METHODS OF MEASURING CARFILZOMIB

BACKGROUND

[0001] Accurate assessment of the concentration of an active pharmaceutical ingredient (API) in a solution prior to formulating is important to ensure that the correct amount of the API is portioned into the resulting formulation. Carfilzomib is an approved API for treating multiple myeloma, and is marketed under the name KYPROLIS®. Accurate measurement of carfilzomib during formulating is required to ensure the resulting formulation contains the desired amount of carfilzomib. Thus, a need exists for methods that provide an accurate measurement of carfilzomib in a sample.

SUMMARY

[0002] Provided herein are methods of measuring carfilzomib concentration in a sample during formulation of the carfilzomib. In one aspect, the present disclosure refers to a method for measuring a carfilzomib concentration of a sample comprising carfilzomib comprising the steps of diluting the sample with a diluent comprising water and 25% to 40% by volume acetonitrile to form an analytical sample; and subjecting the analytical sample to high performance liquid chromatography (HPLC) to determine the carfilzomib concentration in the sample. The methods for measuring a carfilzomib concentration in a sample comprise diluting the sample with a diluent comprising water and less than 50% by volume acetonitrile to form an analytical sample; and subjecting the analytical sample to high performance liquid chromatography (HPLC) to obtain the carfilzomib concentration of the sample. In various examples, the sample is from carfilzomib compounding. In some examples, the sample is from a bulk lyophilization solution of carfilzomib. In some examples, the sample is a solubilization sample. In some examples, the sample is a post-dilution sample. In various cases, the diluent is water and 0% to 45% by volume acetonitrile. In some cases, the diluent is water and 25% to 40% by volume acetonitrile. In some cases the diluent is water and 30% by volume acetonitrile. In some cases the diluent is water and 40% by volume acetonitrile. In various examples, the methods provide a relative standard deviation (RSD) value of less than 2% determined from multiple analytical samples of the sample. In some cases, the RSD% is less than 1%. In some cases, the RSD% is less than 0.5%. In various cases, the concentration of carfilzomib in the sample is 3 mg/mL to 8 mg/mL. In some cases, the concentration of carfilzomib in the sample is 5 mg/mL to 6 mg/mL. In various examples, the analytical sample is at a temperature of 2 to 8 C prior to HPLC analysis. In various examples, the analytical sample is at room temperature prior to HPLC analysis. In various examples, the methods disclosed herein further comprise preparing a lyophilizate from the bulk lyophilization solution. In some cases, the lyophilizate contains 10 mg carfilzomib. In some cases, the lyophilizate contains 30 mg carfilzomib. In some cases, the lyophilizate contains 60 mg carfilzomib.

BRIEF DESCRIPTION OF THE FIGURES

[0003] Figure 1 shows carfilzomib concentration results for samples analyzed using a range of diluents containing varying percentages of acetonitrile by volume in water.

[0004] Figure 2 shows concentration of analytical sample solutions that were prepared with 50% v/v ACN diluent, from samples having a concentration at about 7.8 mg/mL, when the analytical sample is at 5°C prior to HPLC analysis, analyzed on Day 1 and Day 2.

WHAT IS CLAIMED:

1. A method for measuring a carfilzomib concentration of a sample comprising carfilzomib comprising the steps of

diluting the sample with a diluent comprising water and 25% to 40% by volume acetonitrile to form an analytical sample; and

subjecting the analytical sample to high performance liquid chromatography (HPLC) to determine the carfilzomib concentration in the sample.

2. The method of claim 1, wherein the sample is obtained from carfilzomib compounding.

3. The method of claim 1, wherein the sample is obtained from a bulk lyophilization solution of carfilzomib.

4. The method of claim 1, wherein the sample is a solubilization sample.

5. The method of claim 1, wherein the sample is a post-dilution sample.

6. The method of any one of claims 1 to 5, wherein the diluent comprises water and 30% by volume acetonitrile.

7. The method of any one of claims 1 to 5, wherein the diluent comprises water and 40% by volume acetonitrile.

8. The method of any one of claims 1 to 7, wherein the method comprises a relative standard deviation (RSD) value of less than 2%.

9. The method of claim 8, wherein the RSD is less than 1%.

10. The method of claim 8, wherein the RSD is less than 0.5%.

11. The method of any one of claims 1 to 10, wherein the carfilzomib concentration is 3 mg/mL to 8 mg/mL.

12. The method of claim 11, wherein the carfilzomib concentration is 5 mg/mL to 6 mg/mL.

13. The method of any one of claims 1 to 12, wherein the temperature of the analytical sample is 2°C to 8 C prior to HPLC analysis.

14. The method of any one of claims 1 to 12, wherein the temperature of the analytical sample is at room temperature prior to HPLC analysis.

15. The method of any one of claims 3 to 14, further comprising the step of preparing a lyophilizate from the sample.

16. The method of claim 15, wherein the lyophilizate contains 10 mg carfilzomib.

17. The method of claim 15, wherein the lyophilizate contains 30 mg carfilzomib.

18. The method of claim 15, wherein the lyophilizate contains 60 mg carfilzomib.