbed) against tetanus and diphtheria with reduced content of diphtheria antigen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION OF THE MEDICINE

One dose (0.5 ml) contains:

tetanus anatoxin	not less than 40 IU
diphtheria anatoxin	not less than 5 IU
adsorbed to hydrated aluminium hydroxide	not more than 0.5 mg Al^{3+}

For a full list of adjuvants, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
The vaccine is a milky, homogeneous cream-coloured suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

VACDITE is intended for the active immunization of adolescents and adults against tetanus and diphtheria according to the national vaccination schedule.

Primary vaccination
- adolescents and adults not vaccinated against tetanus and diphtheria.

Revaccination
- adults who have undergone complete primary vaccination against tetanus and diphtheria (booster dose every 10-15 years).

Vaccination against tetanus in persons with injury
In case of injury, VACDITE vaccine may be used instead of a vaccine that contains only tetanus anatoxin.

4.2 Dosage and method of administration

Dosage
Primary vaccination
For those who did not receive any diphtheria and tetanus vaccine, the primary vaccination schedule consists of three doses of the vaccine, namely one and six months after the first dose. Primary vaccination of adults against tetanus and diphtheria with three doses will be performed only if there is no credible documentation of the primary vaccination from the past.
Primary diphtheria, tetanus vaccination should be performed at intervals that are consistent with official recommendations.

In case of persons > =40 years of age who received no vaccine against diphtheria and tetanus during the last 20 years (including those who have never been vaccinated or in case of whom there is not known whether or not they have been vaccinated), one dose of VACDITE vaccine protects against tetanus and diphtheria in most cases. Two additional doses of diphtheria and tetanus vaccine will increase the response of the diphtheria and tetanus vaccine when it is administered one and six months after the first dose.
The first vaccination of adults against tetanus and diphtheria is recommended at the age of 30 years. Revaccination of adults against diphtheria and tetanus is performed with a combined vaccine every 10-15 years. If the recommended interval is exceeded, revaccination against diphtheria and tetanus should be performed always with only one dose if the primary vaccination with three doses of the tetanus vaccine is documented in the patient's medical records.
Repeated diphtheria and tetanus vaccination should be performed at the intervals that are consistent with official recommendations.
VACDITE can be used to treat the injuries suspected of tetanus infection and those who have previously been vaccinated with 3 doses of the vaccine within the primary vaccination with a vaccine containing tetanus toxoid and in case of whom an administration of adjuvant dose against diphtheria in indicated. Immunoglobulins against tetanus should be administered simultaneously, namely in accordance with official recommendations.

Children and adolescents

Primary vaccination
The vaccine is administered to adolescents who did not receive the primary vaccination against diphtheria and tetanus according to the national vaccination schedule.

Dosage in case of injury

Data on previous vaccination of the patient	Tetanus risk	
	Low	High
unvaccinated or incompletely vaccinated or uncertain information about previous vaccinations	diphtheria and tetanus vaccine or tetanus vaccine, and subsequent administration of additional doses of primary vaccination according to the scheme: 0; 1; 6 month	diphtheria and tetanus vaccine or tetanus vaccine with antitoxin (specific immunoglobulin 250/500 IU) subsequent administration of additional doses of primary vaccination according to the scheme: 0; 1; 6 month
primary vaccination or revaccination - the last dose before more than 10 - 15 years	diphtheria and tetanus vaccine or tetanus vaccine -one adjuvant dose	diphtheria and tetanus vaccine or tetanus vaccine -one adjuvant dose together with antitoxin (specific immunoglobulin 250/500 IU)
primary vaccination or revaccination - the last dose before 10 - 15 years	diphtheria and tetanus vaccine or tetanus vaccine -one adjuvant dose	diphtheria and tetanus vaccine or tetanus vaccine -one adjuvant dose
primary vaccination or revaccination - the last dose less than 5 years ago	is not required	not required if the risk of infection is particularly high, it is necessary to consider administration of

		diphtheria and tetanus vaccine or tetanus vaccine -one adjuvant dose

Method of administration
One dose of the vaccine (0.5 ml) is administered intramuscularly into the deltoid muscle or deeply subcutaneously.

4.3 Contraindications
- Hypersensitivity to the medicines or to any of the adjuvants referred to in section 6.1.
- Acute fever illness. Moderate forms of infection are not contraindications of vaccination.
- In the event of worsening a chronic disease, vaccination should be postponed until symptoms of the illness are corrected.
- Vaccination against tetanus during the last 5 years.
- Thrombocytopenia or neurological disorders after a previous dose of the vaccine
containing: T, DT, Td, D or d antigens. If there is a contraindication for diphtheria vaccine, a vaccine containing only tetanus toxoid should be administered.

