

3rd October 2006

EU Synchronisation of PSUR¹ submission schemes of medicinal products authorised through national and mutual recognition procedures

Under the auspices of the “Heads of Medicines Agencies” an initiative has been taken to ensure that medicinal products with the same active substance follow the same Periodic Safety Update Report (PSUR) submission scheme in all EU Member States. The submission scheme for PSURs will normally be determined by the marketing authorisation date (‘birth date’) of the concerned medicinal product. If a medicinal product is authorised on different dates in the various Member States, then this currently still results in different PSUR submission schemes in these Member States.

At the start of January 2006, marketing authorisation holders of original medicinal products were requested to make proposals for EU harmonised birth dates (EU HBDs) of their medicinal products. However, due to the transition from 5-yearly to 3-yearly PSURs, a birth date alone is in many cases no longer the determining factor for the new PSUR submission scheme. Therefore, the request was made to provide a corresponding data lock point² (DLP), in addition to the proposal for an EU HBD, for the forthcoming PSUR. The proposals for EU HBDs have been collected and 558 of them have been adopted by the Heads of Medicines Agencies. The list of adopted EU HBDs and accompanying DLPs for the forthcoming PSURs can be found on the HMA website [[HYPERLINK](#)]

Several proposals for EU HBDs received were not clear or two or more proposals were received for the same substance by different companies. This is currently being sorted out and will lead probably to a further 90 EU HBDs which will be published as an addendum to the current list in due time.

Marketing authorisation holders of generic medicinal products are also expected to use the EU HBDs and accompanying DLPs. The consequences for reference safety information used for generic medicinal products are described in the appendix “Reference safety information to be used in PSURs of generic medicinal products for which the submission date is based on an EU HBD” [[HYPERLINK](#)].

The benefits of this project are clear:

- a. Marketing authorisation holders of original medicinal products only have to make a PSUR for the concerned products once every 3 years and this can be simultaneously submitted to all EU Member States.
- b. Marketing authorisation holders of generic medicinal products have the same advantages as those stated under a, and can collaborate on the preparation of PSURs and thereby mutually share the workload.
- c. The marketing authorisation authorities will be able to mutually share the assessment tasks of the PSURs, thus preventing duplicate assessment work.

The member States will share the assessment tasks of the PSURs based on EU HBDs. The Member State in charge of making the PSUR assessment report is called the PSUR Reference Member State (P-RMS) and will be indicated in the list of EU HBDs once known.

The project has the support of EFPIA, AESGP and EGA.

Medicinal products authorised before December 1976 and herbals, homeopathics, vaccines and blood products still, for the time being, fall outside of the scope of the PSUR synchronisation project.

¹ PSUR = Periodic Safety Update Report

² Data lock point: the end point of the period covered by the PSUR

Practical consequences for the submission date of PSURs

a. **New marketing authorisations associated with existing medicinal products, such as new strengths, new pharmaceutical forms, new administration routes, new indications (‘line extensions’)**

If an EU HBD was established for the original medicinal product, then this should also be used for the line extension. However, it might also be considered necessary to follow a separate PSUR scheme for a given period of time for a line extension. Per case agreements will need to be made with the competent authorities (this is the RMS for MRP and DCP products).

b. **New marketing authorisations of generic medicinal products**

If an EU HBD was established for the original medicinal product, then this should also be used for the new marketing authorisation of corresponding generic medicinal products. However, it might be considered necessary in a special case to follow a separate PSUR scheme for the generic medicinal product. Such cases could be:

- the presence of an active substance which is a different salt/ester/derivative (with the same therapeutic moiety), and
- the presence of an excipient without an established safety profile; and
- a Risk Management Plan in place for the corresponding original product requiring specific monitoring of a safety concern.

Per case agreements will need to be made with the competent authorities (this is the RMS for MRP and DCP products). A request for an early renewal of a market authorisation can be made so that an application for the renewal takes place at the same time as the submission of a PSUR on the basis of an EU HBD. For details, see the “Guideline on the Processing of Renewals in Mutual Recognition and Decentralised Procedures, October 2005” on the HMA website: http://heads.medagencies.org/mrfg/docs/bpg/renewal_guide_MRP_DCP.pdf.

Member States have agreed that also for products authorised through national procedures early renewals may be applied for.

c. **Existing market authorisations of original medicinal products for which an EU HBD has been established and corresponding generic medicinal products**

The EU HBD should be used. If a marketing authorisation still needs to be renewed (normally all marketing authorisations should be renewed once after five years, although it has been agreed that a further renewal should take place before 30 April 2009 for MRP products for which the marketing authorisation has already been renewed once before 30 October 2005), then a request for early renewal can be made so that the application for the renewal for the marketing authorisation takes place at the same time as the submission of the PSUR on the basis of the EU HBD. See the aforementioned Renewal Guideline for details.

d. **Existing marketing authorisations of medicinal products for which no EU HBD has been established**

- the current 5-year scheme may be completed if that results in a submission of a PSUR before 30 October 2008. A 3-year scheme should subsequently be followed.
- if the current 5-year scheme results in a submission of a PSUR on or after 30 October 2008, then the marketing authorisation holder must submit a proposal for a submission date that is before 30 October 2008.

Appendices:

- “List of EU HBDs and Related DLPs”, 3 October 2006
- “Reference safety information to be used in PSURs of generic medicinal products for which the submission date is based on an EU HBD”, 4 April 2006