European Medicines Agency

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Questions and answers on the recommendation to suspend the marketing authorisation for Raptiva

The European Medicines Agency (EMEA) has completed a review of Raptiva (efalizumab) at the request of the European Commission, following concerns over the safety of the medicine. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the benefits of Raptiva no longer outweigh its risks, and that the marketing authorisation should be suspended across the European Union (EU). The review was carried out under an 'Article 20' referral[1].

What is Raptiva?
Raptiva is a powder and solvent that are made up into a solution for injection. It contains the active substance efalizumab. Raptiva is used to treat adults with moderate to severe chronic (long-term) plaque psoriasis (a disease causing red, scaly patches on the skin) who have failed to respond to or cannot take other systemic (whole-body) treatments for psoriasis, including ciclosporin, methotrexate and PUVA (psoralen ultraviolet-A).

The active substance in Raptiva, efalizumab, is a monoclonal antibody. Efalizumab blocks a protein called LFA-1 on the surface of lymphocytes, a type of white blood cell that is involved in the inflammation process. As LFA-1 is important in helping the lymphocytes to stick to cells in the skin, efalizumab reduces the inflammation in the skin that causes psoriasis, improving the symptoms of the disease. Raptiva has been authorised in the EU since September 2004 and is marketed in 24 Member States[2].

Why was Raptiva reviewed?
The CHMP reviewed Raptiva after it had received reports of serious side effects associated with the medicine. These included three confirmed cases of 'progressive multifocal leukoencephalopathy' (PML) reported between September 2008 and January 2009 in patients who had been receiving Raptiva for more than three years. Two of these cases resulted in the patient's death. The CHMP also received reports of a suspected case of PML which could not be confirmed and another suspected case which was later judged to be unlikely.

PML is a rare brain infection caused by a virus called the JC virus. The JC virus is commonly found in the general population but only leads to PML if the immune system has been weakened. PML causes damage to the protective sheath surrounding nerves and usually leads to severe disability or death.

As a result of these reports, the European Commission issued a formal request, asking the CHMP to issue an opinion on whether the marketing authorisation for Raptiva should be maintained, varied, suspended or withdrawn across the EU.

Which data has the CHMP reviewed?
The CHMP reviewed information on the benefits and risks of Raptiva provided by the marketing authorisation holder (MAH) that has become available since the medicine has been authorised. This included data on the medicine's effectiveness from 10 studies, information on the medicine's safety from a database of clinical trials, and information on side effects reported to the MAH from healthcare professionals and health authorities.

[1] Article 20 of Regulation (EC) No 726/2004.
[2] Raptiva is marketed in Austria, Bulgaria, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Latvia, Malta, the Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

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What are the conclusions of the CHMP?
The Committee noted that there is a risk of PML in patients receiving Raptiva. Although psoriasis is a disabling condition that can cause social and psychological problems for patients, it is very rarely life-threatening. The Committee concluded that the risk of PML, which is usually fatal, is unacceptable in patients receiving Raptiva. Introducing restrictions on the use of Raptiva was judged to be unlikely to reduce this risk, because there is no reliable way of knowing which patients will develop PML or when the disease is likely to occur. The CHMP also concluded that Raptiva's benefits are modest and that its position as a treatment option for moderate to severe psoriasis is less clear than when it was first authorised, now that other medicines have been authorised for use in the same patients.

The CHMP noted that other serious side effects have also been reported in patients receiving Raptiva, including Guillain Barré and Miller Fisher syndromes (disorders of the immune system that damage the nerves), encephalitis (inflammation of the brain), encephalopathy (brain damage), meningitis (inflammation of the membrane that surrounds the brain) and other infections such as sepsis (blood infection) and tuberculosis.

Therefore, based on evaluation of available data and the scientific discussion within the Committee, the CHMP concluded that the benefits of Raptiva no longer outweigh its risks and recommended that the marketing authorisation for Raptiva be suspended across the EU. The CHMP has recommended that the suspension of Raptiva's marketing authorisation should remain in place until there is enough new evidence to identify a group of patients in which the benefits of Raptiva outweigh its risks. In particular, the Committee would need to see new information on Raptiva's effectiveness in patients who have no other treatment options, and on its safety in these patients who may already have a weakened immune system as result of previous treatment with tumour necrosis factor (TNF)-alpha blockers (other medicines used to treat psoriasis). TNF-alpha blockers also reduce the activity of the immune system.

What is happening with clinical trials of Raptiva?
Decisions on whether clinical trials continue or not are made by individual Member States at a national level. The CHMP is of the opinion that relevant clinical trials with Raptiva should preferably continue as they may provide important information on the safety and effectiveness of the medicine in patients with no other treatment options.

What are the recommendations for patients?
- Patients who are currently receiving Raptiva should make an appointment with the doctor who prescribed it to them.
- Patients should not stop Raptiva treatment abruptly as this could lead to the disease coming back or getting worse. Their doctor will discuss the most appropriate replacement treatment with them.
- Patients currently involved in clinical trials with Raptiva should speak to their investigator.
- Patients who have taken Raptiva in the past and have any questions or concerns should speak to their doctor or pharmacist.

What are the recommendations for prescribers?
- Prescribers should not issue any prescriptions for Raptiva to patients who are not already taking the medicine.
- Prescribers should review the treatment of all patients currently taking the medicine with a view to stopping treatment.
- Prescribers should not stop Raptiva treatment abruptly (which could cause the disease to return or worsen), but should consider alternative treatments and continue to monitor the patients' psoriasis.
- The effects of Raptiva on the immune system last for about eight to 12 weeks. Prescribers should therefore make sure that patients are closely monitored for infections and neurological symptoms (affecting the brain) after they have stopped Raptiva treatment.

The CHMP opinion will now be sent to the European Commission for the adoption of a formal decision, applicable in all EU countries.

The full European Public Assessment Report for Raptiva is available here.