If there is any contraindication for vaccination with VACDITE, it is necessary to evaluate the risk associated with vaccination as for the risk of infection.
In case of injury and detection of contraindications for use of tetanus and diphtheria vaccine (Td) or tetanus (T) vaccines, a specific anti-tetanus immunoglobulin should be given immediately.

4.4 Special warnings and precautions for use
Before vaccination, a detailed history (especially with regard to previous vaccinations and possible occurrence of adverse effects) and clinical examination should be made.
VACDITE should be administered with caution to thrombocytopenic individuals (see section 4.3) or people with blood clotting disorders, since bleeding may occur in these individuals after administration. After administration of the vaccine, the injection site should be firmly pressed (without friction) for at least two minutes.
The occurrence of convulsions in history or family history and the occurrence of adverse reaction after DTP vaccination in the family history do not constitute the contraindications.
As with all injectable vaccines, the appropriate treatment should always be available immediately for the anaphylactic reaction after administration of this vaccine.
Immunosuppressive therapy or immunodeficiency may induce a reduction in the immune response to the administration of the vaccine. Therefore, it is recommended to wait with the vaccination until completing the therapy, respectively, to make sure that the person concerned is properly protected against tetanus and diphtheria.
Thiomersal (an organic compound of mercury) has been used in the production process of this medicine and its residues are present in the final product. Therefore, hypersensitivity reactions may occur.
The vaccine should be administered with caution to persons who have had an allergic reaction or other health problems after a previous administration of the vaccine.

Do not apply intravascularly.
Make sure that the needle does not penetrate into the blood vessel.
After administration of the vaccine, the vaccinated person should be under medical supervision for 30 minutes.

4.5 Medical and other interactions
VACDITE may be administered simultaneously with other vaccines according to the national vaccination schedule, if necessary with immunoglobulins.

In case of simultaneous administration of different injections of vaccines and immunoglobulins, they should be applied at different sites and separate syringes should be used.

4.6 Fertility, pregnancy and lactation

Pregnancy
During pregnancy, only patients in the indicated cases (in the case of injuries) should be vaccinated against tetanus. In the first trimester, the vaccine may only be administered if there is a serious risk of infection. In this case, the doctor will decide on the administration. For women who received the first or second dose before their pregnancy was confirmed, vaccination must be completed during pregnancy, most likely in the second trimester of pregnancy.

Breastfeeding
Breastfeeding is not a contraindication to vaccinations with VACDITE.

4.7 Effects on ability to drive and use machines
VACDITE has no or has a negligible influence on the ability to drive and use machines.

4.8 Adverse effects
Table list of undesirable effects

For classification of adverse effects, the following convention was used:
- very often (>= 1/10)
- often (>=1/100 to <1/10)
- less often (> =1 / 1000 to <1/100)
- rare (>= 1 / 10000 to <1/1000)
- very rare (<1/10000)
- * unknown (can not be estimated from available data)

* From spontaneous reports, these undesirable effects have been reported very rarely. As these side effects are reported from a population of unknown size on a voluntary basis, it is not possible to reliably estimate their frequency or determine their causal relationship to the administration of the vaccine.

Adverse reactions observed in clinical trials and spontaneous reports after the drug has been marketed:

Class of body systems	Frequency	Adverse effects
General disorders and reactions at the site of administration	Very often > =1/10	fever nausea reaction or pain at the injection site

Possible adverse reactions (i.e. adverse reactions reported in other vaccines with the same antigenic composition as VACDITE):

Class of body systems	Frequency	Adverse effects
General disorders and reactions at the site of administration	very often > =1/10	pain at injection site redness at injection site swelling at injection site fatigue
	often: > =1/100 and < 1/10	temperature>= 37.5 ° C eruption attack of fever (shivers)

Skeletal disorders and muscle system and connective tissue	very often: > =1/10	muscle weakness
	rare: >= 1/10 000 to < 1/1 000	pain muscles
	very rare: < 1/10 000	knuckleache
Gastrointestinal tract disorders	very often: > =1/10	diarrhea
	rare: >= 1/100 and < 1/10	nausea vomiting
Nervous system disorders	very often: > =1/10	dizziness headache
	unknown (from available sources)	paresthesia syncope convulsions Guillain - Bairy syndrome brachial neuropathy
Immune system disorders	unknown (from available sources)	allergic reactions: rash urticaria pruritus angioedema anaphylactic shock Arthus phenomenon
Disorders of blood and blood lymphatic system	rare >= 1/10 000 to < 1/1 000	lymphadenopathy

Description of selected adverse reactions

Overall adverse reactions such as fever, shivers, excessive sweating, nausea usually recede within 24-48 hours.

