ACTACEL®

Act-HIB® Reconstituted with TRIPACEL®

Hemophilus B Conjugate Vaccine (Tetanus Protein Conjugate)
Component Pertussis Vaccine Combined with Diphtheria and Tetanus Toxoids Adsorbed

Intramuscular injection
Reconstituted product for injection

Dosage Forms

ACTacel® (Act-HIB® reconstituted with TRIPACEL®) is supplied as a sterile lyophilized white powder in a single dose vial for reconstitution with a sterile, uniform, cloudy, white to off-white suspension provided in a separate single dose vial. After reconstitution, ACTacel® is a sterile, uniform, cloudy, white to off-white suspension.

COMPOSITION
1 dose = about 0.5 mL.

Active Ingredients

Purified Polyribosylribitol Phosphate Capsular Polysaccharide (PRP) of *Haemophilus influenzae* type b covalently bound to 20 µg of Tetanus Protein	10 µg
Diphtheria Toxoid	15 Lf (≥30 IU)
Tetanus Toxoid	5 Lf (≥40 IU)
Acellular Pertussis	
Pertussis Toxoid (PT)	10 µg
Filamentous Haemagglutinin (FHA)	5 µg
Pertactin (PRN)	3 µg
Fimbriae Types 2 and 3 (FIM)	5 µg

Other Ingredients:

Excipients:	
Aluminum Phosphate (adjuvant) (Aluminum 0.33 mg)	1.5 mg
2-phenoxyethanol	0.6% v/v
Sucrose	42.5 mg
Tris (Hydroxymethyl) Aminomethane	0.6 mg
Manufacturing Process Residuals:	
Formaldehyde and glutaraldehyde are present in trace amounts.	

INDICATIONS

Primary vaccination of infants at or above the age of 2 months up to their 6 birthday against diphtheria, tetanus and pertussis and invasive Heamophilus influenzae type b infections.
Currently, Haemophilus b conjugate vaccines are not recommended for infants younger than 2 months of age.
Children who have had invasive *H. influenzae* type b (Hib) infection diphtheria, tetanus or pertussis should still be immunized since these clinical infections do not always confer immunity.
Human Immunodeficiency Virus (HIV)-infected persons, both asymptomatic and symptomatic, should be immunized against *H. influenza* type b, diphtheria, tetanus and pertussis according to standard schedules.
ACTacel® is not to be used for the treatment of diseases caused by *H. influenzae* type b, *Corynebacterium diphtheriae, Clostridium tetani or Bordetella pertussis* infections.

CONTRAINDICATIONS
Allergy to any component of the vaccine (see components listed in composition), or an allergic or anaphylactic reaction to a previous dose of the vaccine is a contraindication to vaccination. Because of uncertainty as to which component of the vaccine may be responsible, none of the components should be administered. Alternatively, such persons may be referred to an allergist for evaluation if further immunizations are considered.

Neurological Disorders

The following events are contraindications to administration of any pertussis-containing vaccine, including ACTacel®:
Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures) within 7 days of a previous dose of a pertussis-containing vaccine that is not attributable to another identifiable cause.

Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, progressive encephalopathy. Pertussis vaccine should not be administered to persons with such conditions until a treatment regimen has been established and the condition has stabilized

SPECIAL WARNINGS AND PRECAUTIONS

General

Before administration of ACTacel®, health-care providers should inform the parent or guardian of the benefits and risks of immunization, inquire about the recent health status of the recipient, review the recipient's history concerning possible hypersensitivity to the vaccine or similar vaccine, previous immunization history, the presence of any contraindications to immunization and comply with any local requirements with respect

to information to be provided to the parent or guardian before immunization and the importance of completing the immunization series.
It is extremely important that the parent or guardian be questioned concerning any signs or symptoms of an adverse reaction after a previous dose of vaccine. (See **Error! Reference source not found.** and **Error! Reference source not found.**.)
The rates and severity of adverse events in recipients of tetanus toxoid are influenced by the number of prior doses and the level of pre-existing antitoxins.
As with any vaccine, ACTacel® may not protect 100% of vaccinated individuals.

