IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

APOTEX CORP.
APOTEX, INC.
Petitioner
v.
ALLERGAN, INC.
Patent Owner

U.S. Patent No. 8,633,162 to Acheampong *et al*.
Issue Date: January 21, 2014
Title: Methods of Providing Therapeutic Effects Using Cyclosporin Components

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Inter Partes Review No. Unassigned

Petition for *Inter Partes* Review of U.S. Patent No. 8,633,162 Under 35 U.S.C. §§ 311-319 and 37 C.F.R. §§ 42.1-.80, 42.100-.123

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I. INTRODUCTION

APOTEX CORP. and APOTEX, INC. petition for *Inter Partes* Review, seeking cancellation of claims of U.S. Patent No 8,633,162 to Acheampong *et al*. ("the '162 patent") (APO1001), which is purportedly owned by ALLERGAN, INC.

II. OVERVIEW

The claims of the '162 patent should be cancelled. They recite methods of administering topical ophthalmic emulsions known to be useful for treating dry eye disease (also referred to as keratocunjunctivitis sicca or KCS (APO1003, 1:14-15) and increasing tear production in humans by administering the emulsion twice a day. APO1003, 1:14-15;APO1005, ¶¶4 and 15. The claimed methods use emulsions that contain cyclosporin A (CsA) at 0.05% and castor oil at 1.25%, along with excipients at identical concentrations to those taught in the art. (Percent values refer to percent weight throughout this petition.) APO1005, ¶¶4 and 168.

Both CsA and castor oil were known in the prior art as useful agents to treat dry eye/KCS and increase tear production. APO1002, 11, 6:25-28; APO1003, 4, 5:9-12; APO1004, 1; APO1005, ¶¶17, 58, and 63. A prior art publication of clinical trials testing 0.05% CsA in a castor oil emulsion reported that such emulsions were safe and efficacious when administered twice a day. APO1004, 1; APO1005, ¶17. And prior art patents taught the use of 1.25% castor oil emulsions with CsA for increasing tear production and for the treatment of dry eye/KCS.

APO1002, 10, 3:49-53; APO1003, 3, 4:33-43; APO1005, ¶60. So, before the September 2003 alleged priority date of the challenged patent, POSAs were well aware of methods of treatment using ophthalmically-acceptable castor oil emulsion formulations containing 0.05% CsA for treatment of dry eye disease/KCS and increasing tear production. APO1003, 3, 4:33-43; APO1004, 1; APO1005, ¶60.

Furthermore, during prosecution of a parent application, Allergan *admitted* that its emulsions containing 0.05% CsA and 1.25% castor oil would have been "readily envisaged" and "would have been obvious" and that the differences between the claimed formulation and the prior art "are insignificant." APO1019, 951; APO1005, ¶98. Allergan also admitted that there would have been a reasonable expectation of success in arriving at a formulation containing 0.05% CsA and 1.25% castor oil because the differences between such a formulation and the prior art "are too small to believe otherwise." APO1019, 951; APO1005, ¶98.

During prosecution of the challenged claims, Allergan asserted that it was unexpected that the combination of 1.25% castor oil and 0.05% CsA would be "*equally* or more therapeutically effective for the treatment of dry eye/keratoconjunctivitis sicca than the [prior art] formulation containing 0.10% by weight cyclosporin A and 1.25% by weight castor oil. . . ." APO1019, 2133, ¶14 (emphasis added). But equivalent performance does not meet the standard for unexpectedly superior results, and in any case, does not control the conclusion of

obviousness over a strong case based on the prior art. *Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc.* 752 F.3d 967, 977 (Fed. Cir. 2014); *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1372 (Fed. Cir. 2007).

Allergan submitted data purporting to show that the tissue penetration of the CsA contained in the prior art 0.1% CsA emulsion was superior to the tissue penetration of the emulsion of the claimed methods containing 0.05% CsA. APO1019, 2157, ¶7; APO1005, ¶242. And because less CsA from the 0.05% CsA emulsion penetrated tissue compared to the 0.10% CsA emulsion, Allergan argued that it was surprising that the claimed (0.05% CsA) composition had equal or better clinical therapeutic value. APO1019, 2157, ¶7; APO1005, ¶242. But as discussed below, Allergan's arguments do not show unexpectedly superior results because the prior art taught that increasing the CsA concentration beyond 0.05% had no clinical benefit, and regardless, Allergan did not show its results were *superior* to the prior art formulations. APO1004, 1; APO1005, ¶242; APO1007, ¶45.

In contrast to Allergan's arguments before the Patent Office, prior art studies demonstrated that 0.05% CsA emulsions were at least as effective in treating dry eye as 0.10% CsA emulsions, or other emulsions containing even more CsA. APO1004, 1; APO1023, 2; APO1005, ¶241. Therefore, POSAs were aware that, at 0.05%, CsA was already at the top of the dose response curve. APO1005, ¶241.

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