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Herpes zoster prevention in multiple sclerosis and neuromyelitis optica spectrum disorders

Consensus of Section of Multiple Sclerosis and Neuroimmunology of Polish Neurological Society, Polish Society of Family Medicine and Polish Society of Vaccinology on supplementary data to recommendations of expert group of Polish Society of Vaccinology, Polish Society of Family Medicine, Polish Dermatological Society, Polish Association for the Study of Pain, and Polish Neurological Society and ECTRIMS/EAN of 2023

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ABSTRACT

A working group convened by the Section of Multiple Sclerosis and Neuroimmunology of the Polish Neurological Society, the Polish Society of Family Medicine, and the Polish Society of Vaccinology has developed a consensus on supplementary data to the recommendations of the expert group of the Polish Society of Vaccinology, the Polish Society of Family Medicine, the Polish Dermatological Society, the Polish Association for the Study of Pain, and the Polish Neurological Society, and ECTRIMS/EAN of 2023 with regard to the currently available in Poland recombinant herpes zoster vaccine (RZV).

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It is intended for the prevention of herpes zoster and postherpetic neuralgia in individuals aged > 50 and individuals aged ≥ 18 who belong to herpes zoster risk groups. In Poland it is available with 50% reimbursement exclusively for patients aged 65 and older who have an increased risk of developing herpes zoster.

This statement is based on the literature available as of 12 July 2024. The guidance will be updated as new data emerges. All data regarding the above-mentioned vaccine comes from clinical trials which have been reviewed, published and approved by the regulatory authorities and an increasing number of recommendations that might have an impact on real world data.

Keywords: herpes zoster, multiple sclerosis, neuromyelitis optica spectrum disorders, risk of herpes zoster, indications for vaccination

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Herpes zoster prevention

Herpes zoster is an infectious viral disease that represents symptomatic reactivation of a latent varicella-zoster virus (VZV) infection. For herpes zoster to develop, the patient has to have a history of primary VZV infection, usually in the form of varicella, less frequently in the form of an oligosymptomatic or intrauterine infection, and occasionally after varicella vaccination with a live product containing an attenuated Oka VZV strain. Varicella vaccination has not been shown to increase the risk of herpes zoster on the population level [1, 2]. Usually, herpes zoster presents as vesicles on an erythematous base, preceded by pain in a single dermatome. Severe complications can develop in the course of the disease, with postherpetic neuralgia being the most clinically significant one. This occurs in up to 30% of patients, leads to a considerable decrease in the quality of life, and causes chronic suffering. Its treatment is long-term, often ineffective and constitutes a significant challenge for the healthcare system.

Multiple sclerosis (MS) and neuromyelitis optica spectrum disorders (NMOSD) are autoimmune disorders managed with disease-modifying therapies (DMTs). According to the ongoing drug programme reimbursed by the Polish National Health Fund (NFZ) 'Treatment of patients with MS' (B.29), patients found eligible for treatment with sphingosine-1-phosphate (S1P) receptor modulators or cladribine tablets have to be tested for the presence of anti-VZV antibodies.

If a high titre of IgG antibodies and no IgM antibodies are found, VZV vaccination is not necessary, although the patient can still be vaccinated against herpes zoster. If there is no history to confirm varicella and the patient has no IgG antibodies against VZV, it is recommended to fully vaccinate them, i.e. administer two doses of a varicella vaccine at least six weeks apart.

Currently, there are two vaccine products against varicella available in Poland: Varilrix® and Varivax®. It should be remembered that the varicella vaccine contains live attenuated viruses and is completely different to the herpes zoster vaccine, which is a recombinant vaccine (Shingrix®). A history of varicella is an indication for herpes zoster vaccination, and varicella vaccination does not rule out the possibility of being given a herpes zoster vaccine.

When discussing the risk of developing herpes zoster, one should remember that a considerable number of DMTs used to treat MS and NMOSD have immunosuppressive effects.

According to the recommendations on herpes zoster vaccination published in 2023, which were developed by experts representing several Polish scientific societies including the Polish Neurological Society, the risk factors for herpes zoster are the following:

1) age > 50 years,
2) congenital or acquired immunodeficiency, including iatrogenic immunosuppression, human acquired immunodeficiency virus (HIV) infection, neoplastic disease (leukaemia, lymphoma, multiple myeloma), solid organ transplantation or haematopoietic stem-cell transplantation (HSCT),
3) chronic heart disease,
4) chronic liver disease,
5) chronic lung disease,
6) chronic kidney disease,
7) autoimmune diseases,
8) diabetes,
9) depression [2].

