British Pharmacopoeia

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Date: 8th May 2025

TO WHOM IT MAY CONCERN

MORPHINE ORAL SOLUTION BP 2025

It has come to our attention that the monograph for Morphine Oral Solution in the BP 2025 requires amendments to both the Related substances test and the Assay section.

RELATED SUBSTANCES

The relative retention time for impurity A should be about 1.4 for impurity A, in line with other Morphine dosage form monographs.

The system suitability criterion will be revised to use a peak-to-valley ratio rather than resolution between two peaks.

The limit for impurity B is should state "the area of any peak corresponding to impurity B is not greater than 0.8 times the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);".

The Related substances test will be amended as follows, with the changed text highlighted:

[...]

When the chromatograms are recorded under the prescribed conditions the retention times relative to morphine (retention time about 12.5 minutes) are: impurity F, about 0.95; impurity E, about 1.1; **impurity A, about 1.4**; impurity C, about 1.6 and impurity B, about 1.9.

[...]

System suitability

The test is not valid unless, in the chromatogram obtained with solution (3), **the peak-to-valley ratio is at least 2.0, where *Hp* is the height above the baseline of the peak due to impurity F and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to morphine.**

[...]

Limits

Identify any peaks in the chromatogram obtained with solution (1) corresponding to impurity E, impurity C and impurity B using the chromatogram obtained with solution (3) and the chromatogram supplied with morphine for system suitability EPCRS. Multiply the area of any peak corresponding to impurity E, impurity C and impurity B by the following correction factors respectively: 0.5, 0.4 and 0.25.

MHRA

In the chromatogram obtained with solution (1):
the area of any peak corresponding to impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);
the area of any peak corresponding to impurity B is not greater than 0.8 times the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);
the area of any peak corresponding to impurity F is not greater than 0.6 times the area of the peak in the chromatogram obtained with solution (2) (0.3%);
the area of any other secondary peaks is not greater than 0.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);
the sum of the areas of all secondary peaks is not greater than 4 times the area of the principal peak in the chromatogram obtained with solution (2) (2.0%).
Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.05%).

[...]

ASSAY

The solvent used for preparing the solutions for the Assay has been changed to the mobile phase. The Assay will be amended as follows, with the changed text highlighted:

[...]

Carry out the method for liquid chromatography, Appendix III D, using the following solutions in the **mobile phase**.

[...]

Please accept this as a notice of intent to amend the monograph on behalf of the British Pharmacopoeia Commission. This letter is for information only and does not represent a legally-enforceable standard. The revised monograph will be published in a future edition of the British Pharmacopoeia - the current target publication is the BP 2026, which will come into force on 1st January 2026.

If you have any questions concerning this letter, please do not hesitate to contact the British Pharmacopoeia Secretariat (BPCOM@mhra.gov.uk).

Yours faithfully,

MR STEVE HOARE

Secretary & Scientific Director

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