Public Assessment Report

VARILRIX

INFORMASI PRODUK

Nama obat	:	Varilrix
Bentuk sediaan	:	Serbuk injeksi
Zat aktif	:	Tiap dosis mengandung : Live attenuated varicella zoster virus (oka strain) >= 2000 pfu
Kemasan	:	Dus, 1 vial @ 1 dosis (0,5 ml) + 1 pre-filled syringe pelarut @ 0,5 ml
Pendaftar	:	PT Glaxo Wellcome Indonesia, Jakarta
Produsen	:	GlaxoSmithKline Biologicals SA, Rixensart, Belgium
Kategori Registrasi	:	Registrasi produk biologi yang sudah terdaftar dengan posologi baru
Indikasi yang disetujui:	:	*Healthy subjects* *Varilrix is indicated for active immunization against varicella of healthy subjects from the age of 12 months onwards.* *Vaccination of susceptible healthy close contacts of subjects at risk of severe varicella is recommended, in order to reduce the risk of transmission of wild-type virus to these patients. Close contacts include parents and siblings of high-risk patients, and medical and paramedical personnel.* *Patients at high risk of severe varicella* *Patients suffering from leukaemia, patients under immunosuppressive treatment (including corticosteroid therapy) for malignant solid tumour, for serious chronic diseases (such as chronic renal failure, auto-immune diseases, collagen diseases, severe bronchial asthma) or following organ transplantation, are predisposed to severe natural varicella. Vaccination with the Oka-strain has been shown to reduce the complications of varicella in these patients.* *There is only limited data from clinical trials available for Varilrix in patients at high risk of severe varicella; should vaccination be considered, it is advised that:* • *Maintenance chemotherapy should be withheld one week before and one week after immunization of patients in the acute phase of leukaemia. Patients under radiotherapy should normally not be vaccinated during the treatment phase. Generally patients are immunized when they are in complete haematological remission from the disease.* • *The total lymphocyte count should be at least 1,200 per mm3 or no other evidence of lack of cellular immune competence exists.* • *Vaccination should be carried out a few weeks before the administration of the immunosuppressive treatment for patients undergoing organ transplantation (e.g. kidney transplant).*
Posologi yang diajukan	:	*Dosage and Administration* *0.5 mL of reconstituted vaccine contains one immunizing dose.* *Posology* *Healthy subjects* • *Children 12 months up to and including 12 years of age.* *Children from the age of 12 months up to and including 12 years of age should receive 2 doses of Varilrix to ensure optimal protection against varicella (see "Pharmacodynamics"). It is preferable to administer the second dose at least 6 weeks after the first dose but in no circumstances less than 4 weeks. [Note: Applicable official recommendations may vary regarding the interval between doses and the need for one or two doses of varicella-containing vaccines in children aged 12 months to*

12 years]

- *Adolescents and adults from 13 years of age and above From 13 years of age and above: 2 doses. It is preferable to administer the second dose at least 6 weeks after the first dose but in no circumstances less than 4 weeks.*

High-risk patients

The same schedule described for healthy subjects should be applied for high-risk patients. In these patients, periodic measurement of varicella antibodies after vaccination may be indicated in order to identify those who may benefit from re-vaccination.

Interchangeability

- *A single dose of Varilrix may be administered to those who have already received a single dose of another varicella-containing vaccine.*
- *A single dose of Varilrix may be administered followed by a single dose of another varicellacontaining vaccine.*

Method of administration.

Varilrix is to be injected ***subcutaneously (SC) or intramuscularly (IM)*** *in the deltoid region or in the anterolateral area of the thigh.* ***Varilrix should be administered subcutaneously in subjects with bleeding disorders (e.g. thrombocytopenia or any coagulation disorder).***

For instructions on reconstitution of the medicinal product before administration see "Instructions for Use/Handling".

