

EMA/90006/2015
EMA/H/C/001104

EPAR summary for the public

Prevenar 13

pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)

This is a summary of the European public assessment report (EPAR) for Prevenar 13. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Prevenar 13.

What is Prevenar 13?

Prevenar 13 is a vaccine. It is available as a suspension for injection that contains parts from 13 different types of the bacterium *Streptococcus pneumoniae* (*S. pneumoniae*).

What is Prevenar 13 used for?

Prevenar 13 is used to protect children aged between six weeks and 17 years against invasive disease, pneumonia (infection of the lungs) and acute otitis media (infection of the middle ear) caused by *S. pneumoniae*. It is also used to protect adults and the elderly against invasive disease and pneumonia caused by *S. pneumoniae*. Invasive disease occurs when the bacterium spreads through the body causing serious infections such as septicaemia (blood infection) and meningitis (infection of the membranes around the brain and spine).

When prescribing Prevenar 13, consideration should be given to the risk of invasive disease and pneumonia in the different age groups, other diseases the vaccinees may have and the type of bacteria in the different geographical areas.

The vaccine can only be obtained with a prescription.

How is Prevenar 13 used?

Adults and children aged two years and above should receive one single dose of Prevenar 13 into the shoulder muscle.

In children below two years of age, the vaccine is given by injection into the thigh muscle. The vaccination schedule depends on the age of the child and should be based on official recommendations:

- children aged between six weeks and six months are normally given four doses. The first three doses are given with an interval of one month between each dose. The fourth dose, the booster, is given between 11 and 15 months of age. Alternatively, when Prevenar 13 is given as part of a routine immunisation programme, two doses can be given at the ages of two and four months, followed by a booster at 11 to 15 months of age;
- children aged between seven months and 11 months should first receive two doses with an interval of at least one month followed by a third dose in the second year;
- children between 12 and 23 months of age should receive two doses with an interval of at least two months;
- children between two and 17 years of age should receive a single dose.

Prevenar 13 can be used in children who have started vaccination with Prevenar (another vaccine authorised in the European Union for *S. pneumoniae*, which contains parts of seven of the 13 types of *S. pneumoniae* included in Prevenar 13).

Further information on the use of Prevenar 13 in people at increased risk of pneumococcal infections (such as patients with HIV or people who have received a haematopoietic stem cell transplant) and on how to switch from Prevenar to Prevenar 13 can be found in the summary of product characteristics (also part of the EPAR).

How does Prevenar 13 work?

Vaccines work by 'teaching' the immune system (the body's natural defences) how to defend itself against a disease. When a person is given the vaccine, the immune system recognises the parts of the bacterium contained in the vaccine as 'foreign' and makes antibodies against them. The immune system will then be able to produce antibodies more quickly when it is exposed to the bacterium. This helps to protect against the disease.

Prevenar 13 contains small amounts of polysaccharides (a type of sugar) extracted from the 'capsule' that surrounds the *S. pneumoniae* bacterium. These polysaccharides have been purified, then 'conjugated' (attached) to a carrier to help them to be recognised by the immune system. The vaccine is also 'adsorbed' (fixed) onto an aluminium compound to enhance the immune response.

Prevenar 13 contains the polysaccharides from 13 different types of *S. pneumoniae* (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F). In Europe, it is estimated that these are responsible for between 73 and 100% of the cases of invasive disease in children under the age of five years, and at least 50 – 76% of the cases of invasive disease in adults, depending on the country. Prevenar 13 is very similar to Prevenar but contains six additional polysaccharides from serotypes which are responsible for between 16 and 60% of the cases.

How has Prevenar 13 been studied?

In children, the ability of Prevenar 13 to trigger the production of antibodies (immunogenicity) was assessed in two main studies involving 1,266 healthy children who were vaccinated between the ages of two and 15 months and in a third study involving 598 children aged between five and 17 years old who had previously been vaccinated with Prevenar or who had never been vaccinated for invasive

pneumococcal disease. Prevenar 13 was compared with Prevenar. The studies compared the immune response for Prevenar 13 with that for Prevenar against the seven polysaccharides that they share in common. In the first two studies they were compared directly, and in the third study the results for Prevenar 13 were compared to those obtained for Prevenar in a previous study. The immune response to the additional six polysaccharides in Prevenar 13 was compared with the lowest immune response to any of the polysaccharides in Prevenar. Additional studies in children looked at the effects of giving booster vaccinations, switching from Prevenar to Prevenar 13 and using Prevenar 13 alongside other vaccines routinely given to children.

