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Crystal et al.

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(54) **NASAL DRUG PRODUCTS AND METHODS OF THEIR USE**

2015/0174061 A1 6/2015 Wyse et al.
2015/0258019 A1 9/2015 Crystal et al.
2016/0008277 A1 1/2016 Crystal et al.

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FOREIGN PATENT DOCUMENTS

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CN 1575795 2/2005
EP 1681057 B1 8/2008
WO WO 8203768 A1 11/1982
WO WO 9830211 A1 7/1998
WO WO 0062757 A1 10/2000
WO WO 0074652 A1 12/2000
WO WO 0158447 A1 8/2001
WO WO 0182931 A1 11/2001
WO WO 0211778 A1 2/2002
WO WO 03084520 A2 10/2003
WO WO 2004054511 A2 7/2004
WO WO 2005020906 A2 3/2005
WO WO 2006089973 A2 8/2006
WO WO 2007083073 A1 7/2007
WO WO 2009040595 A1 2/2009
WO WO 2012026963 A2 3/2012
WO WO 2012156317 A2 11/2012
WO WO 2013128447 A1 9/2013
WO WO 2014016653 A1 1/2014
WO WO 2015095644 A1 6/2015
WO WO 2015136373 A1 9/2015
WO WO 2016007729 A1 1/2016

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This patent is subject to a terminal disclaimer.

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(60) Provisional application No. 61/953,379, filed on Mar. 14, 2014.

(51) **Int. Cl.**
A61M 31/00 (2006.01)
A61M 5/00 (2006.01)
A61F 13/00 (2006.01)
A61K 31/56 (2006.01)
A61K 47/02 (2006.01)

(52) **U.S. Cl.**
CPC **A61M 31/00** (2013.01); **A61K 47/02** (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,181,726 A 1/1980 Bernstein
4,464,378 A 8/1984 Hussain
5,866,154 A 2/1999 Bahal et al.
9,192,570 B2* 11/2015 Wyse A61K 9/0043
2003/0077300 A1 4/2003 Wermeling
2006/0120967 A1 6/2006 Namburi et al.
2009/0017102 A1 1/2009 Stinchcomb et al.
2010/0113495 A1 5/2010 Wermeling et al.
2010/0168147 A1 7/2010 Chapleo et al.
2010/0331354 A1 12/2010 Wermeling
2011/0046172 A1 2/2011 Chapleo et al.
2012/0270895 A1 10/2012 Wermeling
2013/0023825 A1 1/2013 Edwards et al.

OTHER PUBLICATIONS

U.S. Appl. No. 14/942,344, filed Nov. 16, 2015, Crystal et al.
Walley, A Y et al., "Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis," *BMJ* 346:f174, (Published Jan. 31, 2013).
Walley A Y et al., "Opioid overdose prevention with intranasal naloxone among people who take methadone," *J Subst Abuse Treat* 44:2, 241-47 (Epub Sep. 12, 2012).
Weber J M et al., "Can nebulized naloxone be used safely and effectively by emergency medical services for suspected opioid overdose?" *Prehosp Emerg Care* 16:2, 289-92 (Epub Dec. 22, 2011).
Merlin M A et al., "Intranasal naloxone delivery is an alternative to intravenous naloxone for opioid overdoses," *Am J Emerg Med* 28:3, 296-303 (Epub Jan. 28, 2010).
Kerr D et al., "Randomized controlled trial comparing the effectiveness and safety of intranasal and intramuscular naloxone for the treatment of suspected heroin overdose," *Addiction* 104:12, 2067-74 (Epub Nov. 9, 2009).
Robertson T M, "Intranasal naloxone is a viable alternative to intravenous naloxone for prehospital narcotic overdose," *Prehosp Emerg Care* 13:4, 512-15 (Published Oct. 2009).

(Continued)

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(57) **ABSTRACT**

Drug products adapted for nasal delivery, comprising a pre-primed device filled with a pharmaceutical composition comprising an opioid receptor antagonist, are provided. Methods of treating opioid overdose or its symptoms with the inventive drug products are also provided.

45 Claims, 7 Drawing Sheets

(56)

References Cited

OTHER PUBLICATIONS

Doe-Simkins M et al., "Saved by the nose: bystander-administered intranasal naloxone hydrochloride for opioid overdose," *Am J Public Health* 99:5, 788-91 (published May 2009).

Heard C et al., "Intranasal flumazenil and naloxone to reverse over-sedation in a child undergoing dental restorations," *Paediatr Anaesth* 19:8 795-99 (published Aug. 2009).

Dowling J et al., "Population pharmacokinetics of intravenous, intramuscular, and intranasal naloxone in human volunteers," *Ther Drug Monit* 30:4 490-96 (published Aug. 2008).

Ashton H et al., "Best evidence topic report. Intranasal naloxone in suspected opioid overdose," *Emerg Med J* 23:3, 221-23 (published Mar. 2006).

Barton E D et al., "Efficacy of intranasal naloxone as a needleless alternative for treatment of opioid overdose in the prehospital setting," *J Emerg Med* 29:3, 265-71 (published Oct. 2005).

