SCHEDULING STATUS: S2

1. NAME OF THE MEDICINE

TRUMENBA® (Meningococcal B vaccine)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0,5 mL dose contains 60 µg each *Neisseria meningitidis* serogroup B recombinant lipoprotein (rLP2086; subfamily A and B; *E.coli*)

TRUMENBA is sugar-free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection

The vaccine is a homogeneous white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TRUMENBA is indicated in individuals 10 years and older for active immunisation to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroup B.

4.2 Posology and method of administration

Dosing of TRUMENBA should be determined taking into consideration the risk of invasive meningococcal B disease by each country or region. The use of TRUMENBA should be in accordance with official recommendations.

Posology

Standard schedule for routine immunisation

2 doses (0,5 mL each) administered at 0 and 6 months.

Schedule for individuals at increased risk of invasive meningococcal disease

2 doses (0,5 mL each) administered at least 1 month apart, followed by a third dose at least 4 months after the second dose.

Booster dose

A booster dose should be considered following either dosing regimen for individuals at continued risk of invasive meningococcal disease (see section 5.1).

Special populations

Elderly

TRUMENBA has not been studied in adults older than 65 years of age.

Paediatric population

Safety and efficacy of TRUMENBA in children below the age of 10 years of age have not been established.

Method of administration

For intramuscular injection only.

The preferred site for injection is the deltoid muscle of the upper arm.

Separate injection sites and different syringes must be used if more than one vaccine is administered at the same time.

For instructions on handling TRUMENBA before administration, see section 6.6.

4.3 Contraindications

- Hypersensitivity to meningococcal group B rLP2086 vaccine or to any of the excipients of TRUMENBA listed in section 6.1.
- Severe allergic reaction (e.g., anaphylaxis) after any previous dose of TRUMENBA or to any component of this vaccine.

4.4 Special warnings and precautions for use

Do not inject intravenously, intradermally, or subcutaneously.

Appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of TRUMENBA.

Syncope (fainting) can occur in association with administration of TRUMENBA. Procedures should be in place to avoid injury from fainting.

Vaccination should be postponed in individuals suffering from an acute severe febrile illness. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

TRUMENBA should be given with caution to individuals with thrombocytopenia or any coagulation disorder or to those receiving anticoagulant therapy, unless the potential benefit clearly outweighs the risk of administration.

Persons with familial complement deficiencies (for example, C5 or C3 deficiencies) and persons receiving treatments that inhibit terminal complement activation (for example, eculizumab) are at increased risk for invasive disease caused by *Neisseria meningitidis* serogroup B, even if they develop antibodies following vaccination with TRUMENBA.

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to TRUMENBA.

Vaccination with TRUMENBA may not protect all vaccine recipients.

4.5 Interaction with other medicines and other forms of interaction

TRUMENBA can be given concomitantly with any of the following vaccines: Reduced diphtheria toxoid, tetanus toxoid, acellular pertussis and inactivated poliovirus vaccine (dTaP-IPV), quadrivalent human papillomavirus vaccine (HPV4), meningococcal serogroups A, C, Y, W conjugate vaccine (MnACYW) and tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed (Tdap).

There is no data available on the interchangeability of TRUMENBA with other meningococcal group B vaccines to complete the vaccination series.

Individuals with impaired immune responsiveness due to the use of immunosuppressive therapy (including irradiation, corticosteroids, antimetabolites, alkylating medicines, and cytotoxic medicines) may not respond optimally to active immunisation with TRUMENBA.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of TRUMENBA vaccine in pregnant women. Therefore, TRUMENBA should be used during pregnancy only if clearly needed.

Breastfeeding

It is unknown whether TRUMENBA is excreted in human milk.

TRUMENBA should only be used during breastfeeding when the possible advantages outweigh the potential risks.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to fertility in females.

4.7 Effects on ability to drive and use machines

TRUMENBA has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety of TRUMENBA was investigated in 11 completed clinical studies that enrolled a total of 20 803 subjects, of which 15 294 subjects received at least one dose of TRUMENBA administered alone or concomitantly with a licensed vaccine and 5 509 control subjects received either saline alone, a licensed vaccine alone, or saline and a licensed vaccine.

Adverse reactions following booster vaccination in 268 subjects aged 15 to 23 years were similar to adverse reactions during the primary TRUMENBA vaccination series approximately 4 years earlier.
Adverse reactions reported in clinical studies are listed below by system organ class, in decreasing order of seriousness.

Tabulated summary of adverse reactions

Frequencies are categorised as follows:

Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/
1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000), unknown (cannot be estimated from the available data).

MedDRA system organ class	**Frequency**	**Undesirable effects**
Nervous system disorders	Very common	Headache
Gastrointestinal disorders	Very common	Diarrhoea, nausea
	Common	Vomiting
Musculoskeletal and connective tissue disorders	Very common	Muscle pain (myalgia), joint pain (arthralgia)
General disorders and administration site conditions	Very common	Chills, fatigue, redness (erythema), swelling (induration) and pain at injection site
	Common	Fever ≥ 38 °C (pyrexia)

Post-marketing experience

The following are considered adverse reactions for TRUMENBA and was reported in the post-marketing experience. Because this reaction were derived from spontaneous reports, the frequency could not be determined.

