

# New Therapeutic Options for Alcohol Dependence: Long-Acting Intramuscular Formulations of Naltrexone

James C. Garbutt, M.D.

Results of oral therapy for alcohol dependence have been inconsistent, in part because of poor medication adherence. A newly approved, extended-release intramuscular formulation of naltrexone (XR-NTX) may have advantages over oral formulations in terms of adherence. One randomized, double-blind, placebo-controlled trial demonstrated that treatment with XR-NTX significantly decreased the number of heavy-drinking days compared with placebo treatment among patients who had a current DSM-IV diagnosis of alcohol dependence. Another trial, of a different investigational long-acting intramuscular formulation of naltrexone (poly [DL-] lactide polymer; DL-NTX), found that time to first drinking day was significantly greater among alcohol-dependent (DSM-IV) subjects using DL-NTX than among those using placebo. Time to first drinking day and cumulative abstinent days were significantly greater among alcohol dependent (DSM-IV) subjects using DL-NTX than among those using placebo. However, the primary outcome measure, cumulative non-heavy drinking days, was not significantly different between the DL-NTX and the placebo groups. Treatment with long-acting intramuscular formulations of naltrexone is generally well tolerated. Nausea, headache, injection-site reactions, and fatigue are the most common adverse events.

*(J Clin Psychiatry 2006;67[suppl 14]:30-34)*

**A**lcohol dependence is increasingly recognized as a chronic disease in which genetic vulnerability and social and environmental factors are involved in the etiology and course of the disease.<sup>1</sup> As with other chronic diseases, long-term comprehensive management strategies for alcohol dependence are needed to achieve and sustain the benefits of treatment.<sup>2</sup> These strategies include counseling, behavioral therapy, and self-help groups. In addition, pharmacologic agents are an important therapeutic option that can be used by primary care practitioners and addiction specialists in conjunction with the other approaches.<sup>3</sup> Naltrexone, an opioid antagonist, has been approved as an oral formulation for the treatment of alcohol dependence for over 10 years. Recently, naltrexone for extended-release injectable suspension (XR-NTX) has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of alcohol dependence and represents a new treatment opportunity.

Oral naltrexone has been indicated for the treatment of alcohol dependence since 1994. Recently, the efficacy of oral naltrexone was confirmed in the Combined Pharmacotherapies and Behavioral Interventions for Alcohol

Dependence (COMBINE) study,<sup>4</sup> in which naltrexone administered in the context of a compliance-enhancing therapy called *medical management* showed the greatest reductions in heavy drinking compared with placebo or acamprosate. Heavy drinking was defined as 5 drinks or more per day for men and 4 drinks or more per day for women. Reduction in heavy drinking is meaningful for individual patients and for public health because heavy drinking is highly correlated with negative life consequences such as impaired driving, interpersonal problems, and injuries.<sup>5</sup> In addition, increased risk of a variety of adverse health consequences has been detected with each additional alcoholic drink per day.<sup>6</sup> Despite these positive findings for naltrexone, its use has been limited clinically, in part because of lack of knowledge among practitioners and patients of the efficacy and tolerability of naltrexone.<sup>7</sup> Additionally, problems with efficacy have been reported and may be due to poor adherence to a daily medication regimen<sup>8,9</sup> or to adverse events (AEs) associated with the medication.<sup>10,11</sup> In addition, treatment may directly conflict with the behaviors and rewards associated with alcohol consumption.<sup>12</sup> If a medication diminishes or alters the desirable effects of alcohol, the patient may discontinue treatment.<sup>13</sup> Patients with lower rates of adherence to oral naltrexone treatment have been shown to have higher rates of relapse than patients who adhere to the drug regimen.<sup>9</sup> (For additional information about treatment adherence in alcohol dependence, see in this supplement "Improving Medication Adherence in Alcohol Dependence" by Helen M. Pettinati, Ph.D.<sup>14</sup>)

---

*From the Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, N.C.*

*Supported by an educational grant from Alkermes, Inc. and Cephalon, Inc.*

*Corresponding author and reprints: James C. Garbutt, M.D., CB #7160, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599-7160 (e-mail: jc\_garbutt@med.unc.edu).*