Kelly A M et al., "Randomised trial of intranasal versus intramuscular naloxone in prehospital treatment for suspected opioid overdose," *Med J Aust* 182:1 24-27 (published Jan. 3, 2005).

Kelly A M et al., "Intranasal naloxone for lite threatening opioid toxicity," *Emerg Med J* 19:4, 375 (published Jul. 2002).

Barton E D et al., "Intranasal administration of naloxone by paramedics," *Prehosp Emerg Care* 6:1, 54-58 (published Jan. 2002).

Loimer N et al., "Nasal administration of naloxone is as effective as the intravenous route in opiate addicts," *Int J Addict* 29:6, 819-27 (published Apr. 1994).

Loimer N et al., "Nasal administration of naloxone for detection of opiate dependence," *J Psychiatr Res* 26:1, 39-43 (published Jan. 1992).

Bailey A M et al., "Naloxone for opioid overdose prevention: pharmacists' role in community-based practice settings," *Ann. Pharmacother* 48:5, 601-06 (published May 2014).

Wermeling D P et al., "A response to the opioid overdose epidemic: naloxone nasal spray," *Drug Delivery Transl. Res.* 3:1, 63-74 (published Feb. 1, 2013).

Wermeling D P et al., "Opioid harm reduction strategies: focus on expanded access to intranasal naloxone," *Pharmacotherapy* 30:7, 627-31, 2010.

Aptar UnitDose and BiDose product information sheet, available at www.aptar.com/docs/pharma-prescription/uds-bds-datasheet.pdf, publication date unknown, last accessed Mar. 26, 2015.

International Search Report and Written Opinion for Application No. IB/2015/000941; Sep. 2, 2015, 11 pgs.

Notice of Allowance, U.S. Appl. No. 14/659,472, Oct. 9, 2015, 9 pgs.

Corrected Notice Allowance, U.S. Appl. No. 14/659,472, Nov. 2015, 9 pgs.

U.S. Appl. No. 15/183,441, filed Jun. 14, 2016, Keegan F. et al. Krieter P. et al., Pharmacokinetic Properties and Human Use Characteristics of an FDA Approved Intranasal Naloxone Product for the Treatment of Opioid Overdose, *J Clin Pharmacol*, 2016, pp. 1-11. International Search Report and Written Opinion for WO2016/007729, Dec. 4, 2015, 16 pages.

