SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

TYPHIM Vi solution for injection

Vi capsular polysaccharide typhoid fever vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0,5 mL immunising dose contains:

Purified Vi capsular polysaccharide of *Salmonella typhi* (Ty2 strain) – 25 µg

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.

A clear, colourless liquid vaccine.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TYPHIM Vi is indicated for active immunisation against typhoid fever caused by *Salmonella enterica serovar Typhi* (*S. typhi*) in adults or children 2 years of age or older.

TYPHIM Vi is intended both for the inhabitants of endemic zones and for persons travelling to endemic areas, migrants, health care workers, catering and food industry professionals and military personnel.

4.2 Posology and method of administration

Posology

The recommended dose for adults and children is a single injection of 0,5 mL.

The preferred route of administration for this vaccine is intramuscular although it may also be given

subcutaneously.

Revaccination should be carried out every 3 years if the subject is still exposed to the risk.

4.3 Contraindications

Known systemic hypersensitivity reaction to any component of TYPHIM Vi or a life-threatening reaction after previous administration of TYPHIM Vi or a vaccine containing the same substances (see section 6.1).

Vaccination must be postponed in case of febrile or acute diseases.

4.4 Special warnings and precautions for use

This vaccine provides protection against the risk of infection related to *Salmonella typhi,* but gives no protection against *Salmonella paratyphi A* or *B* or against non-typhoidal Salmonellae.

As each dose may contain traces of formaldehyde and casein, which are used during vaccine production, caution should be exercised when the vaccine is administered to subjects with hypersensitivity to these ingredients.

Immunosuppressive treatment or immunodeficiency may reduce the immunogenicity of TYPHIM Vi. It is recommended to postpone the vaccination until the end of the disease treatment. Vaccination of subjects with chronic immunodeficiency such as HIV infection is recommended even if the antibody response is limited.

As with other polysaccharide vaccines, the antibody response may be inadequate in children under 2 years of age.

Vaccination should occur at least 2 weeks prior to potential exposure to infection with *Salmonella typhi.*

Do not administer by intravascular injection: ensure that the needle does not penetrate a blood vessel.

As with all injectable vaccines, the vaccine must be administered with caution to patients with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these patients.

Prior to administration of any dose of TYPHIM Vi, the parent or guardian of the recipient or the adult recipient himself must be asked about his personal history, family history, and recent health status, including immunisation history, current health status and any adverse event after previous immunisations. In subjects who have a history of serious or severe reaction within 48 hours of a previous injection with a vaccine containing similar components, the course of the vaccination must be carefully considered.

Before the injection of any biological product, the person responsible for administration must take all precautions known for the prevention of allergic or any other reactions.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following administration of the vaccine.

As a precautionary measure, epinephrine [adrenaline] 1:1 000 injection and a means for its administration should be available in case of unexpected anaphylactic or serious allergic reactions.

Syncope (fainting) may occur following, or even before any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent falling injury and manage syncopal reactions.

4.5 Interaction with other medicines and other forms of interaction

Separate injection sites must be used in case of concomitant administration.
TYPHIM Vi may be administered during the same vaccination session with other common vaccines (yellow fever, diphtheria, tetanus, poliomyelitis, rabies prepared on Vero cells, meningitis A + C,

hepatitis A and hepatitis B).

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal reproduction studies have not been conducted with TYPHIM Vi.

Data on the use of this vaccine in pregnant woman are limited. Therefore, the administration of the vaccine during pregnancy is not recommended. TYPHIM Vi should be given to pregnant women only if clearly needed and following an assessment of the risks and benefits.

Lactation

It is not known whether TYPHIM Vi is excreted in breast milk. Caution must be exercised when administered to nursing mothers.

4.7 Effects on ability to drive and use machines

No studies of the effect of TYPHIM Vi on the ability to drive and use machines have been performed.

4.8 Undesirable effects

In clinical studies, more than 15 000 subjects were involved and received TYPHIM Vi either in a single injection or as a second injection.

The most frequently reported adverse reactions, in all age groups, after administration of TYPHIM Vi were injection site pain. In adults from 18 years of age, myalgia and fatigue were the most frequently reported systemic reactions. In children and adolescents (from 2 to 17 years of age), myalgia and headache were the most frequently reported systemic reactions.

The adverse reactions observed during clinical trials were generally of mild to moderate intensity and appeared within 3 days after vaccination. Most reactions resolved spontaneously within 1 to 3 days after onset.

The table below summarises the frequencies of subjects experiencing at least one solicited adverse reaction that were recorded within 7 days following vaccination in 1 435 adults and 97 children and adolescents from 2 to 17 years of age.

Frequencies are reported as:

Very common: ≥ 1/10 (≥ 10 %)

Common: ≥ 1/100 and < 1/10 (≥ 1 % and < 10 %)

Uncommon: ≥ 1/1 000 and < 1/100 (≥ 0,1 % and < 1 %)

Rare: ≥ 1/10 000 and < 1/1 000 (≥ 0,01 % and < 0,1 %)

Very rare: < 1/10 000 (< 0,01 %)

Subjects experiencing at least one:	**Children and adolescents** 2 – 17 years (N=97)	**Adults** ≥ 18 years (N=1 435)
Adverse Reactions	% † - Frequency	% † - Frequency
Nervous system disorders		
Headache	13,5 % - Very common	7,8 % - Common
Musculoskeletal and connective tissue disorders		
Myalgia	14,6 % - Very common	47,1 % - Very common
General disorders and administration site condition		
Injection site pain	52,6 % - Very common	75,6 % - Very Common
Injection site erythema	14,4 % -Very common	7,7 % - Common
Injection site swelling/oedema/ induration	16,5 % - Very common	6,0 % - Common
Malaise	6,3 % - Common	13,3 % - Very Common
Fever	1,0 % - Common	0 %
Fatigue/asthenia	4,8 % - Common	25,0 % - Very Common

N: Number of subjects analysed according to safety analyses set.

