European Medicines Agency

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Questions and answers on the referral for Ciclosporin IDL and associated names capsules containing ciclosporin 25 mg, 50 mg and 100 mg

On 23 April 2009, the European Medicines Agency completed an arbitration procedure following a disagreement among Member States of the European Union (EU) regarding the authorisation of the medicine Ciclosporin IDL. The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that the benefits of Ciclosporin IDL do not outweigh its risks, and that the marketing authorisation granted in the Netherlands cannot be recognised in other Member States of the EU and that the marketing authorisation in the Netherlands should be suspended.
The company that markets Ciclosporin IDL, International Drug Licensing, requested a re-examination of the opinion. After having considered the grounds for this request, the CHMP re-examined the initial opinion, and confirmed the recommendation for the refusal and suspension of the marketing authorisation on 23 July 2009.
The review was carried out under an 'Article 29' referral[1].

What is Ciclosporin IDL?

Ciclosporin IDL is an immunosuppressive medicine (a medicine that reduces the activity of the immune system, the body's natural defences). It is used in patients who have had a transplant, to prevent rejection (when the immune system attacks the transplanted organ). It is also used to treat or prevent graft-versus-host disease (when the immune system of the transplanted organ attacks the patient's tissues).
Ciclosporin IDL is also used to treat autoimmune diseases. An autoimmune disease is a disease which is caused by the body's own defence system attacking normal tissue, such as psoriasis (a disease causing red, scaly patches on the skin), atopic dermatitis (eczema, an itchy red rash), nephrotic syndrome (a kidney disease) and rheumatoid arthritis (inflammation of the joints).
The active substance in Ciclosporin IDL, ciclosporin, acts on some special cells in the immune system called T-cells that are responsible for attacking transplanted organs or, in auto-immune diseases, normal tissue.
Ciclosporin IDL is a generic medicine that is based on a reference medicine authorised in Germany (Sandimmun Optoral 25 mg capsules).

Why was Ciclosporin IDL reviewed?

The company International Drug Licensing (IDL) submitted Ciclosporin IDL for mutual recognition on the basis of the initial authorisation granted by the Netherlands on 10 August 2007. The company wanted the authorisation to be recognised in Belgium, Germany, Italy, Spain, Sweden and the United Kingdom (the 'concerned Member States'). However, because the concerned Member States were not able to reach an agreement, the Dutch medicines regulatory agency referred the matter to the CHMP for arbitration on 2 December 2008.
The grounds for the referral were that five of the concerned Member States did not agree that enough evidence had been presented to show that Ciclosporin IDL was 'bioequivalent' to the reference medicine. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

[1] Article 29 of Directive 2001/83/EC as amended, referral on the grounds of potential serious risk to public health

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What are the conclusions of the CHMP?
Based on evaluation of the currently available data and the scientific discussion within the Committee, the CHMP was of the opinion that bioequivalence between Ciclosporin IDL and the reference medicine had not been sufficiently demonstrated. The CHMP therefore concluded that the benefits of Ciclosporin IDL do not outweigh its risks, and that the marketing authorisation should not be granted in the concerned Member States. In addition the Committee has also recommended that the marketing authorisation for Ciclosporin IDL in the Netherlands and other member states in the EU where the product has been authorised should be suspended until satisfactory bioequivalence data are obtained. The CHMP opinion was confirmed after re-examination.

The European Commission issued a decision on 22 July 2010.

	Initial	Re-examination
Rapporteur:	Prof. Pieter de Graeff	Dr Ondřej Slanař
Co-rapporteur:	Dr Robert James Hemmings	Dr Tomas Salmonson
Procedure start date:	18 December 2008	20 June 2009
Company responses provided on:	16 January 2009	n/a
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