**PROCEDURAL STEPS TAKEN AND SCIENTIFIC DISCUSSION AFTER AUTHORISATION**

For procedures finalised after 1 September 2000 please refer to module 8B**.**

- On 24 November 1999 the CPMP issued a notification to the Commission relating to changes in the Package Leaflet and Labelling not connected to the Summary of Product Characteristics. The European Commission amended the Decision on 15 February 2000.

- On 19 January 2000, recognising that respiratory symptoms are an important part of the hypersensitivity reactions (HSR) the Marketing Authorisation Holder requested an update of the Summary of Product Characteristics and Package Leaflet through an Urgent Safety Restriction (USR) procedure in accordance with article 1(2) of Commission Regulation (EC) No. 542/95 as amended.

  The scope of the procedure was to introduce and highlight information regarding respiratory symptoms associated with HSR. It has been recognised that these patients may initially be thought of as having respiratory disease of other origin. As a consequence new warnings have been introduced in the Summary of Product Characteristics (sections 4.4 and 4.8), the labelling (alert card) and in the Package Leaflet. These new warnings are aimed for physicians and patients to better recognise these HSR with respiratory symptoms.

  On 4 February 2000, the MAH submitted an application for a Type II variation in accordance with Commission Regulation (EC) No. 542/95. The scope of the variation was to update the Summary of Product Characteristics (SPC), and as a consequence the Labelling and Package Leaflet following new information provisionally introduced through the above USR and following the availability of new interaction data of abacavir with methadone, and other new safety data. The CPMP considered the changes related to the variation acceptable and issued on 25 May 2000 the Opinion on the Type II variation. The respective Commission Decision was issued on 22 February 2001.

- On 10 August 2000, the Marketing Authorisation Holder requested an update of the Summary of Product Characteristics, Package Leaflet and Labelling through an Urgent Safety Restriction procedure in accordance with article 1(2) of Commission Regulation (EC) No. 542/95 as amended. This was due to reports of hypersensitivity reactions occurring when therapy with Ziagen was restarted following a break in therapy.

  The scope of the Urgent Safety restriction was to provide information to prescribers and patients regarding the recognition of hypersensitivity reactions, their occurrence after interruption of therapy and the management of restarting. As a consequence new warnings have been introduced in the Summary of Product Characteristics (sections 4.4 and 4.8), the Labelling (alert card) and in the Package Leaflet.