PENGANTAR

Varilrix merupakan vaksin yang mengandung Live attenuated varicella zoster virus (oka strain) ≥2000 PFU/dosis yang diproduksi oleh GlaxoSmithKline Biologicals SA, Rixensart, Belgium. Vaksin ini sudah disetujui di Indonesia untuk usia 12 bulan ke atas, saat ini melakukan variasi penambahan rute pemberian baru yaitu intramuskular.

ASPEK MUTU

N/A

ASPEK KHASIAT DAN KEAMANAN

Studi Non Klinik

N/A

Studi Klinik

Diserahkan 1 studi klinik fase 3b yang menggunakan produk Priorix Tetra yaitu studi MMRV-048. Open, multicenter, randomized, controlled phase IIIb study evaluating the immunogenicity and safety of subcutaneous versus intramuscular administration of GlaxoSmithKline Biologicals's combined measles-mumps-rubella-varicella vaccine (MeMuRu-OKA) to healthy children aged 11 to 21 months.

Justifikasi penggunaan studi klinik Priorix-tetra untuk mendukung rute administrasi intramuskular pada Varilrix: 1. Mengandung strain virus Varicella yang sama 2. Diformulasikan dari bulk Varicella yang sama (dengan end-of-shelf life [EOSL] specification of 103,3 pfu/dose untuk Varicella pada kedua vaksin) 3. Mengandung eksipien yang sama.

Tujuan primer studi ini adalah untuk mengevaluasi geometric mean titre (GMT) dan seroconversion rate terhadap varicella zoster virus (VZV) sebelum dan setelah pemberian Priorix-Tetra secara intramuskular dan subkutan. Tujuan sekunder yaitu mengevaluasi Cell Mediated Immunity terhadap varicella dan measles;

mengevaluasi nilai GMT dan serokonversi MMR setelah pemberian Priorix-Tetra secara intramuskular dan subkutan; serta untuk mengevaluasi profil keamanan.

Sebanyak 328 subyek (usia 11-21 bulan, berat > 2000 g, sehat) dirandomisasi menjadi 2 kelompok (MMRV IM dan MMRV SC) dengan rasio 1:1. Kedua kelompok mendapatkan 2 dosis Priorix-Tetra dengan interval waktu 6 minggu. Durasi studi adalah selama 12 minggu pengamatan.

Hasil evaluasi terhadap studi di atas sebagai berikut:

1. Data imunogenisitas untuk Varicella yang diberikan secara intramuskular (IM) sebanding dengan subkutan (SC) berdasarkan parameter GMT (3388.8 vs 2575.7) dan seropositivity rate (100% vs 100%) dengan lower limit of the two-sided 95% CI on the difference sebesar -4.10% menggunakan formula Priorix-tetra yang mengandung Measles, Mumps, Rubella, dan Varicella.
2. Mempertimbangkan bahwa Varilrix mengandung Varicella yang merupakan salah satu komponen pada Priorix-tetra, mempunyai formula yang mirip, dan diproduksi oleh produsen yang sama, maka imunogenisitas Varicella (Varilrix) dapat mengacu ke data imunogenisitas Varicella yang dikandung oleh Priorix-tetra.
3. Profil keamanan secara umum dapat ditoleransi. AE lokal yang paling sering terjadi adalah nyeri pada tempat suntikan, redness, dan swelling yang lebih rendah pada pemberian IM dibandingkan dengan SC, sedangkan untuk kejadian AE sistemik, yang paling sering terjadi adalah demam dan rash, dengan kejadian demam yang sedikit lebih tinggi pada kelompok IM.

KEPUTUSAN

Mempertimbangkan data khasiat dan keamanan tersebut di atas, diputuskan registrasi perubahan posologi Varilrix serbuk injeksi dapat **diterima** sebagai berikut:

Dosage and Administration

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0.5 mL of reconstituted vaccine contains one immunizing dose.

Posology

Healthy subjects

- *Children 12 months up to and including 12 years of age.*
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