Although MS is typically diagnosed in people aged between 20 and 40, it is a chronic disorder that patients usually live with for many years. Data provided by the Polish National Health Fund (NFZ, Narodowy Fundusz Zdrowia) shows that patients aged 56 to 65 were the largest age cohort of MS patients receiving healthcare services in 2019 [2]. Moreover, as MS or NMOSD patients age, and thus the duration of their treatment (including immunosuppressive treatment) increases, they often develop other chronic disorders such as depression, which can result from, among other factors, the effects of some DMTs.

Consequently, MS and NMOSD patients are in a group of patients at a particularly high risk of herpes zoster. According to the summary of product characteristics of the approved herpes zoster vaccine (recombinant protein vaccine) [4] and the published recommendations, due to the epidemiology of herpes zoster and the occurrence of its complications,

the vaccination is recommended to all people aged > 50 and younger adults (≥ 18) with risk factors for herpes zoster [2, 5].

ECTRIMS/EAN recommendations on administration of recombinant herpes zoster vaccine

According to the ECTRIMS/EAN recommendations published in 2023, herpes zoster vaccine is recommended for MS patients aged > 18 if they have a history of varicella or were vaccinated against varicella and in whom treatment with drugs increasing the risk of herpes zoster, e.g. cladribine tablets, alemtuzumab, S1P receptor modulators, natalizumab, or anti-CD20 monoclonal antibodies, is being planned. Varicella vaccination should be considered in other cases [6]. Moreover, herpes zoster vaccination is recommended in older MS patients, who according to the recommendations should also receive a pneumococcal vaccine and flu vaccine every year [6]. Polish recommendations for this population take into consideration RSV vaccine (for those over 60) and diphtheria tetanus pertussis vaccine (once every 10 years) [5]. Vaccinations against hepatitis B and COVID should also be recommended for this group of patients [6]. Herpes zoster vaccination should optimally be done at least two weeks before the start of immunosuppressive treatment, or as early as possible if the treatment has already started. Ideally, it should be during the period when the likelihood of achieving an immune response is the highest.

Herpes zoster vaccine

The recombinant herpes zoster vaccine (RZV) available in Poland (Shingrix®) was approved in the European Union in 2018; it has been available in Poland since the spring of 2023. Due to the epidemiology of herpes zoster and the occurrence of its complications, the vaccine is intended for the prevention of herpes zoster and postherpetic neuralgia in individuals aged > 50 and individuals aged ≥ 18 who belong to herpes zoster risk groups. The full vaccination schedule consists of two doses of the vaccine given 2–6 months apart. In special cases, the interval between doses may be shortened to one month. The need for booster doses has not been determined [4], but based on the duration of follow-up and previous experience with the use of the vaccine [7], the administration of two doses results in effective immunisation lasting c.10 years. New information on the durability of vaccination efficacy is expected to be obtained over time as the vaccine remains on the market. No data on the need for booster doses is currently available. Observational studies that are ongoing are assessing the efficacy of the vaccine beyond 10 years after completion of the full vaccination schedule. The need for booster doses requires confirmation in further studies.

The vaccine product for herpes zoster prevention that is approved in Poland may be given to people previously vaccinated with a live attenuated varicella vaccine. It is not, however, indicated for use in the prevention of varicella as a primary VZV infection. The RZV vaccine is only intended for prevention, and should not be used to treat clinically confirmed disease [4]. Due to the risk of recurrent herpes zoster, the vaccination is also recommended in patients who previously had herpes zoster, but not until acute herpes zoster symptoms have resolved.

Efficacy

The recombinant vaccine has a very high efficacy. It has been shown to reduce the risk of developing herpes zoster by > 90% over an average follow-up of 3.1 years in people aged ≥ 50 and to reduce the risk of postherpetic neuralgia by 91.2% over an average follow-up of 3.1 years in people aged ≥ 50 and by 88.8% over 4 years in people aged ≥ 70. The safety and efficacy of the vaccine have also been demonstrated in groups at high risk of herpes zoster i.e. autologous HSCT recipients, patients with haematological or solid neoplasms, patients with HIV infection, and individuals after kidney transplantation [7].

Safety

The most common (> 1/10) side effects of the RZV vaccine include injection site reactions such as pain, redness, and swelling, also fatigue, chills, fever and headache, gastrointestinal symptoms including nausea, vomiting, diarrhoea and/or abdominal pain.

