SINGAPORE, 4 OCTOBER 2016

HSA UPDATES

"HSA UPDATES" addresses topics of current public interest, and is subject to change as more information becomes available.

HSA UPDATES NO 5/2016

HSA APPROVES DENGVAXIA® VACCINE

The Health Sciences Authority (HSA) has approved the dengue vaccine Dengvaxia® for the prevention of dengue infection caused by dengue virus serotypes 1, 2, 3 and 4 in individuals aged 12 to 45 years. The vaccination regime requires three doses to be administered over 12 months. Each dose is given at the 0, 6th and 12th month.

2 Two groups of experts from HSA's Medicines Advisory Committee and Dengue Expert Panel, comprising medical doctors and infectious diseases specialists, were consulted during the review to ensure that the vaccine is relevant and the benefits outweigh the risks for the Singapore population.

Scientific Review and Findings

3 HSA's regulatory approval is based on a review of the 24 clinical studies conducted by Sanofi in over 41,000 subjects. This comprised:

- 2 major clinical studies conducted in Latin America and Asia assessing the safety and efficacy of the vaccine against dengue in highly endemic countries in individuals aged 2 to 16 years; and
- 22 supportive studies assessing the antibody levels in individuals following vaccination.

The key findings of HSA's evaluation/assessment on the 2 major clinical studies in individuals aged 2 to 16 years submitted by Sanofi are:

4 Vaccine efficacy was defined as the percentage reduction of dengue disease in a vaccinated group of people compared to an unvaccinated group. Overall, the vaccine was effective in reducing dengue illness by 60%, and reducing severe dengue illness by 84%. Efficacy differed by serotypes, age groups and prior dengue exposure in the patient.

5 The vaccine was less effective against DENV-1 and DENV-2, which are the predominant strains in Singapore. The vaccine efficacy was 50% for DENV-1 and 40% for DENV-2 versus 75% for DENV-3 and 77% for DENV-4 infection.

6 In the Asia and Latin American efficacy studies, there was consistent risk reduction of hospitalised dengue observed in the vaccinated group aged 12 and above during the follow-up period. On the other hand, there was inconsistent risk reduction in the vaccinated group aged 9 to 11 years old in the Asian study.

7 In the Asian study, subjects were monitored for up to 5 years after receiving the first dose. During the first 2 years after the first dose, vaccinated children in this age group were 80% less likely to be hospitalised due to dengue and 87% less likely to have clinically severe dengue. However, during the subsequent 3 years (i.e. the 3rd to 5th years after the first dose of vaccination), preliminary long-term follow up data collected up to 31 October 2015 by Sanofi and provided in their regulatory submission to HSA showed an observed 30% increased risk of hospitalisation and three times the risk of severe dengue in vaccinated children aged between 9 to 11 years old. In contrast, in the Latin American efficacy study, a continued reduction of the risks was observed in the same age group and during the same period of time.

8 Taking into consideration the specific epidemiological situation in Singapore where the incidence of dengue is much lower in children than in young adults, the low immune response amongst the younger age group seen in the clinical trial conducted in Singapore, and the inconsistent risk reduction in the vaccinated group aged 9 to 11 years old, the vaccine was approved for use in the population 12 to 45 years of age.

9 The vaccine was shown to have provided significantly better protection to those who have had a prior exposure to dengue, as compared to those without previous dengue infection (i.e., 81% vs 38% protection respectively against all four strains) in individuals aged between 2 to 16 years. The vaccine is less likely to benefit those who did not previously have dengue.

10 There was insufficient evidence on the safety and efficacy of the vaccine for use in individuals above 45 years old.

- HSA's recommended cut-off age is 45 years old, which is in line with countries which have approved the vaccine.

11 The safety profile of the vaccine was generally consistent with that expected of a vaccine. All vaccines can cause side effects. Most of these are minor (for example, a sore arm or low-grade fever) and they usually go away within a few days.

12 HSA is prepared to review the approved age range when more clinical data becomes available that reduces the concern on those under 12 years old, and that provides more data on those above 45 years old.

13 As the vaccine is more effective in those who had previous dengue infection, and that there is a postulated risk of severe dengue in those who do not have past dengue infections when they become infected subsequently, it is recommended that

individuals interested in getting the vaccine consult their doctors on the benefits and risks of the vaccination. Doctors may consider a blood test, when available, to determine their past infection status. This may provide additional information to enable the individual to make an informed decision on the benefits versus risks of vaccination.

14 Educational materials detailing the approved indications and limitations of the vaccine – particularly for individuals without previous dengue infection – will be provided to doctors and patients to enable them to make an informed decision about vaccination.

15 HSA will monitor the vaccine closely to ensure its continued safety and efficacy.

Approval of Dengvaxia®

16 Dengvaxia®, developed by Sanofi Pasteur, is the first available dengue vaccine against all four strains of dengue virus (DEN-1, DEN-2, DEN-3, and DEN-4). The vaccine is approved in Singapore for the prevention of dengue infection caused by dengue virus serotypes 1, 2, 3 and 4 in individuals aged 12 to 45 years.

17 Dengvaxia® has been approved in countries including Mexico, Brazil, Philippines, El Salvador, Costa Rica, Guatemala, Peru, Indonesia and Paraguay.

HEALTH SCIENCES AUTHORITY
SINGAPORE
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- **About the Health Sciences Authority (HSA)**

The Health Sciences Authority (HSA) applies medical, pharmaceutical and scientific expertise through its three professional groups, Health Products Regulation, Blood Services and Applied Sciences, to protect and advance national health and safety. HSA is a multidisciplinary authority. It serves as the national regulator for health products, ensuring they are wisely regulated to meet standards of safety, quality and efficacy. As the national blood service, it is responsible for providing a safe and adequate blood supply. It also applies specialised scientific, forensic, investigative and analytical capabilities in serving the administration of justice. For more details, visit http://www.hsa.gov.sg/.

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