**Table 1. Adverse Events According to Treatment: DL Naltrexone (DL-NTX) (N = 167) Versus Placebo (N = 166)<sup>a</sup>**

| Adverse Event                        | DL-NTX, N (%) | Placebo, N (%) | p Value |
|--------------------------------------|---------------|----------------|---------|
| One or more injection site reactions | 123 (73.7)    | 103 (62.1)     | < .03   |
| Headache                             | 37 (22.2)     | 33 (19.9)      | .69     |
| Nausea                               | 23 (13.8)     | 17 (10.2)      | .40     |
| Fatigue                              | 19 (11.4)     | 13 (7.8)       | .35     |
| Back pain                            | 16 (9.6)      | 9 (5.4)        | .22     |
| Nasopharyngitis                      | 15 (9.0)      | 23 (13.9)      | .17     |
| Upper abdominal pain                 | 9 (5.4)       | 0              | .02     |
| Chest pain                           | 1 (0.6)       | 7 (4.2)        | .03     |
| Irritability                         | 0             | 5 (3.0)        | .03     |

<sup>a</sup>Adapted with permission from Kranzler et al.<sup>13</sup>  
Abbreviation: DL = poly (DL-) lactide polymer.

Since the 1970s, efforts have been made to develop a parenteral extended-release formulation of naltrexone. Two formulations have been tested in phase 2 and phase 3 trials. One is a preparation of microspheres of poly (DL-) lactide polymers (DL-NTX), and the other is a preparation of microspheres of polylactide-co-glycolide (PLG) polymers (XR-NTX) that has been recently approved by the FDA to treat alcohol dependence.<sup>15</sup> This latter formulation releases naltrexone from drug-encapsulated microspheres for 1 month after a single injection.<sup>16</sup> Once injected into the body, PLG, a commonly used biodegradable substance, slowly hydrolyzes into lactic and glycolic acids, which are further metabolized into water and carbon dioxide. As the polymer degrades, naltrexone is released continuously by the microspheres.<sup>17</sup>

Injectable, long-acting medications may have advantages over oral medications because bioavailability is maintained over time and medication adherence problems related to fluctuating patient motivation and daily dosing decisions are minimized. Long-acting formulations also can overcome problems with oral drug absorption, yielding more predictable and consistent plasma concentrations.<sup>18</sup>

## PIVOTAL CLINICAL TRIALS

### DL Naltrexone (DL-NTX)

**Trial design.** Kranzler et al.<sup>13</sup> in 2004 reported the results of a phase 3, multicenter, double-blind, placebo-controlled trial of the investigational intramuscular DL-NTX in 333 patients who had a current diagnosis of alcohol dependence defined by the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV). Eighteen patients were excluded from the efficacy analysis but included in the safety analysis because of protocol violations at one site. For efficacy, the trial compared DL-NTX (N = 158) with placebo (N = 157) in patients who had at least 3 consecutive days of abstinence during the screening period and who then tolerated 4 days of 50 mg oral naltrexone. Both groups received monthly injections for 3 months. At the start of the study, patients in the nal-

trexone group received 300 mg of DL-NTX (two 150-mg intramuscular injections) followed by monthly 150-mg injections. Placebo patients received 2 injections at the start of the study, which were followed by single monthly injections. All patients also received an adaptation of motivational enhancement therapy. The primary outcome measure was the cumulative number of non-heavy-drinking days (heavy drinking was defined as  $\geq 5$  drinks/day for men and  $\geq 4$  drinks/day for women). The secondary outcome measure was cumulative abstinent days.

**Efficacy results.** No significant treatment group differences were seen in the primary outcome measure, cumulative non-heavy-drinking days ( $p = .29$ ); 23% of the DL-NTX group reported no heavy drinking over the 3 months compared with 16% of placebo subjects ( $p = .12$ ). However, several secondary measures showed evidence of a positive DL-NTX effect. There was an increase in time to first heavy drinking in the DL-NTX group compared with the placebo group (median, 11 days vs. 6 days;  $p = .05$ ). There was a significant benefit for the DL-NTX group in time to any drinking (median, 5 days vs. 3 days;  $p = .003$ ), and the DL-NTX group had more cumulative abstinent days (mean, 52.8 vs. 45.6 days;  $p = .018$ ) compared with placebo. In addition,  $\gamma$ -glutamyltransferase (GGT) level, which when elevated can be an indicator of heavy drinking, decreased significantly over the course of the study for both groups ( $p < .001$ ). The reduction was 15% greater in the DL-NTX group compared with the placebo group.

