June 2020

BCG - Bacillus Calmette Guérin, BCG-medac – Implementation Patient Alert Card

Dear Healthcare Professional,
medac GmbH in agreement with the Health Products Regulatory Authority (HPRA) would like to inform you of the following:

Summary

- Case reports have shown that there is a risk of a flare-up of latent BCG infections, with potentially fatal outcome.
- Adequate treatment of flare-up of latent BCG infections is of utmost importance.
- To ensure that patients and general practitioners are aware of the ongoing risk that a BCG infection can occur even years after BCG treatment, a patient alert card will be included in the packaging of BCG-medac soon. Until implementation please find some cards attached. Contact details where additional cards could be ordered are found below.

→ Please hand over the patient alert card to the patient and answer her/his questions on this topic.

Background on the safety concern

BCG-medac is indicated for the treatment of non-invasive urothelial bladder carcinoma (curative treatment of carcinoma *in situ*, prophylactic treatment of recurrence of urothelial carcinoma limited to mucosa; urothelial carcinoma in lamina propria but not the muscular layer of the bladder; carcinoma *in situ*).

An uncommon side effect of the treatment with BCG-medac is a disseminated BCG infection which can occur even years after the treatment. It might lead to a latent BCG infection, which can persist for several years. Those latent BCG infections might flare-up years after the initial infection and arise particularly from granulomatous pneumonitis, abscesses, infected aneurysms, and infections of implants, grafts or the surrounding tissues and which remain undetected and persistent for a long time even after termination of BCG therapy. There have also been case reports in which such a systemic infection had a fatal outcome due to challenging diagnosis and delayed treatment. Flare-up of these infections thus presents a risk for patient safety, with potentially fatal outcome.

Consultation of a specialist for infectious diseases is recommended once BCG has disseminated because the course of disease is similar to *M. tuberculosis* infections. However, BCG (attenuated *M. bovis)* is far less pathogenic for humans than *M. tuberculosis* and the patient does not need to be isolated once a systemic infection is diagnosed.

Patient Alert Card

A patient alert card was developed to minimise the risk of undetected severe systemic BCG infection with potentially fatal outcome and can now be found in the package.

Before the first instillation with BCG-medac is performed, the patient should be educated on the symptoms of a severe systemic reaction/infection, and the patient alert card should be completed with the patient's and urologist's name. Patients should carry the patient alert card at all times and hand it over to any physician they visit (general practitioner, hospital physician) to ensure adequate treatment in case of a systemic infection.

The patient alert card also includes a short description of the symptoms of a systemic infection and a short notice regarding BCG and the risk of a flare-up of latent BCG infection to make general practitioners and hospital physicians who are not directly involved in the treatment with BCG-medac aware of such a complication. In case a systemic BCG infection or other adverse reaction occurs it should be reported via the national reporting system.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Website: www.hpra.ie.

Adverse drug reactions can also be reported directly to the marketing authorisation holder:

medac Gesellschaft für klinische Spezialpräparate mbH
Theaterstr. 6
22880 Wedel
Germany
E-mail: Drugsafety@medac.de
Tel.: +49 4103 8006-0
Fax: +49 4103 8006-100

The SmPC has been updated in section 4.4 Special warnings and precautions for use, and section 4.8 Undesirable effects. The PIL has been updated in section 2 Warnings and precautions, accordingly.

Please find attached to this letter a patient alert card. Additional cards can be ordered at Quality@Fannin.eu

The HPRA has agreed at this time for the initial communication to be sent electronically with postal dissemination including copies of the printed patient alert card to follow.

DATE OF APPROVAL BY COMPETENT AUTHORITY: 06/2020

Sincerely,

B. Jogereit

Dr. med. Barbara Jogereit
EU-QPPV medac GmbH