Public Assessment Report
(Variation, New Indication)
ADACEL

INFORMASI PRODUK

Nama obat	:	Adacel
Bentuk sediaan	:	Injeksi
Zat aktif	:	Tiap 0,5 mL mengandung : Tetanus toxoid 5 Lf Diptheria toxoid 2 Lf Pertusis toxoid 2,5 Lf Filamentous Haemagglutinin 5 mcg Fimbriae types 2 and 3 5 mcg Pertactin 3 mcg
Kemasan	:	Dus, 1 vial @ 0,5 mL (1 dosis)
Pendaftar	:	PT Aventis Pharma
Produsen	:	Sanofi Pasteur Ltd, Ontario, Kanada
Kategori Registrasi	:	Produk Biologi yang sudah terdaftar dengan indikasi baru
Indikasi yang diajukan:	:	*ADACEL® is indicated for active booster immunization for the prevention of tetanus, diphtheria and pertussis (whooping cough) in person 4 to 6 years of age and 10 years or older.* *ADACEL® is indicated for passive protection against pertussis in early infancy following maternal immunization during pregnancy (see sections DOSAGE AND ADMINISTRATION, WARNING AND PRECAUTION, and PREGNANT WOMEN).* *ADACEL® should be used in accordance with official recommendations.* *In accordance with local recommendations, Adacel may be considered as an alternative for the fifth dose of tetanus, diphtheria and acellular pertussis vaccine (DTaP) in children 4 through 6 years of age, concomitantly administered with inactivated Poliomyelitis Vaccine (IPV) at separate sites to complete the vaccination series of this age when indicated.* *ADACEL® is not to be used for the treatment of disease caused by Bordetella pertussis, Corynebacteriuyn diphtheriae or Clostridium tetani infections.* *ADACEL® is not to be used for the treatment of disease caused ny Bordetella pertussis, Corynebacteriuyn diphtheriae or Clostridium tetani infections.* *PEDIATRICS* *ADACEL® is not indicated for immunization of children below the age of 4 years.* *TETANUS PROPHYLAXIS IN WOUND MANAGEMENT The need for active immunization with a tetanus toxoid-containing preparation such as Td adsorbed vaccine or Adacel, with or without passive immunization with tetanus Immune Globulin.*
Posologi yang diajukan:	:	*Recommended Dose* *ADACEL® (0.5 mL) should be administered as a booster injection by the intramuscular route.* *Re-dosing with ADACEL® can be used to boost immunity to diphtheria, tetanus and pertussis at 5 to 10 years intervals.* *The preferred site is into the deltoid muscle. Fractional doses (doses<0,5 mL) should not be given.*

ADACEL® may be administered to pregnant women during the second or third trimester to provide passive protection of infants against pertussis (see sections INDICATION, DOSAGE AND ADMINISTRATION, WARNING AND PRECAUTION and PREGNANT WOMEN).

The effect of fractional doses on the safety and efficacy has not been determined.

Table 2: NACI Recommended Use of Immunizing Agents in Wound Management.

History of Tetanus Immunization	*Clean, Minor Wounds*		*All Other Wounds*	
	*Td**	*TIG † (Human)*	*Td**	*TIG † (Human)*
Uncertain or < 3 doses of an immunization series ‡	*Yes*	*No*	*Yes*	*Yes*
≥ 3 doses receiverd in an immunization series ‡	*No§*	*No*	*No***	*No††*

**Adult-type tetanus and diphtheria toxoids.*

†Tetanus immune globulin, given at a separate site from the Td.

‡ Primary immunization is at least 3 doses at age appropriate intervals §Yes, if >10 years since last booster.

***Yes, if >5 years since last booster*

††Yes, if individuals are known to have a significant humoral immune deficiency state (e.g. HIV gammaglobulinemia) since immune response to tetanus toxoid may be suboptimal.

A thorough attempt must be made to determine whether a patient has completed primary immunization. Persons who have completed primary immunization against tetanus and who sustain wounds that are minor and uncontaminated, should receive a booster dose of a tetanus toxoid-containing preparation if they have not received tetanus toxoid within the preceding 10 years. For tetanus-prone wounds (e.g., wounds contaminated with dirt, feces, soil and saliva, puncture wounds, avulsions and wounds resulting from missiles, crushing, burns or frostbite), a booster is appropriate if the patient has not received a tetanus toxoid-containing preparation within the preceding 5 years.