In adults, Prevenar 13 was investigated in four main studies. The first study involved 835 adults aged 50 to 64 years who had not previously been vaccinated against invasive disease caused by *S. pneumoniae*. The second study involved 938 adults aged 70 years or older who had already been vaccinated against invasive disease caused by *S. pneumoniae* at least five years earlier. In both studies, Prevenar 13 was compared with a similar vaccine containing the polysaccharides from 23 different types of *S. pneumoniae* (23-valent polysaccharide vaccine). The studies compared the immune responses one month after vaccination with the two vaccines. A third study, which involved 900 adults aged 18 to 49, compared the immune response to Prevenar 13 with the response in adults aged 60 to 64. A fourth study involved approximately 85,000 adults over 65 years of age who had not previously been vaccinated with the 23-valent polysaccharide vaccine, and compared Prevenar 13 with placebo (a dummy treatment). The main measure of effectiveness was based on the number of subjects who developed a first episode of pneumonia caused by a type of *S. pneumoniae* covered by Prevenar 13.

What benefit has Prevenar 13 shown during the studies?

In children under five years of age, Prevenar 13 produced a response that was at least as good as Prevenar for six of the seven *S. pneumoniae* polysaccharides they share in common in the first main study, and for five of the seven in the second. Where the response to Prevenar 13 was lower than the comparator, the differences were considered to be small. All six of the additional polysaccharides in Prevenar 13 produced a response at least as good as the lowest response seen with Prevenar in the first main study. This was true for five of the six additional polysaccharides in the second study.

In children aged between five and 17 years old, Prevenar 13 produced a response that was at least as good as Prevenar for all seven *S. pneumoniae* polysaccharides they share in common. All six of the additional polysaccharides in Prevenar 13 produced a response that was similar to the response seen with Prevenar against the seven polysaccharides.

The additional studies showed that Prevenar 13 led to an increase in antibody production following booster vaccinations and supported a switch to Prevenar 13 in children who had started vaccination with Prevenar. Prevenar 13 was not shown to affect the immunogenicity of other vaccines routinely given to children.

In adults aged 50 and older, in the first two main studies Prevenar 13 produced an immune response that was at least as good as the 23-valent polysaccharide vaccine for all 12 of the *S. pneumoniae* polysaccharides they share in common, and for several of these serotypes the immune response was better with Prevenar 13. Adults aged 18 to 49 had an immune response with Prevenar 13 which was as good as the response in adults aged 60 to 64.

The fourth study in adults over 65 years of age showed that Prevenar 13 reduced the incidence of pneumonia by almost half: 49 out of 42,240 (around 0.1%) subjects fell ill with pneumonia caused by

S. pneumoniae in the vaccine group, compared with 90 out of 42,256 (around 0.2%) subjects in the placebo group.

What is the risk associated with Prevenar 13?

The most common side effects with Prevenar 13 (seen in more than 1 patient in 10) in children are decreased appetite, fever (only very common in children aged 6 weeks to 5 years), irritability, reactions at the site of injection (reddening or hardening of the skin, swelling, pain or tenderness), somnolence (sleepiness) and poor quality sleep. In adults and the elderly, the most common side effects (seen in more than 1 patient in 10) are decreased appetite, headaches, diarrhoea, fever (only very common in adults aged 18 to 29 years), vomiting (only very common in adults aged 18 to 49 years), rash, reactions at the site of injection, limitation of arm movement, arthralgia and myalgia (joint and muscle pain), chills and fatigue. For the full list of all side effects reported with Prevenar 13, see the package leaflet.

Prevenar 13 must not be used in people who are hypersensitive (allergic) to the active substances, to any of the other ingredients or to diphtheria toxoid (a weakened toxin from the bacterium that causes diphtheria). People who have a severe fever should not receive the vaccine until they have recovered, but they can still be given the vaccine if they have a mild infection such as a cold.

Why has Prevenar 13 been approved?

The CHMP decided that Prevenar 13's benefits are greater than its risks and recommended that it be granted marketing authorisation. The CHMP noted that in children the immune system's response to Prevenar 13 was comparable to that of Prevenar, which is already authorised for the protection of children against *S. pneumoniae* in the EU. The Committee also noted that Prevenar 13 contains additional polysaccharides from the types of *S. pneumoniae* that are responsible for causing disease in children in Europe.

In adults and the elderly, the Committee noted that community-acquired pneumonia and invasive pneumococcal disease may be an important health problem and that the benefit in terms of protection outweighed the risk of adverse reactions. For the prevention of pneumonia, although the use of Prevenar 13 was only investigated in adults over 65 years of age, the CHMP considered that the results could also be applied to younger adults as studies have shown that their immune response is similar or higher than that among adults older than 65.

What measures are being taken to ensure the safe and effective use of Prevenar 13?

A risk management plan has been developed to ensure that Prevenar 13 is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Prevenar 13, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Prevenar 13

The European Commission granted a marketing authorisation valid throughout the European Union for Prevenar 13 on 9 December 2009.

The full EPAR for Prevenar 13 can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports. For more information about

treatment with Prevenar 13, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 02-2015.