**Adverse events.** There were no significant differences between the DL-NTX and placebo groups in terms of serious adverse events (SAEs) or AEs other than injection site reactions. In the DL-NTX group, a significantly greater percentage of patients reported 1 or more injection site reactions compared with the placebo group ( $p < .03$ ). The most common injection site reactions in the DL-NTX group were pain, induration, and contusion, but none of these reactions were significantly more prevalent compared with placebo. Overall, the most common AEs from naltrexone were headache, nausea, and fatigue (Table 1).

### XR Naltrexone (XR-NTX)

**Trial design.** Garbutt et al.<sup>2</sup> in 2005 reported the results of a 6-month, multicenter, randomized, double-blind, placebo-controlled study of the efficacy and safety of 2 doses (380 mg or 190 mg) of XR-NTX versus matched volumes of placebo injections (4 mL and 2 mL). The study involved 624 subjects: 423 men and 201 women, 18 years and older, with a current diagnosis of alcohol dependence defined by the DSM-IV. Most participants were actively drinking at study initiation; only about 8% of patients were abstinent for the week prior to study start. For a period of 6 months, patients received XR-NTX every 4 weeks and standardized supportive therapy (12 sessions) using the BRENDA (Biopsychosocial, Report, Empathy, Needs, Direct Advice, and Assessment) model,<sup>19</sup> a 6-stage,

**Table 2. Primary and Secondary Efficacy Outcomes: Intramuscular Extended-Release Naltrexone 380 mg Versus Placebo<sup>a</sup>**

| Outcome                         | Hazard Ratio (95% CI) | p Value |
|---------------------------------|-----------------------|---------|
| Primary outcome, overall        |                       |         |
| Event rate of heavy drinking    | 0.75 (0.60 to 0.94)   | .02     |
| 7-Day lead-in drinking subgroup |                       |         |
| Yes (N = 571)                   | 0.79 (0.62 to 1.00)   | .05     |
| No (N = 53)                     | 0.20 (0.07 to 0.62)   | .005    |
| Secondary outcomes, overall     |                       |         |
| Risky drinking <sup>b</sup>     | 0.90 (0.76 to 1.07)   | .23     |
| Nonabstinent days               | 0.96 (0.83 to 1.11)   | .58     |

<sup>a</sup>Adapted with permission from Garbutt et al.<sup>2</sup> Copyright ©2005 American Medical Association. All rights reserved.

<sup>b</sup>National Institute on Alcohol Abuse and Alcoholism definition of > 2 drinks/day for men and > 1 drink/day for women.

Abbreviation: CI = confidence interval.

low-intensity intervention designed to facilitate direct feedback of addiction-related consequences.

In this study of XR-NTX,<sup>2</sup> the primary efficacy endpoint was the event rate of heavy drinking, which combined the frequency and pattern of heavy-drinking days ( $\geq 5$  drinks/day for men and  $\geq 4$  drinks/day for women) for the 24 weeks of treatment. Secondary study endpoints included the rate of risky-drinking days (> 2 drinks/day for men and > 1 drink/day for women) and of any-drinking days. Exploratory endpoints included changes in serum GGT concentration over time and time to study discontinuation.

**Efficacy results.** Retention rates were similar across the 3 groups, with approximately 65% of subjects in each group receiving all 6 injections and 60% of subjects in each group completing the study.

Patients treated with XR-NTX 380 mg experienced a 25% greater reduction in the rate of heavy drinking compared with placebo-treated patients ( $p = .02$ ) (Table 2). Patients treated with XR-NTX 190 mg reported a 17% greater reduction in the rate of heavy drinking than that reported by placebo-treated patients ( $p = .07$ ). These numbers represent mean reductions, which may have been disproportionately affected by the patients who were drinking most heavily. Thus, if the median number of heavy-drinking days is considered across the groups, the 380-mg XR-NTX group had a 48% greater reduction in heavy-drinking days compared with the placebo group. Neither the rate of risky drinking nor the rate of any drinking was significantly lower with either dose of XR-NTX compared with placebo. During the study, an overall 15% reduction in GGT level was observed for all participants.