Adverse reactions at the injection site such as redness, swelling and itching, and itching lymphatic infiltration are most common in revaccinated patients. Subcutaneous nodules - granulomas that occasionally form an aseptic abscess (1: 100,000) may occur. Granulomas that do not recede within 6 weeks may result from developing hypersensitivity to aluminium.

Report of suspicions of adverse reactions

It is important to report the suspicion of adverse reactions after medicine registration. It allows continuous monitoring of the benefit/ risk balance of the medicine. Healthcare professionals are required to report any suspicion of adverse reactions to the National Reporting Centre referred to in Annex V.

4.9 Overdosage

Overdosage is unlikely because the package contains only one dose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, tetanus vaccine, ATC code: J07AM51

Mechanism of action

VACDITE induces or strengthens active immunity against tetanus and diphtheria. The vaccine contains a reduced dose of diphtheria toxoid compared to the DTP, DTaP and DT vaccines that are intended for children under 6 years of age.
The therapeutic vaccines are tetanus toxoid (T) and diphtherial toxoid (d) adsorbed to aluminium hydroxide. Toxoids are obtained by inactivating bacterial toxins originating from the cultures of *Clostridium tetani* and *Corynebacterium diphtheriae*. Toxoids are further concentrated and purified.
Toxoids retain the antigenic properties of natural toxins but are not pathogenic. Thus, toxoids activate an immune system response, consisting of antibody production (seroconversion), and trigger the mechanism of immune memory. Immunizing properties of the vaccine are supported by aluminium hydroxide (adjuvant).
Studies of immunity levels against diphtheria and tetanus in different age groups have justified the need for revaccination, particularly in those aged 30-60 years, who belong to poorly revaccinated groups. The study results confirm safety along with the high immunogenicity of VACDITE.
An adequate level of protection of antibodies against tetanus and diphtheria is achieved only after the complete vaccination cycle (primary and booster), according to the national vaccination schedule.

5.2 Pharmacokinetic properties
Not applicable.

5.3 Preclinical safety data
Preclinical data from available published studies obtained based on usual pharmacological studies of safety, toxicity after repeated administering, genotoxicity, carcinogenic potential, reproductive toxicity and development did not reveal any special hazard for humans.

6. PHARMACEUTICAL INFORMATION

6.1 List of adjuvants

sodium chloride
water for injections

Adjuvant: see section 2 above

6.2 Incompatibility
No compatibility studies have been performed, so this medicine should not be mixed with other medicines.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Store in a refrigerator (2 ° C - 8 ° C).
Do not store in the freezer. In case of freezing, degrade the vaccine.
Keep in a vertical position.
Keep the ampoules in the original package for protection from light.

6.5 Type of package and contents of packing
0.5 ml suspension in ampoule made of type 1 glass.
Package size:
1 x 0.5 ml ampoule

Rectangular stamp with the text:
State Institute for Drug Control
825 08 Bratislava, Kvetná 11
-7/4-

15 x 0.5 ml ampoule

Not all packing sizes may be marketed.

6.6 Special precautions for disposal and other handling the medicine
After shaking, the vaccine is a milky, homogeneous suspension, creamy shade.
During storage, white sediment with clear liquid on the surface can be observed.

Before application shake the ampoule properly until a homogeneous suspension is obtained. The vaccine should be visually inspected for the presence of foreign particles and/or a change in physical appearance.
The vaccine must not be used in the event of any change in appearance.

Any unused medicine or waste material from the medicine should be disposed in accordance with the national requirements.

7. MARKETING AUTHORIZATION HOLDER

BIODRUG s.r.o.
Boženy Nemcovej 8
811 04 Bratislava
Slovak Republic

8. MARKETING AUTHORIZATION NUMBER

59/0044/17-S

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first registration: 8 March 2017

10. DATE OF TEXT REVISION

July 2017

Detailed information on this medicine is available on the website of the State Institute for Drug Control (www.sukl.sk)

Block stamp:

I certify that this document literary corresponds to the presented original ~~(certified copy)~~ consisting of 7 pages. It is the complete (~~partial)~~ copy. No (T~~he following)~~ modifications, supplements were made in the document.

In Bratislava, on 9 October 2018

Round seal with the text: JUDr. Lýdia Kliská Uhrinová - Notary – Bratislava III

/signature/

Rectangular stamp with the text:
JUDr. Magdaléna Kršková
notarial trainee
entrusted by the notary
JUDr. Lýdia Kliská Uhrinová

Round seal with the text: JUDr. Lýdia Kliská Uhrinová - Notary – Bratislava III

Round seal with the text: JUDr. Lýdia Kliská Uhrinová - Notary – Bratislava III

Round seal with the text: JUDr. Lýdia Kliská Uhrinová - Notary – Bratislava III