SUMMARY

[0007] The present disclosure relates to topical pharmaceutical compositions comprising diethylene glycol monoethyl ether (DEGEE). The inventors of the present disclosure have made the surprising discovery that topical pharmaceutical compositions comprising diethylene glycol monoethyl ether (DEGEE) maintained at an acidic pH were fully preserved without the addition of a traditional antimicrobial preservative. In preferred examples, the pharmaceutical composition is maintained at a pH of less than about 6.3, or alternatively, less than about 6.0. In preferred examples, the pharmaceutical composition further comprises an emulsifier blend of cetearyl alcohol, dicetyl phosphate, and ceteth-10 phosphate, which is manufactured by Croda under the tradename Crodafos™ CES or Crodafos™ CES PHARMA.

[0008] In certain examples, the present disclosure relates to a topical pharmaceutical composition comprising a pharmaceutically effective amount of an active ingredient, diethylene glycol monoethyl ether, and water. The topical pharmaceutical composition has a pH that is less than or equal to 6.3, or alternatively less than or equal to 6.0. In certain examples, the pharmaceutical composition has a pH between 5.0 and 6.3 or alternatively, a pH between 5.0 and 6.0.

[0009] In certain examples, the pharmaceutical composition is a cream or gel.

[00010] In certain examples, the pharmaceutical composition satisfies the European Pharmacopeia Efficacy of Antimicrobial Preservation Criteria A and/or the United States Pharmacopeia ("USP") Criteria for Category 2 (Topical) Products. The pharmaceutical composition can satisfy the European Pharmacopeia Efficacy of Antimicrobial Preservation Criteria A and/or USP Criteria for Category 2 Products despite the fact that the formulation does not comprise an antimicrobial preservative. In certain examples, the pharmaceutical composition does not comprise traditional antimicrobial preservatives such as benzyl alcohol,

parabens (e.g., methylparaben, ethylparaben, propylparaben, and butylparaben), phenoxyethanol, propylene glycol, bronopol, benzylkonium chloride, or benzethonium chloride.

[00010a] In one aspect, the present disclosure relates to a topical pharmaceutical composition comprising: a pharmaceutically effective amount of an active ingredient; diethylene glycol monoethyl ether; and water, and wherein the topical pharmaceutical composition has a pH that is less than or equal to 6.3, wherein the pharmaceutical composition satisfies European Pharmacopeia Efficacy of Antimicrobial Preservation Criteria A, and wherein the pharmaceutical composition does not comprise an antimicrobial preservative.

[00011] In certain examples, the pharmaceutical composition comprises between about 10% and about 40% w/w of diethylene glycol monoethyl ether. In certain examples, the pharmaceutical composition comprises between about 20% and about 35% w/w of diethylene glycol monoethyl ether.

[00012] In certain examples, the pharmaceutical composition further comprises an emulsifier blend of cetearyl alcohol, dicetyl phosphate, and ceteth-10 phosphate. In certain examples, the pharmaceutical composition comprises between about 8% and about 15% w/w of the emulsifier blend of cetearyl alcohol, dicetyl phosphate, and ceteth-10 phosphate.

[00013] In certain examples, the active ingredient is a poorly water-soluble drug. In certain examples, the active ingredient is roflumilast.

[00014] In certain examples, the present disclosure relates to a topical pharmaceutical composition comprising a pharmaceutically effective amount of an active ingredient, diethylene glycol monoethyl ether, an emulsifier blend of cetearyl alcohol, dicetyl phosphate, and ceteth-10 phosphate, and water. In certain examples, the

topical pharmaceutical composition has a pH that is less than or equal to 6.3, or alternatively, less than or equal to 6.0. In certain examples, the pharmaceutical composition has a pH between 5.0 and 6.0, or alternatively, a pH between 5.0 and 6.3.

[00015] In certain examples, the pharmaceutical composition is a cream or gel.

[00016] In certain examples, the pharmaceutical composition satisfies the European Pharmacopeia Efficacy of Antimicrobial Preservation Criteria A and/or the USP Criteria for Category 2 (Topical) Products. The pharmaceutical composition can satisfy the European Pharmacopeia Efficacy of Antimicrobial Preservation Criteria A and/or USP

Criteria for Category 2 Products despite the fact that the formulation does not comprise an antimicrobial preservative. In certain examples, the pharmaceutical composition does not comprise traditional antimicrobial preservatives such as benzyl alcohol, parabens (e.g., methylparaben, ethylparaben, propylparaben, and butylparaben), phenoxyethanol, propylene glycol, bronopol, benzylkonium chloride, or benzethonium chloride.

[00016a] In another aspect, the present disclosure relates to a topical pharmaceutical composition comprising: a pharmaceutically effective amount of an active ingredient; diethylene glycol monoethyl ether; an emulsifier blend of cetearyl alcohol, dicetyl phosphate, and ceteth-10 phosphate; and water, and wherein the pharmaceutical composition satisfies European Pharmacopeia Efficacy of Antimicrobial Preservation Criteria A.

[00017] In certain examples, the pharmaceutical composition comprises between about 10% and about 40% w/w of diethylene glycol monoethyl ether. In certain examples, the pharmaceutical composition comprises between about 20% and about 35% w/w of diethylene glycol monoethyl ether. In certain examples, the pharmaceutical composition comprises between about 8% and about 15% w/w of the emulsifier blend of cetearyl alcohol, dicetyl phosphate, and ceteth-10 phosphate.

[00018] In certain examples, the active ingredient is a poorly water-soluble drug. In certain examples, the active ingredient is roflumilast.

[00018a] In another aspect, the present disclosure relates to a topical pharmaceutical composition comprising: roflumilast; diethylene glycol monoethyl ether; an emulsifier blend of cetearyl alcohol, dicetyl phosphate, and ceteth-10 phosphate; and water, wherein the topical pharmaceutical composition has a pH that is less than or equal to 6.3, and wherein the pharmaceutical composition satisfies European Pharmacopeia Efficacy of Antimicrobial Preservation Criteria A.

DETAILED DESCRIPTION OF THE INVENTION

[00019] Before the present invention is described in detail below, it is to be understood that this invention is not limited to the particular methodology, protocols, and reagents described herein as these may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims. Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs.

[00020] All publications, patents and patent applications cited herein are hereby incorporated by reference in their entirety unless otherwise stated. Where the same term is defined in a publication, patent, or patent application and the present disclosure incorporated