European Medicines Agency

Doc. Ref.: EMA/756630/2009
EMEA/H/C/264

Agenerase
amprenavir

EPAR summary for the public

This document is a summary of the European Public Assessment Report (EPAR). It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the studies performed, to reach their recommendations on how to use the medicine.
If you need more information about your medical condition or your treatment, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist. If you want more information on the basis for the CHMP recommendations, read the Scientific Discussion (also part of the EPAR).

What is Agenerase?
Agenerase is a medicine that contains the active substance amprenavir. It is available as cream capsules (50 and 150 mg) and as an oral solution (15 mg/ml).

What is Agenerase used for?
Agenerase is used in combination with other antiviral medicines to treat patients over four years of age who are infected with human immunodeficiency virus type 1 (HIV-1), a virus that causes acquired immune deficiency syndrome (AIDS). Agenerase should only be used in patients who have previously been treated with the same type of medicine as Agenerase (protease inhibitors). Doctors should prescribe Agenerase after they have looked at the antiviral medicines the patient has taken before and the likelihood that the virus will respond to the medicine.
The medicine can only be obtained with a prescription.

How is Agenerase used?
Treatment with Agenerase should be started by a doctor who has experience in the management of HIV infection. In adults, Agenerase capsules are usually given with low-dose ritonavir (another antiviral medicine). The oral solution is for patients who cannot swallow the capsules but it cannot be given with ritonavir. The recommended dose of Agenerase for patients over 12 years of age is 600 mg twice a day, taken with 100 mg ritonavir twice a day and with other antiviral medicines. If ritonavir is not used, Agenerase is taken at a higher dose (1,200 mg twice a day). In children aged between four and 12 years and in patients who weigh less than 50 kg, the recommended dose of Agenerase depends on body weight. Taking Agenerase with ritonavir should be avoided in children. The dose of Agenerase should be reduced in patients who have problems with their liver, and it should be taken without ritonavir by patients who have severe liver problems. Because amprenavir is less easily absorbed with the oral solution than with the capsules, the two formulations are not interchangeable on a milligram-for-milligram basis. For more information, see the Package Leaflet.

How does Agenerase work?
The active substance in Agenerase, amprenavir, is a protease inhibitor. It blocks an enzyme called protease, which is involved in the reproduction of HIV. When the enzyme is blocked, the virus does not reproduce normally, slowing down the spread of infection. Ritonavir is another protease inhibitor that is used as a 'booster'. It slows down the rate at which amprenavir is broken down, increasing the

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levels of amprenavir in the blood. This allows a lower dose of amprenavir to be used for the same effect. Agenerase, taken in combination with other antiviral medicines, reduces the amount of HIV in the blood and keeps it at a low level. Agenerase does not cure HIV infection or AIDS, but it may delay the damage to the immune system and the development of infections and diseases associated with AIDS.

How has Agenerase been studied?
Agenerase boosted with low-dose ritonavir has been compared with other protease inhibitors in 206 adults who had taken protease inhibitors in the past. Of these, 43 had HIV that was resistant to four other protease inhibitors. Agenerase without ritonavir has also been studied in 268 HIV-infected children and adolescents aged between six months and 18 years, all of whom had previously taken treatment for HIV infection, and 135 of whom had been treated with protease inhibitors. Agenerase without ritonavir has also been compared with placebo (a dummy treatment) and with invirase (another protease inhibitor) in 736 HIV-infected adults who had not previously been treated with protease inhibitors. The main measures of effectiveness were the number of patients with undetectable levels of HIV in the blood (viral load) and the change in viral load after treatment.

What benefit has Agenerase shown during the studies?
In adults who had taken protease inhibitors in the past, Agenerase boosted with ritonavir was as effective as other protease inhibitors in reducing viral loads after 16 weeks of treatment: around two thirds of the patients in both groups had viral loads below 400 copies/ml. In the patients with HIV that was resistant to four other protease inhibitors, patients taking Agenerase with ritonavir had a greater fall in viral load after four weeks than those continuing to take their previous protease inhibitors. Agenerase reduced viral loads in children and adolescents, although very few of those who had taken protease inhibitors in the past responded to treatment and there were very few children aged below four years. In the studies of adults who had not previously taken protease inhibitors, Agenerase taken without ritonavir was more effective than placebo but less effective than indinavir.

What is the risk associated with Agenerase?
The most common side effects with Agenerase (seen in more than 1 patient in 10) are hypercholesterolaemia (high blood cholesterol levels), headache, diarrhoea, flatulence (gas), nausea (feeling sick), vomiting, rash and fatigue (tiredness). For the full list of all side effects reported with Agenerase, see the Package Leaflet.
Agenerase should not be used in people who may be hypersensitive (allergic) to amprenavir or any of the other ingredients. Agenerase must not be used in patients who are taking St John's wort (a herbal preparation used to treat depression) or medicines that are broken down in the same way as Agenerase and are harmful at high levels in the blood. See the Package Leaflet for the full list of these medicines.
Agenerase boosted with ritonavir must not be taken by patients who have severe problems with their liver, or by patients taking rifampicin (used to treat tuberculosis) or medicines that are broken down in the same way as ritonavir, such as flecainide and propafenone (used to correct irregular heartbeat).
As with other anti-HIV medicines, patients taking Agenerase may be at risk of lipodystrophy (changes in the distribution of body fat), osteonecrosis (death of bone tissue) or immune reactivation syndrome (symptoms of infection caused by the recovering immune system). Patients who have problems with their liver may be at an elevated risk of liver damage when taking Agenerase.

Why has Agenerase been approved?
The Committee for Medicinal Products for Human Use (CHMP) decided that Agenerase benefits are greater than its risks, but noted that the benefit of Agenerase taken with ritonavir has not been demonstrated in patients who have not taken protease inhibitors in the past. The Committee recommended that Agenerase be given marketing authorisation.
Agenerase was originally authorised under 'Exceptional Circumstances', because, for scientific reasons, limited information was available at the time of approval. As the company had supplied the additional information requested, the 'Exceptional Circumstances' ended on 10 March 2004.

Other information about Agenerase:
The European Commission granted a marketing authorisation valid throughout the European Union for Agenerase to Glaxo Group Limited on 20 October 2000. After five years, the marketing authorisation was renewed for a further five years.

The full EPAR for Agenerase can be found here.

This summary was last updated in 12-2009.