Interactions with 3 pretreatment factors defined before randomization were also assessed. These factors were sex, pretreatment abstinence (no drinking 7 days before the first randomized injection), and having a treatment goal of abstinence. Treatment effects were highly significant among men receiving XR-NTX 380 mg compared with those receiving placebo ( $p < .001$ ) and were greater for

patients with pretreatment abstinence ( $N = 53$ ) ( $p = .005$ ) than for patients who drank during the lead-in period ( $N = 571$ ) ( $p = .05$ ). In patients who were abstinent for 1 week prior to treatment and received XR-NTX 380 mg, there was an 80% greater reduction in heavy drinking compared with patients receiving placebo ( $p = .005$ ); in patients who did not abstain and received XR-NTX, the reduction was still significant ( $p = .05$ ) but of a lesser magnitude (21% reduction).

In a retrospective analysis of this data set, O'Malley et al.<sup>20</sup> examined heavy drinking and abstinence in patients who had abstained from alcohol 4 days before treatment ("4-day lead-in abstinence"). The 4-day lead-in abstinence group represented a larger data set ( $N = 82$ ) than did the 7-day lead-in abstinence analysis reported by Garbutt et al.<sup>2</sup> Compared with patients who did not abstain, patients in all groups (active and placebo) who abstained for 4 days before treatment initiation had greater improvements in heavy drinking and abstinence measures.<sup>20</sup> Subjects who abstained from drinking and received XR-NTX had a 74% greater reduction in heavy drinking compared with abstaining placebo subjects. Subjects who did not abstain and received XR-NTX had a 19% greater reduction in heavy drinking compared with non-abstaining placebo subjects. Overall, the percentage of patients who maintained complete abstinence during the trial did not differ significantly among the groups (7% in the 380-mg XR-NTX group, 6% in the 190-mg XR-NTX group, and 5% in the placebo group). It is of interest that subjects who received XR-NTX 380 mg and who were actively drinking at the time of injection showed reductions in heavy drinking but not a greater likelihood of sustained abstinence, whereas those who initiated abstinence prior to the injection had marked improvements in heavy drinking and were more likely to have sustained abstinence. These findings point to the importance of the motivation and state of the patient at the time of injection in determining the type of response one might anticipate.

**Adverse events.** The most common adverse events for XR-NTX were nausea, headache, and fatigue; nausea and fatigue were significantly more common in the 380-mg XR-NTX group compared with placebo (Table 3). Nausea was mild or moderate in approximately 95% of cases, and most of the episodes occurred only during the first month of treatment. The most common injection site reaction was tenderness. Seven (1.1%) of the patients discontinued injections because of site reactions: 4 patients in the 380-mg and 2 in the 190-mg XR-NTX groups, and 1 patient in the 4-mL placebo group. The percentage of patients who experienced SAEs during treatment was similar among the treatment groups. The most common SAE was hospitalization for alcohol detoxification. Two SAEs were judged by the investigators to be possibly related to the study medication. There were 1 diagnosed case and 1 suspected case of eosinophilic pneumonia. Both cases required hos-

Table 3. Adverse Events for XR-NTX 380 mg (N = 205), XR-NTX 190 mg (N = 210), and Placebo (N = 209)<sup>a</sup>

| Adverse Event                                 | XR-NTX<br>380 mg, N (%) | XR-NTX<br>190 mg, N (%) | Placebo, N (%) | p Value <sup>b</sup> |
|---|-------------------------|-------------------------|----------------|----------------------|
| Nausea  | 68 (33)                 | 53 (25)                 | 23 (11)        | < .001               |
| Headache                                      | 45 (22)                 | 33 (16)                 | 34 (16)        | .17                  |
| Fatigue                                       | 41 (20)                 | 34 (16)                 | 23 (11)        | .01                  |
| Insomnia                                      | 28 (14)                 | 27 (13)                 | 25 (12)        | .66                  |
| Vomiting                                      | 28 (14)                 | 22 (11)                 | 12 (6)         | .20                  |
| Decreased appetite                            | 26 (13)                 | 12 (6)                  | 3 (1)          | < .001               |
| Diarrhea                                      | 26 (13)                 | 23 (11)                 | 18 (9)         | .20                  |
| Dizziness                                     | 26 (13)                 | 23 (11)                 | 8 (4)          | .001                 |
| Injection site pain                           | 24 (12)                 | 18 (9)                  | 19 (9)         | .04                  |
| Nasopharyngitis                               | 22 (11)                 | 32 (15)                 | 24 (12)        | > .99                |
| Upper respiratory tract infection             | 21 (10)                 | 15 (7)                  | 18 (9)         | .62                  |
| Study discontinuation due<br>to adverse event | 29 (14)                 | 14 (7)                  | 14 (7)         | .01                  |
| Serious adverse event                         | 11 (5)                  | 10 (5)                  | 15 (7)         | NA                   |

