US008993548B2

(12) **United States Patent**
Bernick et al.

(10) **Patent No.: US 8,993,548 B2**
(45) **Date of Patent: *Mar. 31, 2015**

(54) **NATURAL COMBINATION HORMONE REPLACEMENT FORMULATIONS AND THERAPIES**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **14/475,814**

(22) Filed: **Sep. 3, 2014**

(65) **Prior Publication Data**

US 2014/0371182 A1 Dec. 18, 2014

Related U.S. Application Data

(60) Continuation of application No. 14/099,545, filed on Dec. 6, 2013, now Pat. No. 8,846,648, which is a division of application No. 13/684,002, filed on Nov. 21, 2012, now Pat. No. 8,633,178.

(60) Provisional application No. 61/662,265, filed on Jun. 20, 2012, provisional application No. 61/661,302, filed on Jun. 18, 2012, provisional application No. 61/563,408, filed on Nov. 23, 2011.

(51) **Int. Cl.**

A01N 45/00	(2006.01)
A61K 9/48	(2006.01)
A61K 31/57	(2006.01)
A61K 9/16	(2006.01)
A61K 31/565	(2006.01)
A61K 9/70	(2006.01)

(52) **U.S. Cl.**

CPC . ***A61K 31/57*** (2013.01); ***A61K 9/16*** (2013.01); ***A61K 31/565*** (2013.01); ***A61K 9/4858*** (2013.01); ***A61K 9/7023*** (2013.01)

USPC **514/169**; 424/452

(58) **Field of Classification Search**

CPC A61K 31/57; A61K 31/565

USPC 514/169; 424/452

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2,232,438	A		2/1941	Butenandt
4,900,734	A	*	2/1990	Maxson et al. 514/171
5,538,736	A		7/1996	Hoffmann et al.
5,556,635	A		9/1996	Istin et al.
5,580,572	A		12/1996	Mikler et al.
5,605,702	A		2/1997	Teillaud et al.
5,607,691	A		3/1997	Hale et al.
5,607,693	A		3/1997	Bonte et al.
5,609,617	A		3/1997	Shealy et al.
5,626,866	A		5/1997	Ebert et al.
5,653,983	A		8/1997	Meybeck et al.
5,660,839	A		8/1997	Allec et al.
5,662,927	A		9/1997	Ehrlich et al.
5,663,160	A		9/1997	Meybeck et al.
5,686,097	A		11/1997	Taskovich et al.
5,693,335	A		12/1997	Xia et al.
5,700,480	A		12/1997	Hille et al.
5,719,197	A		2/1998	Kanios et al.
5,770,220	A		6/1998	Meconi et al.
5,770,227	A		6/1998	Dong et al.
5,780,044	A		7/1998	Yewey et al.
5,780,050	A		7/1998	Jain et al.
5,788,984	A		8/1998	Guenther et al.
5,820,878	A		10/1998	Hirano et al.
5,840,327	A		11/1998	Gale et al.
5,843,468	A		12/1998	Burkoth et al.
5,843,979	A		12/1998	Wille et al.
5,858,394	A		1/1999	Lipp et al.
5,863,552	A		1/1999	Yue

(Continued)

FOREIGN PATENT DOCUMENTS

WO	WO9619975	7/1996
WO	WO0241878	5/2002

(Continued)

OTHER PUBLICATIONS

Abitec Corporation, Excipients for the Pharmaceutical Industry—Regulatory and Product Information, 2013, 2 pages.

Corbett et al., "Trends in Pharmacy Compounding for Women's Health in North Carolina: Focus on Vulvodynia," Southern Medical Journal, vol. 107, No. 7, Jul. 2014, pp. 433-436.

Shrier et al., "Mucosal Immunity of the Adolescent Female Genital Tract," Journal of Adolescent Health, 2003; 32:183-186.

Gattefossé Sas, Material Safety Data Sheet, Gelot 64, 2012, 8 pages.

Gattefossé Sas, Regulatory Data Sheet, Gelot 64, 2012, 6 pages.

Gattefossé Sas, Regulatory Data Sheet, Lauroglycol 90, 2012, 5 pages.

(Continued)

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(57) **ABSTRACT**

Estrogen and progesterone replacement therapies are provided herein. Among others, the following formulations are provided herein: solubilized estradiol without progesterone; micronized progesterone without estradiol; micronized progesterone with partially solubilized progesterone; solubilized estradiol with micronized progesterone; solubilized estradiol with micronized progesterone in combination with partially solubilized progesterone; and solubilized estradiol with solubilized progesterone.

6 Claims, 4 Drawing Sheets