Vaccines that contain Hib antigen do not provide protection against infections with other types of *H. influenzae,* or against meningitis of other origin.
Under no circumstances can the tetanus protein contained in conjugate vaccines containing tetanus toxoid as protein carrier be used to replace the usual tetanus vaccination.
Edematous reaction affecting one or both lower limbs has occurred following vaccination with *Haemophilus influenzae* type b-containing vaccines. When this reaction occurs, it does so mainly after primary injections and is observed within the first few hours following vaccination. Associated symptoms may include cyanosis, redness, transient purpura and severe crying. In reported cases, all events resolved spontaneously without sequelae within 24 hours.
Inflammatory cellulitis without bacterial infection, drowsiness and high fever (>40.5º) have been associated with similar antigen containing vaccines.
Administration Route-Related Precautions: Do not administer ACTacel® by intravascular injection; ensure that the needle does not penetrate a blood vessel.
Intradermal or subcutaneous routes of administration are not to be utilized.
ACTacel® should not be administered into the buttocks.
Febrile or Acute Disease: Vaccination should be postponed in cases of acute or febrile disease. However, a disease with low-grade fever should not usually be a reason to postpone vaccination.
If any of the following events occur within the specified period after administration of a whole-cell pertussis vaccine or a vaccine containing an acellular pertussis component, the decision to administer ACTacel® should be based on careful consideration of potential benefits and possible risks.

- Temperature of ≥40.5°C (105°F) within 48 hours, not attributable to another identifiable cause;
- Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours;
- Persistent crying lasting ≥3 hours within 48 hours;
- Convulsions with or without fever within 3 days.

Hematologic

Because any intramuscular injection can cause an injection site hematoma in persons with any bleeding disorders, such as hemophilia or thrombocytopenia, or in persons on anticoagulant therapy, intramuscular injections with ACTacel® should not be administered to such persons unless the potential benefits outweigh the risk of administration. If the decision is made to administer any product by intramuscular injection to such persons, it should be given with caution, with steps taken to avoid the risk of hematoma formation following injection.

Immune

The possibility of allergic reactions in persons sensitive to components of the vaccine should be evaluated. Hypersensitivity reactions may occur following the use of ACTacel® even in persons with no prior history of hypersensitivity to the product components. Cases of allergic or anaphylactic reaction have been reported after receiving some preparations containing diphtheria and tetanus toxoids and/or pertussis antigens.

Epinephrine hydrochloride solution (1:1,000) and other appropriate agents should be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs. Health-care providers should be familiar with current recommendations for the initial management of anaphylaxis in non-hospital settings, including proper airway management.
Immunocompromised persons (whether from disease or treatment) may not obtain the expected immune response. If possible, consideration should be given to delaying vaccination until after the completion of any immunosuppressive treatment. Nevertheless, vaccination of persons with chronic immunodeficiency such as HIV infection is recommended even if the antibody response might be limited.
Anaphylactic reaction, hives and urticaria have been associated with similar antigen containing vaccines.

Neurologic

A review by the US Institute of Medicine (IOM) found evidence for a causal relationship between tetanus toxoid and both brachial neuritis and Guillain-Barré syndrome (GBS). If GBS occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give ACTacel® or any vaccine containing tetanus toxoid should be based on careful consideration of potential benefits and possible risks.
For infants or children at higher risk for seizures than the general population, an appropriate antipyretic may be administered (in the dosage recommended in its prescribing information) at the time of vaccination with a vaccine containing an acellular pertussis component (including ACTacel®) and for the following 24 hours, to reduce the possibility of post-vaccination fever.
Hypotonic-hyporesponsive episodes (HHEs) rarely follow vaccination with whole-cell pertussis-containing DTP vaccines and occur even less commonly after acellular

pertussis-containing DTP vaccines and DT vaccines. A history of HHEs is not a contraindication to the use of acellular pertussis vaccines but recommends caution in these cases.
Febrile convulsions, convulsions (partial seizures, grand mal convulsion), polyradiculopathies and demyelinating diseases (including Guillain-Barré syndrome) have been associated with similar antigen containing vaccines

Pregnant Women.
This vaccine is not indicated for persons 6 years of age and older.

Nursing Women

This vaccine is not indicated for persons 6 years of age and older.

Drug Interactions
Immunosuppressive treatments may interfere with the development of the expected immune response. (See **Error! Reference source not found.**.)

Concomitant Vaccine Administration

Administering the most widely used live and inactivated vaccines during the same patient visit has produced seroconversion rates and rates of adverse reactions similar to those observed when the vaccines are administered separately. Vaccines administered simultaneously should be given using separate syringes at separate sites. Simultaneous administration is suggested, particularly when there is concern that a person may not return for subsequent vaccination. Simultaneous administration of childhood vaccines such as ACTacel®, MMR, varicella, pneumococcal conjugate and hepatitis B vaccines, is encouraged for children who are at the recommended age to receive these vaccines and for whom no contraindications exist.
ACTacel® should not be mixed in the same syringe with other parenterals.

