

Division: Weesp

PR ID: 31471

Project: Change Request

PR State: Closed

Description of Change

Description of change:

Update Process Changes instead of description below dashed line (see attached email):

Stage 1: introduction of an additional process for eprosartan and increase of the batch size.

Stage 2: widening of parameter ranges and increase of the batch size.

Overall result: only one quality of eprosartan mesylate.

Specification Changes:

Eprosartan mesylate (due to method change for psd);

SB201999 (due to method change for assay and impurities; introduction of new supplier with different route of synthesis)

Acetonitrile (for recovery)

Method Changes:

Update column description in methods for assay and impurities eprosartan, assay and impurities eprosartan mesylate;

Update equipment description in PSD method;

New method for assay and impurities SB201999.

Suppliers of starting materials:

Update document because of new suppliers for SB201999 and SB290160

If possible remove suppliers that will be no longer used

Stage 1 and 2: New route F2, which is an optimized version of route F1.

In stage 1 several washes and distillation steps are omitted and the concentration is increased.

In stage 2 the drying after the salt formation step is omitted and the quantities and ratio of solvents in the final recrystallization step are changed.

The overall yield in the F2 process is higher and waste streams are considerably less than in F1.

As a result the cost price of eprosartan mesylate, purchased from Lonza, will decrease from € 201.50 per kg to

€ 185.00 per kg.



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Update of the psd method (Method Change).

Additional Information

Approvers:

M. van der Hulst (Global Scientific Approval)

U. Rettenmaier (Global RA-CMC)

E. Spieser (QA Chatillon)

M. A. Lalo (Global QA)

Justification

See attached documents:

Epro F1/F2 idea - new approach for the process,

Comparison of the Process.

Change Strategy

See attached document:

Document list API variations.

Committee Comments

06/15/2010 10:35 AM (GMT+2:00) added by Ute Rettenmaier (PID-002785):

Variation package consists of 4 Type IA variations, 2 Type IB variations and 4 Type II variations. Implementation country by country after approval only.



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12/15/2008 11:15 AM (GMT+1:00) added by Ute Rettenmaier (PID-002785):
Implementation only after approval. This Type IB variation for the process change (+Type IA variation for PSD method change) will be followed by a Type IA variation for the batch size change.
Only after approval of all variations above, Route F2 can be implemented country by country.