<sup>a</sup>Adapted with permission from Garbutt et al.<sup>2</sup> Copyright ©2005 American Medical Association. All rights reserved.

<sup>b</sup>XR-NTX 380 mg vs. placebo.

Abbreviations: NA = not available, XR-NTX = intramuscular extended-release naltrexone.

pitalization and resolved after treatment.<sup>2,15</sup> Discontinuation rates due to AEs are shown in Table 3.

### INCREASING ADHERENCE USING LONG-ACTING INTRAMUSCULAR FORMULATIONS OF NALTREXONE

Poor adherence to therapy can limit the efficacy of any medication. XR-NTX was designed to facilitate adherence by providing therapeutic levels of the drug for a period of 1 month, thus eliminating the need for daily dosing.<sup>17</sup> Clinicians can further improve adherence to XR-NTX therapy by informing patients that nausea usually is short-lived and less common after the first dose. In the study by Garbutt et al.,<sup>2</sup> nausea was mild or moderate in almost all patients and resolved during the first month of treatment in most patients. Clinicians should discuss typical side effects of the injection itself, such as tenderness, and treat reactions as necessary. Patients who may fear injections should understand that only a very small number of patients discontinue treatment because of injection site reactions alone. In fact, 88% of subjects who completed the 6-month trial of XR-NTX by Garbutt et al.<sup>2</sup> enrolled in an open-label extension study lasting an additional 12 months to assess the durability and safety of XR-NTX.<sup>21</sup> Those who received XR-NTX 190 mg or 380 mg in the initial trial were continued on their respective doses, while those originally getting the 4-mL and 2-mL placebo injections were converted to XR-NTX 380 mg and 190 mg, respectively. Psychosocial therapy was offered at each clinic visit.

The median number of heavy-drinking days per month continued to decline in all treatment groups, but the greatest reduction was seen in the group that switched from placebo injections to XR-NTX 380-mg injections. Patients who switched to XR-NTX 380 mg had a median of 5.2 heavy-drinking days per month at the start of the extension study, and this declined to 1.8 days per month by the end of the 12-month extension. In the group that was originally

randomly assigned to XR-NTX 380 mg and maintained on that dose through the extension, median heavy-drinking days declined from 2.6 days per month at the start of the extension to 1.6 days at the end of the 12-month extension (76 weeks total).<sup>21</sup>

XR-NTX was well tolerated in the extension study; 8.4% of patients withdrew as a result of adverse events. There were no significant increases in aspartate aminotransferase or alanine aminotransferase levels,<sup>21</sup> consistent with the original 6-month trial.<sup>2</sup> This extension study confirmed the efficacy and safety of using XR-NTX for 1.5 years.

### CONCLUSIONS

Pivotal studies have demonstrated that long-acting intramuscular formulations of naltrexone are safe and well tolerated. When used in conjunction with psychosocial treatment, extended-release injectable naltrexone (XR-NTX) was shown to significantly reduce heavy drinking in alcohol-dependent patients. Treatment effects were greater in patients who were abstinent before beginning therapy. Patients who were abstinent before treatment and received XR-NTX were more likely to maintain abstinence than were initially abstinent patients receiving placebo.

Long-acting intramuscular formulations of naltrexone have the potential to improve intervention strategies by reducing the need for daily dosing and providing a predictable pharmacologic foundation for treatment that should include psychosocial therapy and possibly other medications.

*Drug names:* acamprosate (Campral), naltrexone (ReVia, Vivitrol, and others).

*Disclosure of off-label usage:* The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents that is outside U.S. Food and Drug Administration–approved labeling has been presented in this article.