PENGANTAR

- Vaksin Adacel merupakan vaksin Diphtheria-Tetanus-Pertussis (acellular) dengan 5 komponen pertusis PT, FHA, PRN, FIM-2, FIM-3.
- Produk sudah disetujui di Indonesia, melakukan variasi perubahan indikasi dan posologi untuk pencegahan PERTUSIS di bayi baru lahir dengan melakukan vaksinasi pada ibu hamil.
- The Advisory Committee on Immunization Practices (ACIP) dan WHO merekomendasikan boosters Tdap pada ibu hamil trimester kedua atau ketiga, lebih baik 15 hari sebelum akhir kehamilan, untuk mencegah kejadian/kematian pada bayi baru lahir akibat pertussis sebelum

menerima imunisasi primer (Centers for Disease Control and Prevention (CDC), 2013; WHO, 2015).

ASPEK KHASIAT DAN KEAMANAN

Studi Klinik

Sebanyak 35 artikel dimasukkan dalam pengajuan berbasis literatur dengan keterangan sebagai berikut:

- 3 publikasi dan 1 artikel di media melaporkan uji klinis *randomized* yang mendukung keamanan dan imunogenisitas Tdap pada Ibu hamil dan bayinya saat lahir melalui seri vaksinasi pada bayi atau dosis booster
- 18 publikasi mendukung keamanan, 12 di antaranya merupakan studi observasional dengan penggunaan merek vaksin Tdap yang diketahui dan 6 merupakan studi observasional yang merek vaksin Tdap tidak disebutkan
- 9 publikasi yang mendukung imunogenesitas:
  - 1 publikasi melaporkan studi observasional yang mendukung imunogenisitas vaksin Tdap pada kehamilan pada Ibu dan bayi saat lahir melalui dosis booster bayi.
  - 4 publikasi melaporkan studi observasional yang mendukung imunogenisitas vaksin Tdap pada kehamilan pada Ibu dan bayinya saat lahir
  - 1 publikasi melaporkan dosis booster bayi dari uji klinis *randomized* yang mendukung imunogenisitas vaksin Tdap pada bayi dari Ibu yang menerima Tdap selama kehamilan
  - 3 publikasi melaporkan studi observasional yang mendukung imunogenisitas Tdap pada bayi dari Ibu yang menerima Tdap selama kehamilan melalui seri vaksinasi pada bayi atau dosis booster.
- 4 publikasi mendukung efektivitas vaksin

Hasil evaluasi terhadap studi tersebut di atas adalah sebagai berikut:

1. Efektivitas

   - Studi case coverage/control dan kohort mengenai efektivitas vaksinasi pertusis pada ibu hamil dengan usia kehamilan 28 – 38 minggu dan > 37 minggu vaksinasi untuk mencegah pertusis pada bayi baru lahir menunjukkan efektivitas vaksin sebesar 93%, dengan efektivitas pada bayi < usia 3 bulan sebesar 91%, pada bayi usia <2 bulan sebesar 90-91%.

2. Imunogenisitas

   - Vaksinasi pada trimester ke-2/ke-3 memberikan respons perlindungan terbaik bagi bayi muda.
   - Bayi dari ibu yang divaksinasi Adacel memiliki titer antibodi pertusis darah tali pusat yang lebih tinggi dibandingkan bayi dari ibu yang tidak divaksinasi Adacel sebelum pemberian DTaP dosis pertama
   - Antibodi maternal mempengaruhi antibodi vaksinasi primer dengan GMC bayi dari ibu yang divaksinasi lebih rendah tetapi tidak ada pengaruh klinis dan seluruh subjek mencapai seroproteksi.

3. Keamanan

- Vaksin Adacel diberikan pada trimester kedua dan ketiga kehamilan dalam studi keamanan.
- Penelitian-penelitian ini menunjukkan bahwa vaksin Adacel atau Tdap dapat ditoleransi dengan baik oleh orang hamil.
- Efek samping yang paling umum pada wanita hamil adalah reaksi di tempat suntikan.
- AE lokal dan sistemik pada wanita hamil yang menerima vaksinasi Adacel/Adacel-Polio serupa dengan yang terlihat pada wanita tidak hamil.
- Secara keseluruhan, tidak ada peningkatan risiko keamanan klinis pada perempuan hamil dan bayinya yang menerima vaksinasi dibandingkan dengan perempuan dalam kelompok kontrol/plasebo dan bayinya.