System organ class	Undesirable effects
Immune system disorders	Allergic reactions
Nervous system disorders	Syncope (fainting)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Experience of overdose is limited. Overdose with TRUMENBA is unlikely because it is provided in a prefilled syringe.

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 30. 2 (antigens)

Mechanism of action

Bivalent rLP2086 is a vaccine composed of two recombinant lipidated factor H binding proteins (fHBPs), one each from subfamily A and B, which stimulate production of broadly protective bactericidal antibodies, necessary for antibody-dependent complement-mediated killing of epidemiologically diverse serogroup B meningococci and consequent protection against invasive meningococcal B disease. fHBPs segregate into two immunologically distinct subfamilies, A and B, and > 95 % of serogroup B strains express fHBPs from either subfamily. This process is measured *in vitro* with serum bactericidal assay (SBA) using human

complement (hSBA) for serogroup B, which is the accepted correlate of protection from meningococcal B disease.

Clinical efficacy

The efficacy of bivalent rLP2086 has not been evaluated through clinical trials but has been inferred by demonstrating the induction of serum bactericidal antibody responses to four meningococcal serogroup B test strains, two each expressing fHBP variants from either subfamily A or B, which are representative of prevalent strains causing invasive disease in Europe. hSBA titres ≥ 1:8 or ≥ 1:16, depending on the strain are considered protective, which is higher than the accepted correlate of protection titre ≥ 1:4.

Immunogenicity

Following vaccination with two or three doses of bivalent rLP2086 in individuals 11 to 18 years of age in Europe on a 0-, 1-, 6-month; 0-, 2-, 6-month or 0-, 6-month schedule or following three vaccinations in individuals 10 to 25 years of age globally on a 0-, 2-, 6-month schedule, protective titres against 4 hSBA test strains were achieved in a high proportion of individuals after the final dose, ranging from 77,5 % to 99,5 %, depending on the test strain. A composite response (protective hSBA titres against all 4 primary test strains) was achieved by 73,5 % of individuals vaccinated according to the 0-, 6-month two dose schedule and by 81,7 % to 84,9 % of individuals vaccinated according to the 0-, 1-, 6-month and 0-, 2-, 6-month 3 dose schedules. Additionally, when serum obtained after the third vaccination in the same individuals from the 10 to 25 years of age group was tested against 10 additional test strains, each expressing different fHBP variants, protective titres range from 71,3 % to 99,3 %, which along with the composite responses, confirms broad protection encompassing diverse heterologous serogroup B strains.

Concomitant vaccine administration

Clinical studies also demonstrated that bivalent rLP2086 may be co-administered with meningococcal serogroups A, C, Y, W conjugate vaccine (MCV4) and tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed (Tdap) in adolescents 10 to < 13 years of age, quadrivalent human papillomavirus

vaccine (HPV4) in adolescents 11 to < 18 years of age, and reduced diphtheria toxoid, tetanus toxoid, acellular pertussis and inactivated poliovirus vaccine (dTap-IPV) in adolescents 11 to < 19 years of age and that immunogenicity remains unchanged (non-inferiority criteria met for all antigens) by concomitant administration with these vaccines when compared to results with each vaccine given alone.

Persistence of immunity and response to booster vaccination

Among adolescents completing a primary vaccination series on a 0-, 1-, 6-month; 0-, 2-, 6-month; or 0-, 6-month schedule, the proportion of individuals with protective titres declines by month 12 and remains relatively steady thereafter through four years following completion of the primary series. A booster dose administered approximately 4 years following completion of the primary series results in a memory response with equal or higher proportions of individuals with protective titres than 1 month after completion of the primary series.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

aluminium phosphate

histidine

polysorbate 80

sodium chloride

water for injection

6.2 Incompatibilities

Do not mix TRUMENBA with other vaccines or medicines in the same syringe.

6.3 Shelf life

48 months

6.4 Special precautions for storage

Store in a refrigerator (2 °C - 8 °C).

Syringes should be stored in the refrigerator horizontally to minimise the re-dispersion time.

Do not freeze. Discard if the vaccine has been frozen.

6.5 Nature and contents of container

TRUMENBA 0,5 mL suspension is available in a pre-filled syringe (Type I glass) with plastic Luer Lok adapter, chlorobutyl rubber plunger stopper, and a synthetic isoprene bromobutyl rubber tip cap with a plastic rigid tip cap cover with or without a needle. The tip cap and rubber plunger of the pre-filled syringe are not made with natural rubber latex.

Pack sizes of 1, 5, and 10 pre-filled syringes, with or without needles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

During storage, a white deposit and clear supernatant may be observed in the pre-filled syringe containing the suspension.

TRUMENBA should be shaken vigorously to ensure that a homogeneous white suspension is obtained.

Do not use TRUMENBA if it cannot be re-suspended.

TRUMENBA should be visually inspected for particulate matter and discoloration prior to administration. TRUMENBA should not be used if particulate matter or discoloration is found.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBER

52/30.2/0987

9. DATE OF FIRST AUTHORISATION

09 December 2019

10. DATE OF REVISION OF THE TEXT

26 November 2020