* cited by examiner

FIG. 1

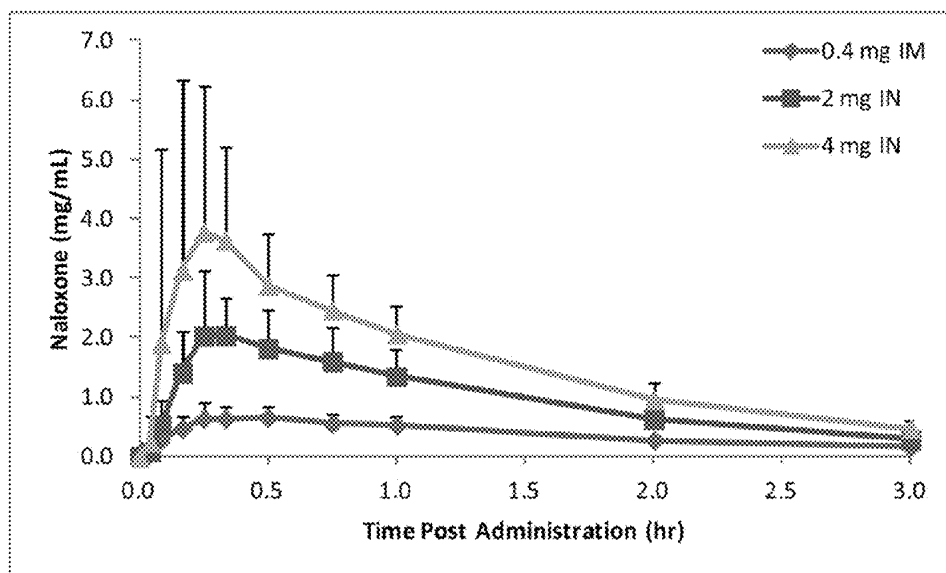


FIG. 2

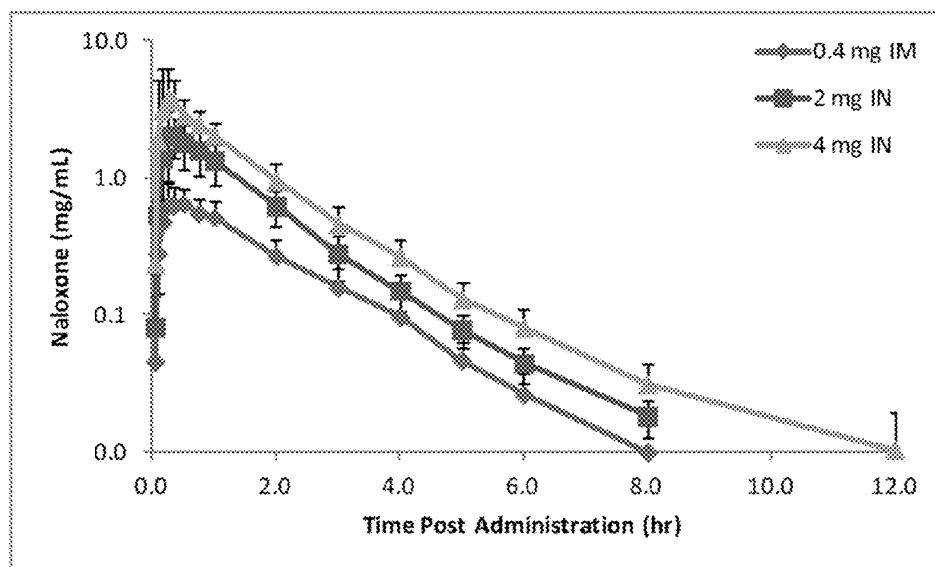
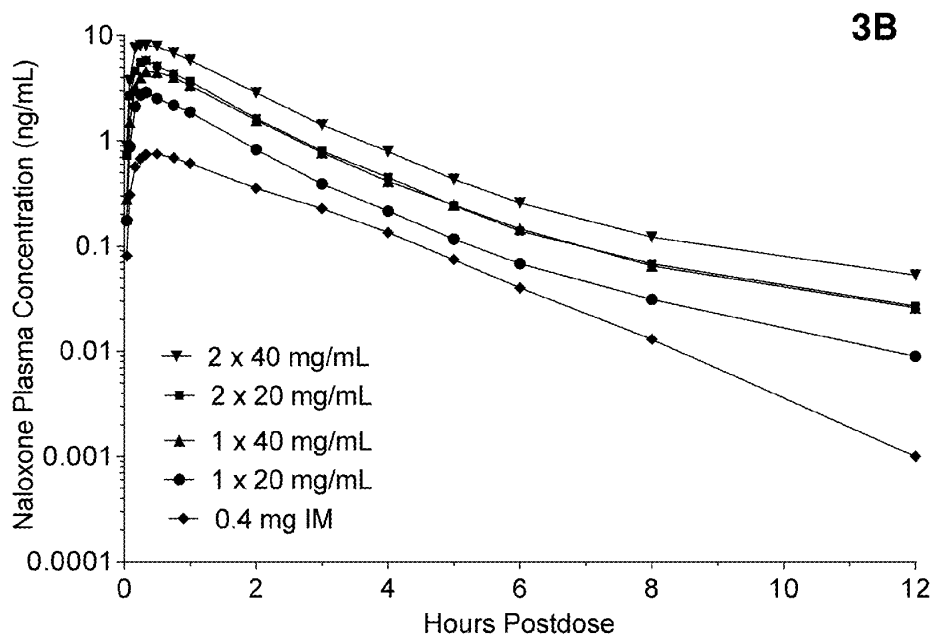
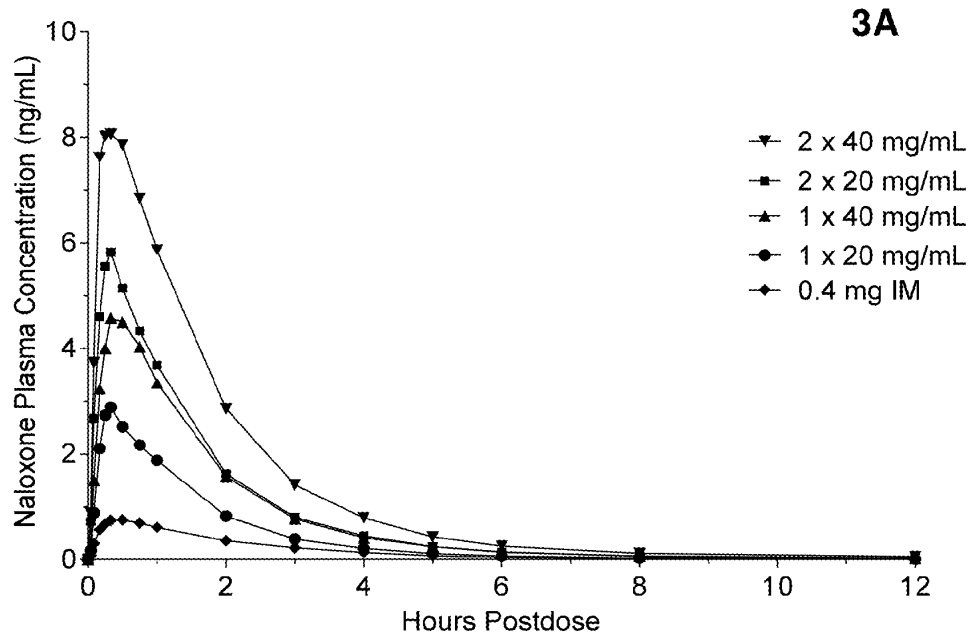


FIG. 3



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