4. Meskipun penelitian yang diajukan mencakup ibu hamil dengan usia kehamilan <20 minggu hingga >37 minggu, namun vaksinasi Adacel pada ibu hamil dianjurkan diberikan pada usia kehamilan 24 hingga 36 minggu dengan pertimbangan sebagai berikut:
   - Pada kelahiran prematur, diperkirakan berat janin sudah cukup besar (sudah mencapai 1 kg) pada usia kehamilan 28 minggu sehingga pemberian vaksin pada usia kehamilan 24 minggu akan menghasilkan pembentukan antibodi yang optimal pada minggu ke-28 (1 bulan setelahnya). vaksinasi)
   - Pemberian pada usia kehamilan maksimal 36 minggu akan menghasilkan pembentukan antibodi yang optimal pada 1 bulan setelah vaksinasi yaitu minggu ke-40 (kelahiran normal).

KEPUTUSAN

Mempertimbangkan data khasiat dan keamanan tersebut di atas, diputuskan registrasi variasi Adacel dengan **indikasi dan posologi** baru pada wanita hami sebagai berikut:

Indication

ADACEL® is indicated for active booster immunization for the prevention of tetanus, diphtheria and pertussis (whooping cough) in person 4 to 6 years of age and 10 years or older. ADACEL® is indicated for passive protection against pertussis in early infancy following maternal immunization during pregnancy (see sections DOSAGE AND ADMINISTRATION, and WARNING AND PRECAUTION). ADACEL® should be used in accordance with official recommendations In accordance with local recommendations, Adacel may be considered as an alternative for the fifth dose of tetanus, diphtheria and acellular pertussis vaccine (DTaP) in children 4 through 6 years of age, concomitantly administered with inactivated Poliomyelitis Vaccine (IPV) at separate site to complete the vaccination series of this age when indicated. ADACEL® is not to be used for the treatment of disease caused by Bordetella pertussis. Corynebacterium diphtheriae or Clostridium tetani infections.

PEDIATRICS ADACEL® is not indicated for immunization of children below the age of 4 years. TETANUS PROPHYLAXIS IN WOUND MANAGEMENT The need for active immunization with a tetanus toxoid-containing preparation such as Td adsorbed vaccine or Adacel, with or without passive immunization with tetanus Immune Globulin depends on both the condition on the wound and the patients vaccination history.

Dosage and administration

Recommended Dose

ADACEL® (0.5 mL) should be administered as a booster injection by the intramuscular route.

Re-dosing with ADACEL® can be used to boost immunity to diphtheria, tetanus and pertussis at 5 to 10 years intervals.

The preferred site is into the deltoid muscle. Fractional doses (doses<0,5 mL) should not be given.

ADACEL® may be administered to pregnant women during the 24-36 weeks to provide passive protection of infants against pertussis (see section INDICATION, DOSAGE AND ADMINISTRATION, WARNING AND PRECAUTION and PREGNANT WOMEN)

The effect of fractional doses on the safety and efficacy has not been determined.

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*Adult-type tetanus and diphtheria toxoids.
†Tetanus immune globulin, given at a separate site from the Td.
‡ Primary immunization is at least 3 doses at age appropriate intervals §Yes, if >10 years since last booster.
**Yes, if >5 years since last booster
††Yes, if individuals are known to have a significant humoral immune deficiency state (e.g. HIV gammaglobulinemia) since immune response to tetanus toxoid may be suboptimal.

A thorough attempt must be made to determine whether a patient has completed primary immunization. Persons who have completed primary immunization against tetanus and who sustain wounds that are minor and uncontaminated, should receive a booster dose of a tetanus toxoid-containing preparation if they have not received tetanus toxoid within the preceding 10 years. For tetanus-prone wounds (e.g., wounds contaminated with dirt, feces, soil and saliva, puncture wounds, avulsions and wounds resulting from missiles, crushing, burns or frostbite), a booster is appropriate if the patient has not received a tetanus toxoid-containing preparation within the preceding 5 years.