Boehringer Ingelheim
Roxane Laboratories

February 2, 2004

RE: DISCONTINUED PRODUCT NOTIFICATION
Roxane Laboratories, Inc. (RLI)

Richard A. Feldman, R.Ph.
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Dear Pharmaceutical Buyer,

As a follow up to the letter dated August 23, 2003 (see attached) regarding the discontinuation of **ORLAAM®** (Levomethadyl Hydrochloride Acetate) Oral Solution, please be advised that effective April 1, 2004 RLI will discontinue the distribution of **ORLAAM®**. All product currently in your inventory can continue to be sold. This will be the only notice sent to you so please adjust your records accordingly.

NDC # 00054	Product Description	Unit Dose Package
3649-63	**ORLAAM®** (Levomethadyl Hydrochloride Acetate)	Oral Solution

Should you have any questions please contact your account representative or customer service at 1-800-520-1631. As always, thank you for your support.

Sincerely,

Richard A. Feldman, R. Ph.
Executive Director, Trade Relations
RAF/mbm

Boehringer Ingelheim
Roxane Laboratories

August 23, 2003

PRODUCT DISCONTINUATION NOTICE
ORLAAM® (Levomethadyl hydrochloride acetate) Oral Solution, 10 mg/mL, CII
NDC 0054-3649-63

Dear Healthcare Professional:

Roxane Laboratories, Inc. is discontinuing the sale and distribution of ORLAAM® (Levomethadyl hydrochloride acetate) Oral Solution, 10 mg/mL after the current inventory is depleted. We estimate that this will occur early in the first quarter of 2004. Since the introduction of ORLAAM in 1995, Roxane Laboratories has received increasing reports of severe cardiac-related adverse events, including QT interval prolongation (15), Torsades de Pointes (8) and cardiac arrest (6). Other cardiac-related adverse events have also been reported, including arrhythmias, syncope, and angina. These events led to the removal of ORLAAM from the European market in March 2001, and extensive changes (including additional warnings & contraindications) were made to the US package insert in April 2001 (Dear Healthcare Professional letter dated April 11, 2001). Since these changes, the use of ORLAAM has decreased dramatically over the last two years. While there may be a very small number of patients who may benefit from ORLAAM, it is our belief that the risks of continued distribution and use in the face of less toxic treatment alternatives no longer outweigh the overall benefits.

ORLAAM is a synthetic opioid agonist solution indicated for the management of opiate dependence, reserved for the treatment of opiate-addicted patients who fail to show acceptable response to other adequate treatments for opiate addiction. Other first-line treatment options are available for the management of opiate dependence, including methadone and the recently FDA-approved buprenorphine. Methadone hydrochloride is available as an oral solution and a dispersible tablet, both which will continue to be manufactured by Roxane Laboratories and distributed by Cebert Pharmaceuticals. Buprenorphine hydrochloride is available in two sublingual formulations: one containing naloxone hydrochloride (Suboxone®, Reckitt Benckiser Pharmaceuticals) and one without naloxone (Subutex®, Reckitt Benckiser Pharmaceuticals). With these first-line agents available for the treatment of opiate addiction, it is our hope that existing patients can be converted to alternate therapies with minimal disruption to them and the centers that treat them.

Due to the forecasted unavailability shortly after the beginning of 2004, no new patients should be initiated on ORLAAM therapy. For existing ORLAAM patients, it is extremely important for healthcare providers to transfer patients to alternative treatments as soon as possible prior to the product's unavailability. To make sure this transition occurs with minimal disruption to all patients involved, we will reserve the right to limit purchase quantities based upon historical annual volumes. Careful consideration should be given to the appropriate conversion regimens. The information on the next page is from the current package insert for ORLAAM:

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Transfer from ORLAAM® to Methadone:
Patients maintained on ORLAAM may be transferred directly to methadone. Because of the difference between the two compounds' metabolites and their pharmacological half-lives, it is recommended that methadone be started on a daily dose at 80% of the ORLAAM dose being replaced; the initial methadone dose must be given no sooner than 48 hours after the last ORLAAM dose. Subsequent increases or decreases of 5 to 10 mg in the daily methadone dose may be given to control symptoms of withdrawal or, less likely, symptoms of excessive sedation, in accordance with clinical observations.

For further information about ORLAAM, please contact our Technical Information Department at 1-800-962-8364 or our Customer Service Department at 1-800-520-1631.

Respectfully,

Michael J. Sehobelock, PharmD
Associate Director
Medical Affairs Department
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