Vaccine-Laboratory Test Interactions

Antigenuria has been detected in some instances following administration of a vaccine containing Hib antigen. Therefore, urine antigen detection may not have definite diagnostic value in suspected Haemophilus influenzae type b disease within two weeks of immunization

DOSAGE AND ADMINISTRATION

Recommended Dose

1 dose = 0.5 mL
The routine immunization schedule with ACTacel® should follow local recommendations.

As a guide, ACTacel® may be given as a 3-dose immunization series, with an interval of 2 months between each dose, followed by a fourth dose administered approximately 6 to 12 months after the third dose. Whenever feasible, ACTacel® should be used for all 4 doses in the vaccination series as there are no clinical data to support the use of ACTacel® with any other licensed acellular pertussis combination vaccine in a mixed sequence.
Premature infants whose clinical condition is satisfactory should be immunized with full doses of vaccine at the same chronological age and according to the same schedule as full-term infants regardless of birth weight.
Fractional doses (<0.5 mL) should not be given. The effect of fractional doses on safety and efficacy has not been determined.
ACTacel® should not be administered to persons less than 2 months of age or to persons 6 years of age or older. (See **Error! Reference source not found.**.)

Administration

Inspect for extraneous particulate matter and/or discolouration before use. If these conditions exist, the product should not be administered.
Reconstitution of Freeze-Dried Product and Withdrawal from Stoppered Vial
Reconstitute Act-HIB® with the TRIPACEL® vaccine.
Cleanse the TRIPACEL® and Act-HIB® vial stoppers with a suitable germicide before reconstitution. Do not remove from either vial, the stoppers or the metal seals holding them in place. Thoroughly but gently shake the vial of TRIPACEL®, withdraw the entire contents of the liquid vaccine and inject slowly into the vial of lyophilized Act-HIB®. Shake the vial now containing ACTacel® thoroughly until a uniform, cloudy, white to off-white suspension results. Withdraw the total volume of reconstituted, combined vaccine. ACTacel® should be used immediately after reconstitution.
Aseptic technique must be used. Use a separate sterile needle and syringe, or a sterile disposable unit, for each individual patient to prevent disease transmission. Needles should not be recapped, but should be disposed of according to biohazard waste guidelines.
Before injection, the skin over the site to be injected should be cleansed with a suitable germicide.
Administer the total volume of reconstituted vaccine **intramuscularly** (I.M.). In infants younger than 1 year, the anterolateral aspect of the thigh provides the largest muscle and is the preferred site of injection. In older children, the deltoid muscle is usually large enough for injection.

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for

identifying the adverse events that appear to be related to vaccine use and for approximating rates of those events.
The frequency of solicited systemic and injection site adverse reactions observed within 48 to 72 hours after any dose of ACTacel® given at 2, 4, 6 and 17 to 21 months of age in clinical trials in Canada and Taiwan is presented below (N = 241).
Very Common: ≥10%

Common: ≥1% and <10%

General Disorders and Administration Site Conditions

Very Common: Injection site tenderness, swelling, redness, fever, fussiness (irritability), less active (reduced activity), eating less (anorexia), crying

Gastrointestinal Disorders

Very Common: Diarrhea
Common: Vomiting

Data from Post-Marketing Experience

The following additional adverse events have been spontaneously reported during the post-marketing use of ACTacel® worldwide. Because these events are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Psychiatric Disorders

Irritability, screaming, prolonged or unusual high-pitched crying, restlessness

Nervous System Disorders

Hypotonic-hyporesponsive episodes, hypotonia, encephalopathy,

Vascular Disorders

Pallor

Gastro-intestinal Disorders

Nausea

Skin and Subcutaneous Tissue Disorders

Erythema, rash, pruritus

General Disorders and Administration Site Conditions

Injection site reactions, including pain and inflammation; large injection site reactions, including limb swelling which may extend from the injection site beyond one or both joints.
Somnolence, sleepiness

STORAGE AND SHELF LIFE

Store at 2° to 8°C (in a refrigerator). **Do not freeze**. Discard product if exposed to freezing.
The vaccine should be used immediately after reconstitution.
Do not use after expiration date.

Packaging

ACTacel® (Act-HIB® reconstituted with TRIPACEL®) is supplied in a 3 mL single dose vial and a 2 mL single dose vial (diluent). The vials are made of type 1 glass. The stoppers of the vials do not contain latex (natural rubber).
ACTacel® is available in a package of:

1 single dose vial of Act-HIB® and 1 single dose vial of TRIPACEL® (diluent)
5 single dose vials of Act-HIB® and 5 single dose vials of TRIPACEL® (diluent)
Not all packages may be marketed

Manufacturer:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

License holder: Medici Medical Ltd, 2 Hapnina st., Raanana 43000

The format of this leaflet was determined by the Ministry of Health and its content was checked and approved on October 2010.