## REFERENCES

1. McLellan AT, Lewis DC, O'Brien CP, et al. Drug dependence, a chronic medical illness: implications for treatment, insurance, and outcomes evaluation. *JAMA* 2000;284:1689–1695
2. Garbutt JC, Kranzler HR, O'Malley SS, et al. Efficacy and tolerability of long-acting injectable naltrexone for alcohol dependence: a randomized controlled trial. *JAMA* 2005;293:1617–1625
3. O'Malley SS, Rounsaville BJ, Farren C, et al. Initial and maintenance naltrexone treatment for alcohol dependence using primary care vs specialty care: a nested sequence of 3 randomized trials. *Arch Intern Med* 2003;163:1695–1704
4. Anton RF, O'Malley SS, Ciraulo DA, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. *JAMA* 2006;295:2003–2017
5. Dawson DA. Alternative measures and models of hazardous consumption. *J Subst Abuse* 2000;12:79–91
6. Corrao G, Bagnardi V, Zambon A, et al. A meta-analysis of alcohol consumption and the risk of 15 diseases. *Prev Med* 2004;38:613–619
7. Mark TL, Kranzler HR, Song X. Understanding US addiction physicians' low rate of naltrexone prescription. *Drug Alcohol Depend* 2003;71:219–228
8. Chick J, Anton R, Chęcinski K, et al. A multicentre, randomized, double-blind, placebo-controlled trial of naltrexone in the treatment of alcohol dependence or abuse. *Alcohol Alcohol* 2000;35:587–593
9. Volpicelli JR, Rhines KC, Rhines JS, et al. Naltrexone and alcohol dependence: role of subject compliance. *Arch Gen Psychiatry* 1997;54:737–742
10. Croop RS, Faulkner EB, Labriola DF. The safety profile of naltrexone in the treatment of alcoholism: results from a multicenter usage study. The Naltrexone Usage Study Group. *Arch Gen Psychiatry* 1997;54:1130–1135
11. Rohsenow DJ, Colby SM, Monti PM, et al. Predictors of compliance with naltrexone among alcoholics. *Alcohol Clin Exp Res* 2000;24:1542–1549
12. Littleton J, Zieglsangberger W. Pharmacological mechanisms of naltrexone and acamprosate in the prevention of relapse in alcohol dependence. *Am J Addict* 2003;12(suppl 1):S3–S11
13. Kranzler HR, Wesson DR, Billot L. Naltrexone depot for treatment of alcohol dependence: a multicenter, randomized, placebo-controlled clinical trial. *Alcohol Clin Exp Res* 2004;28:1051–1059
14. Pettinati HM. Improving medication adherence in alcohol dependence. *J Clin Psychiatry* 2006;67(suppl 14):23–29
15. Vivitrol (naltrexone for extended-release injectable suspension)[package insert]. Cambridge, MA: Alkermes, Inc; April 2006
16. Bartus RT, Emerich DF, Hotz J, et al. Vivitrex, an injectable, extended-release formulation of naltrexone, provides pharmacokinetic and pharmacodynamic evidence of efficacy for 1 month in rats. *Neuropsychopharmacology* 2003;28:1973–1982
17. Johnson BA, Ait-Daoud N, Aubin HJ, et al. A pilot evaluation of the safety and tolerability of repeat dose administration of long-acting injectable naltrexone (Vivitrex) in patients with alcohol dependence. *Alcohol Clin Exp Res* 2004;28:1356–1361
18. Johnson DAW. Observations on the use of long-acting depot neuroleptic injections in the maintenance therapy of schizophrenia. *J Clin Psychiatry* 1984;45(5, sec 2):13–21
19. Volpicelli JR, Pettinati HM, McLellan AT, et al. Combining Medication and Psychosocial Treatments for Addictions: The BRENDA approach. New York, NY: The Guilford Press; 2001
20. O'Malley SS, Illeperuma A, Loewy J, et al. Effects of lead-in drinking/treatment goal with long-acting naltrexone. Presented at the 158th annual meeting of the American Psychiatric Association; May 21–26, 2005; Atlanta, Ga
21. Gastfriend DR, Dong Q, Loewy J, et al. Durability of effect of long-acting injectable naltrexone. Presented at the 158th annual meeting of the American Psychiatric Association; May 21–26, 2005; Atlanta, Ga