DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 202535

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April 5, 2017

Re: Exclusivity decision for Prepopik on remand

Dear Mr. Thygesen:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Prepopik (sodium picosulfate, magnesium oxide, citric acid) and approved under section 505(c) on July 16, 2012.

Please also refer to the September 9, 2016 Memorandum Opinion of the U.S. District Court for the District of Columbia in *Ferring Pharms, Inc. v. Burwell*, CA No. 15-0802 (RC) (D.D.C. Sept. 9, 2016). As you know, on November 7, 2016, the government filed a notice of appeal from the district court's decision, but the appeal was voluntarily dismissed on March 17, 2016. Accordingly, the matter is currently with the Food and Drug Administration (FDA or the Agency) on remand from the district court.

Pursuant to the district court's order, FDA is evaluating the eligibility of Prepopik for 5-year new chemical entity (NCE) exclusivity. As you also know, throughout these proceedings, Ferring has asserted that Prepopik could potentially be eligible for 5-year NCE exclusivity based on the fact that sodium picosulfate is a previously unapproved active ingredient.[1] Nevertheless, the proper test is whether sodium picosulfate contains any previously approved active moiety,[2] as Ferring has also acknowledged.[3] In the past, FDA has taken the position that sodium picosulfate did not

[1] See, e.g., Ferring Petition, Docket FDA-2013-P-0119, at 2 (Jan. 29, 2013) ("Sodium picosulfate is a novel active ingredient that has never been a component of an approved NDA. Both magnesium oxide and citric acid are prodrugs of the active ingredient magnesium citrate, and both have previously been components of approved NDAs."); Complaint, CA No. 15-0802, at ¶ 3 (RC) (D.D.C. June 1, 2015) ("PREPOPIK® is a fixed-dose combination drug product that contains a novel active ingredient, sodium picosulfate, as well as ingredients that FDA had previously approved in other drug applications.").

[2] See 21 CFR 314.3 (defining active moiety as the molecule or ion, excluding, among other things, appended portions of a drug substance that cause the molecule to be an ester or salt).

[3] See Complaint at ¶ 27 ("Thus, the only permissible interpretation of Section 505(j)(5)(F)(ii) is that a drug substance is entitled to five-year exclusivity if it contains no active moiety that has previously been approved."), ¶ 30 ("A drug product contains one or more drug substances, which contain one or more active moieties. If any drug substance in the product is novel, that is contains no previously approved active moiety, the product must be awarded NCE exclusivity.").

contain any such active moiety.[4] Upon further review, it appears that bis-(p-hydroxyphenyl)-pyridyl-2-methane (BPHM, CAS: 603-41-8, UNII: R09078E41Y), the active moiety of sodium picosulfate (CAS: 10040-45-6, UNII: VW106606Y8), also seems to be the active moiety in bisacodyl [(4,4'-diacetoxydiphenyl(2-pyridyl)methane), CAS: 603-50-9, UNII: 10X0709Y6I. Bisacodyl was approved in Halflytely (NDA 021551) on May 10, 2004.[5] Based on the foregoing, it appears that Prepopik does not contain any active ingredient which contains no previously approved active moiety.

Given the unusual circumstances in which this issue has arisen, FDA would like to give you (and other stakeholders) an opportunity to provide your views before the Agency finalizes its remand decision. We are also aware of the need to resolve this issue expeditiously. Therefore, within fourteen days, please submit any scientific and/or legal arguments or analysis regarding Prepopik's eligibility for 5-year NCE exclusivity to Orange Book staff at OrangeBook@fda.hhs.gov

Sincerely,

Kendra S. Stewart -A

Digitally signed by Kendra S. Stewart -A
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300222579, cn=Kendra S. Stewart -A
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[4] See, e.g., FDA, Consolidated Response, Docket Nos. FDA-2013-P-0058 & FDA-2013-P-0119, at 1 (Oct 10.2014) ("Prepopik . . . contains sodium picosulfate, which was a new active moiety at the time of approval.").
[5] Please see Appendix A for a depiction of the chemical structures of sodium picosulfate and bisacodyl.

APPENDIX A -- Chemical structures of the relevant molecules.