Common (≥ 1/100 to < 1/10) adverse effects are pruritus at the injection site and malaise. Severe side effects occur in a small percentage of patients, and overall the frequency of some side effects is higher in younger age groups, for example:

- pain at the injection site, fatigue, muscle pain, headache, chills and fever are more frequent in people aged 18–49 compared to people aged 50 and older,
- muscle pain, fatigue, headache, chills, fever and gastrointestinal symptoms are more frequent in people aged 50–69 compared to people aged 70 and older.

The analysis of data from a passive reporting system for suspected adverse events following immunisation (VAERS, the Vaccine Adverse Event Reporting System) from the first eight months of the use of Shingrix®, after the distribution of c.3.2 million doses, showed that the safety profile of the vaccine was similar to that seen in premarketing clinical studies. Reports of serious adverse events following the administration of the vaccine have been published, including several cases of herpes zoster both in immunocompetent individuals and in patients with immunodeficiency. However, once the reported cases had been analysed, it was determined that the relationship was only temporal, and the cases were not confirmed as having been caused by the administration of the vaccine [8].

Reimbursement in Poland

According to the Polish national recommendations on vaccinations [5] and a position paper of several Polish Medical Associations [2] on herpes zoster vaccination, the administration of recombinant herpes zoster vaccine (RZV) should be also considered in all individuals over > 50 and in individuals aged ≥ 18 who undergo immunosuppressive treatment. Moreover, the vaccine should be considered in all patients with chronic conditions which increase the risk of herpes zoster. These are:

- inherited or acquired immunosuppression, including: iatrogenic immunosuppression, HIV, cancer, haematological malignancies, haematopoietic cell transplant, solid organ transplant,
- chronic pulmonary conditions (i.e. asthma, COPD),
- chronic cardiological conditions (i.e. heart failure),
- chronic kidney disease,
- chronic liver disease,
- autoimmune diseases,
- diabetes,
- depression.

The announcement by the Polish Minister of Health on 11 December 2023 concerning the list of reimbursed medicines and foodstuffs intended for particular nutritional uses and medical devices [9] as of 1 January 2024, included the herpes zoster and postherpetic neuralgia vaccine to be available in Poland, with 50% reimbursement for patients aged 65 and older who have an increased risk of developing herpes zoster [10]. This 50% reimbursement for Shingrix® is accessible for individuals aged 65 and older from the following risk groups:

- chronic heart disease,
- chronic lung disease,
- diabetes,
- chronic renal failure,
- congenital or acquired immunodeficiency,
- generalised neoplastic disease,
- HIV infection,
- Hodgkin's lymphoma,
- iatrogenic immunosuppression,
- leukaemia,
- multiple myeloma,
- following solid organ transplantation,
- rheumatoid arthritis,
- psoriasis,
- psoriatic arthritis,
- inflammatory bowel disease,
- ankylosing spondylitis,
- multiple sclerosis,
- systemic lupus erythematosus.

50% reimbursement of the vaccine's cost means that the price of the product available in Poland for patients is c.400 PLN per dose (c.800 PLN for a full vaccination schedule; data as of 4 March 2024). It is worth noting that reimbursement before the start of treatment is available to patients with multiple sclerosis, but only those aged 65 and older. Taking into consideration the risk factor that is iatrogenic immunosuppression, the reimbursement may apply to MS and NMOSD patients (aged at least 65) during immunosuppressive treatment.

Conclusions

A. Herpes zoster develops in people who have previously had varicella. Varicella vaccination does not protect against herpes zoster and its complications, including postherpetic neuralgia.
B. Vaccination against herpes zoster should be considered in every newly diagnosed MS/NMOSD patient before the initiation of DMTs, especially ones with immunosuppressive effects, regardless of previous infection caused by the varicella zoster virus (VZV) or previous immunisation against the varicella zoster virus.
C. Herpes zoster vaccination in this group should optimally be done at least two weeks before the start of immunosuppressive treatment, or at the earliest possible date if the treatment has already been started (ideally, it should be during the period when the likelihood of achieving an immune response is the highest).
D. Use of the RZV vaccine while taking DMTs is possible and safe (the product available in Poland is not a live vaccine), but it is difficult to fully predict its efficacy based on the available data.
E. The reimbursement of the RZV vaccine is limited to the risk groups. It is important to note that these are not the same as the risk groups listed in the SPC and in the previously published recommendations provided by scientific societies, including the Polish Neurological Society. Reimbursement is also needed in adult patient groups with MS and NMOSD who are at risk of herpes zoster, including all adults found eligible for the use of medicines that significantly increase the risk of developing herpes zoster, such as cladribine, alemtuzumab, S1P receptor modulators, natalizumab, and anti-CD20 monoclonal antibodies, regardless of their age.

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