PSUR review for Gardasil

Introduction

This PSUR covered the reporting perriod from 1 June 2006 to 30 November 2006. No regulatory actions to revoke or withdraw this product for safety reasons has been taken worldwide. Regulatory action was taken in Norway to temporarily withhold product due to concerns with the instructions for the pre-filled safety syringe. These were addressed by amendments to the product information.

The Core Data Sheet has been amended to include updated information about syncope and that haemorrhage and pruritus have been included as injection site reactions.

It was estimated that approximately 2,024,839 doses were distributed during the reporting period. Many of these doses will remain as product inventory due to recent approval/ registration in some countries. In clinical trials 3,337 subjects were given Gardasil. During this reporting period there were 687 spontaneous reports received frm healthcareproviders, including 37 serious reports.

Newly analysed studies

Two studies were newly analysed. A dose ranging study (Protocol 007-10) and Protocol 023-00, an immunogenicity and safety study of Gardasil in females aged 9 to 23 years in Korea. 117 subjects were enrolled in this study. 3 Ongoing and 1 newly commenced study were mentioned. Safety analyses of the ongoing studies is planned for an upcoming PSUR.

Risk Management Programs

Routine pharmacovigilance had been planned for Gardasil. This is in addition to the current conditions of registration which require reporting of 4 studies. Data from those sstudies were not presented.

The sponsor proposes to specifically monitor the following adverse events: Autoimmune disorders, Rheumatologic/ Connective tissue disorders, Non-specific inflammatory reactions, Immunologic/Allergic Conditions and Skin and subcutaneous tissue disorders. A pregnancy registry is to be established in the USA, France and Canada. This is an enhanced surveillance program for women exposed to the vaccine within 1 month prior to the Last Menstruation Period of anytime during pregnancy. A report will be provided annually. To date 26 pregnancies have been reported via the spontaneous reporting system and 2 occurred in clinical trials. At data lock point, 1 first trimester miscarriage and 1 elective termination had been reported. The remaining pregnancy outcomes were pending delivery.

Spontaneous reports

The most frequently reported events concerned medical device complication or device malfaunction with use of pre-filled safety syringes (149 reports) and inappropriate schedule of administration (84 reports). The enxt most frequently reported adverse events concerned local injection site pain (50 reports and pyrexia (36 reports).

3 reports concerning autoimmune disorders were received, these include 2 reports of Guillain-barre, both from the US discussed in the cases included in the VAER database. The third case was of a 14 yr girl who had an upper respiratory infection from 23-26 September who was vaccinated with Gardasil. On 7 October she was admitted to hospital with a 1 day history of clumsiness left hand, slurred speech and difficulty walking. Resonance imaging showed multiple acute demyelinating lesionsof white matter. She was diagnosed with acute disseminated encephalomyelitis (ADEM) and given high dose steroids. She was reported to still have some left hemiparesis (partial recovery). The reporter considered this case was certainly related to vaccination. (It was also included in the VAER database.

No rheumatologic/Connective tissue or Non-specific inflammatory reactions were reported. There were 5 reports of immunologic/ Allergic events: 1 each of anaphylactic reaction, asthma. Allergy to vaccine, hypersensitivity and 1 report which included hypersensitivity and wheezing. 4 of these reports involved subjects with contributing medical histories which included allergies, hives, asthma and anaphylaxis. The remaining case had concomitant immunisations. The subject with anaphylaxis reported had a rechallenge which was negative.

There were 16 reports of Skin and subcutaneous tissue disorders, 15 of these were of urticaria and 1 of drug eruption.