†: For each reaction, the frequency has been defined by the number of subjects experiencing the

reaction divided by the number of subjects with available data

The table below summarises the frequencies of subjects experiencing at least one unsolicited adverse reaction that were recorded within 28 days following vaccination in 1 435 adults and 97 children and adolescents from 2 to 17 years of age.

Subjects experiencing at least one:	**Children and adolescents** 2 - 17 years (N=97)	**Adults** ≥ 18 years (N=1 435)
Adverse Reactions	% † - Frequency	% † - Frequency
General disorders and administration site condition		
Injection site pruritus	0 %	0,1 % - Uncommon

N: Number of subjects analysed according to safety analyses set.

†: For each reaction, the frequency has been defined by the number of subjects experiencing the reaction divided by the number of subjects with available data

Data from post-marketing experience:

Based on spontaneous reporting, the following additional adverse events have been reported during the commercial use of TYPHIM Vi. These events have been very rarely reported, however exact incidence rates cannot be precisely calculated.

Immune system disorders

Anaphylactic/anaphylactoid reactions, including shock, serum sickness

Nervous system disorders

Vasovagal syncope

Respiratory, thoracic and mediastinal disorders

Asthma

Gastrointestinal disorders

Nausea, vomiting, diarrhoea, abdominal pain

Skin and subcutaneous tissue disorders

Allergic type reactions such as pruritus, rash, urticaria

Musculoskeletal and connective tissue disorders

Arthralgia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of TYPHIM Vi is important. It allows continued monitoring of the benefit/risk balance of TYPHIM Vi. Health care providers are asked to report any suspected adverse reactions to:

- The Pharmacovigilance Unit at Sanofi: za.drugsafety@sanofi.com (email) or 011 256-3700 (tel), or
- SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Not documented.

5. PHARMACOLOGICAL PROPERTIES

Category and class: A 30.2 Antigens

Pharmacotherapeutic group: Typhoid vaccines, ATC code: J07AP03

5.1 Pharmacodynamic properties

This vaccine contains purified Vi capsular polysaccharide of *Salmonella typhi* (Ty2 strain). Immunity appears within 1 to 3 weeks after injection and lasts around 3 years.

A double-blind, randomised, controlled efficacy clinical trial was conducted in a highly endemic area in Nepal, in both paediatric and adult populations. A total of 3 457 subjects received TYPHIM Vi. The level of protection conferred by a single dose of the vaccine was 74 % against blood culture-confirmed cases of typhoid fever throughout the 20 months of active surveillance when compared with the control group.

Seroconversion rate (defined as 4-fold rise of anti-Vi antibody levels) was collected in 19 clinical trials. These trials were conducted in endemic and non-endemic areas in both paediatric and adult populations representing a total of 2 137 evaluable subjects. In adult population, seroconversion rate ranged from 62,5 % to 100 % four weeks after a single injection, with similar magnitude of anti-Vi immune response in non-endemic areas compared to endemic areas.

Anti-Vi antibody persistence depends on endemicity, with a trend for better persistence in endemic areas (documented up to 10 years in 83 children at levels equal or above serological correlate of protection of 1 µg/mL). In non-endemic areas, anti-Vi antibodies persist for 2 to 3 years. Revaccination should be carried out with an interval of not more than 3 years if the subject is still exposed to the risk.

Paediatric population

In a double-blind, randomised, controlled efficacy clinical trial conducted in a highly endemic area in South Africa, a total of 5 692 subjects from 5 to 15 years of age received TYPHIM Vi. The level of protection conferred by a single dose of the vaccine was 55 % against blood culture- confirmed cases of typhoid fever during the 3-year follow-up period when compared with the control group.

Immunogenicity was assessed in both endemic and non-endemic areas in paediatric population aged from 2 to 17 years. In 9 clinical trials representing a total of 733 evaluable children, four weeks after a single injection of TYPHIM Vi, seroconversion rate ranged from 67 % to 100 %, demonstrating similar magnitude of anti-Vi immune response to what was documented with adult participants.

5.2 Pharmacokinetic properties

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenol (preservative)

Isotonic buffer solution:

Disodium phosphate dihydrate

Sodium dihydrogen phosphate dihydrate

Sodium chloride

Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

36 months.

Store between +2 °C and +8 °C.

6.4 Special precautions for storage

Protect from light.

Shake well before use.

DO NOT FREEZE.

6.5 Nature and contents of container

1 x single dose pre-filled syringe (type 1 neutral glass) with a black elastomer plunger stopper (chlorobromobutyl or chlorobutyl or bromobutyl) and black needle shield covering a 25-gauge needle.

6.6 Special precautions for disposal and other handling

The vaccine should be visually inspected before administration for discolouration or any particulate matter.

For needle free syringes, the needle should be pushed firmly on to the end of the pre-filled syringe and rotated through 90 degrees.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

sanofi-aventis south africa (pty) ltd

2 Bond Street

Grand Central Ext. 1

Midrand 1685

8. REGISTRATION NUMBER

29/30.1/0091

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20 February 1996

10. DATE OF REVISION OF THE TEXT

27 March 2024